Abstracts of Nutrient Depletion from Tobacco Smoking

Confidential

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Index

A Multi-Nutrient Supplement for Smokers

Rationale for Expectation of Efficacy

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This narrative is written in support of the proposal to offer a nutritional supplement focused on offsetting the adverse health consequences of cigarette smoke exposure. It is a simple statement of expert opinion regarding a scientific rationale based on understanding of events that tend to be triggered by smoke exposure. Scientific citation support is supplied only for the nexus issue of magnesium status, since it is largely supplied for other concepts in separate documents by the patent holder of the proposed product.

For a simple nutritional supplement capsule to be effective in reducing adverse health consequences of tobacco smoke exposure it must focus on key pathophysiological triggers. A sound rationale can be built for such an effect focused on the oxidative stress widely known to be a consequence of smoking. The key pathophysiological sequelae of this added oxidative stress are (1) depletion of glutathione reserves, (2) limitation of magnesium entry into cells, and (3) the manifold consequences of magnesium insufficiency on energetic and cell regulatory pathways.

The well-known carcinogenic potential of cigarette smoke is mediated via two convergent factors: (1) induction of phase I carcinogenesis and (2) favoring of tumorigenesis via uncontrolled propagation of errant cells due to poor immune responses and impaired cellular plasticity for resisting the redirection of energetic metabolism by transformed cells. One potential avenue of offsetting factor (1) would be to focus on detoxification pathways to help removal of carcinogens. This approach would require relatively high amounts of multiple nutrient factors, and its efficacy would be limited due to the great individual variability in innate potential for detoxification. On the other hand, the combination of glutathione reserve depletion and consequential lowering of magnesium-driven oxidative metabolism is quite easily offset with relatively low doses of focused nutrients. And this mechanism can exacerbate not only tumorigenesis, but it can also lead to manifold degenerative effects on multiple tissues that contribute to the disease outcomes of smoke exposure.

Precise mechanisms explaining the restriction of magnesium entry into cells under conditions of depleted glutathione status are still under investigation. However, substantial evidence of such an effect has been reported. Following numerous studies that indicated their metabolic associations[1-8], a definitive study of normotensive and hypertensive humans demonstrated a strong, linear relationship between erythrocyte magnesium and the ratio of reduced to oxidized glutathione.[9] This relationship has been further supported and its association with human disease has been demonstrated.[10-13] The magnesium restriction effect seems to be mediated by effects on cellular energetic metabolism.[12,13] So, there is strong support for the concept of magnesium restriction due to loss of glutathione reserve. Restriction of magnesium entry into cells has manifold impacts on human health. [14-18]

Based on this rationale, a nutritional supplement that effectively offsets the oxidative stress of cigarette exposure by supplying glutathione precursors and simultaneously supplies doses of magnesium to fulfill the latent cellular demands for this critical element has the potential to avert human disease and decrease smoking-associated morbidity and mortality. In addition to supplying nutritional precursors that are known to support hepatic glutathione synthesis, the product should supply a broad range of other essential nutrients that become accessory agents for healthy tissue formation when the magnesium restriction is removed. In the complex web of interactions required for maintaining human health, the weakest link becomes the limiting factor. Nutrients generally operate in tandem for full cellular function restoration.

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Vitamin A

Eur J Obstet Gynecol Reprod Biol. 2011 Apr;155(2):132-6. Epub 2011 Jan 7.

The effect of tobacco smoking during pregnancy on plasma oxidant and antioxidant status in mother and newborn.

Chelchowska M, Ambroszkiewicz J, Gajewska J, Laskowska-Klita T, Leibschang J.

Source

Screening Test Department, Institute of Mother and Child, ul. Kasprzaka 17A, 02-211 Warsaw, Poland.

Abstract

OBJECTIVE:

The aim of the study was to estimate the effect of tobacco smoking during pregnancy on oxidative damage and antioxidant defense in matched samples of maternal blood and cord blood.

STUDY DESIGN:

Healthy, pregnant women (n=140) were divided into non-smoking and smoking groups according to the concentration of cotinine in serum and urine. Oxidative damage was measured through levels of malondialdehyde (MDA) and plasma antioxidant status was evaluated by measuring concentrations of total radical trapping parameters (TRAP) and selected antioxidants (β-carotene, vitamin A, vitamin E, uric acid). Statistical analysis was done using the SAS System for Windows (SAS Institute, Cary, NC).

RESULTS:

In the course of pregnancy the concentration of MDA increased, but to higher values in smoking women than in non-smoking ones. It was accompanied by significantly lower TRAP in the smoking group than in the controls ($p<0.05$). Plasma concentration of uric acid ($p<0.05$) and antioxidant vitamins E ($p<0.01$), A and β-carotene ($p<0.0001$) were all reduced in smokers as compared with non-smoking pregnant women especially in the third trimester. Concentration of MDA in plasma of cord blood of newborns of smoking mothers was significantly higher ($p<0.01$) but the antioxidant defence was lower ($p<0.0001$) than in non-smoking ones. It was particularly pronounced for β-carotene (32%; $p<0.0001$) and vitamin A (28%; $p<0.001$). A significant negative correlation was found between MDA and TRAP levels of maternal plasma (non-smoking and smoking: $r=-0.50$, $p<0.0001$) and cord plasma (non-smoking: $r=-0.54$, $p=0.0057$; smoking: $r=-0.71$, $p=0.0004$) in all the study subjects. Total antioxidant status positively correlated with concentrations of uric acid and vitamin E in non-smoking and smoking mothers as well as their newborns.

CONCLUSION:

Tobacco smoke enhances lipid peroxidation and depletes antioxidant potential in the plasma of pregnant women and umbilical cord blood. Therefore smoking during pregnancy may stimulate free radical damage in the mother and the growing fetus.

Am J Med Sci. 2007 Jun;333(6):346-53.

Exhaustive exercise modifies oxidative stress in smoking subjects.

Gochman E, Reznick AZ, Avizohar O, Ben-Amotz A, Levy Y.

Source

Department of Anatomy and Cell Biology, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.

Abstract

BACKGROUND:
Exhaustive exercise is associated with increased metabolic rate and accelerated generation of reactive oxygen species. Cigarette smoke also contains oxidants that may participate in the development of atherosclerosis. However, data on the association between exercise and smoking are sparse.

METHODS:
A homogenous group of 30 young men (15 smokers and 15 nonsmokers; mean age, 23.7 +/- 2.6 years), healthy, trained subjects, were assessed before and after a standard maximal exercise test.

RESULTS:
Exercise led to increased protein oxidation (carbonyl assay) in both smokers (+17.7%, $P < 0.001$) and nonsmokers (+19.1%, $P < 0.05$), elevation in plasma conjugated dienes (+ 157%, $P < 0.04$), and plasma lipid peroxides (+14%, $P < 0.059$) in smokers versus nonsmokers after exercise. Plasma antioxidants levels were significantly lower in the smoking group, with reduction in total carotenoids (-36.5%, $P < 0.001$), vitamin A (-80%, $P < 0.001$), and vitamin E (-64%, $P < 0.002$), compared with nonsmokers. A significant rise in leakage of muscle enzymes (CPK, LDH) and urine proteins (microalbumin and myoglobin) occurred in all subjects after exercise. CRP levels were higher in smokers compared with nonsmokers before and after exercise.

CONCLUSIONS:
Our results suggest that unnoticed interaction exists between smoking and intense exercise, which indicates that smokers are more susceptible to oxidative insults probably due to lower antioxidant capacity.

Vitamin B-2

Clin Chem. 2010 May;56(5):755-63. Epub 2010 Mar 18.

Long- and short-term effects of tobacco smoking on circulating concentrations of B vitamins.

Ulvik A, Ebbing M, Hustad S, Midttun Ø, Nygård O, Vollset SE, Bønaa KH, Nordrehaug JE, Nilsen DW, Schirmer H, Ueland PM.

Source

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Abstract

BACKGROUND:
Smoking is associated with decreased concentrations of several antioxidant vitamins. We sought to determine the relation between circulating concentrations of selected B vitamins and smoking status, with particular attention to longitudinal associations.

METHODS:
We used baseline data from 2 B-vitamin intervention trials that included 6837 patients with ischemic heart disease. Smoking habits were ascertained by interview. Vitamins and metabolites, including the nicotine metabolite cotinine, were measured in plasma and serum by microbiological assays or gas/liquid chromatography-tandem mass spectrometry.

RESULTS:
The highest circulating concentrations of folate and pyridoxal 5'phosphate (PLP) and lowest concentrations of total plasma homocysteine, a functional marker of folate status, were observed for self-reported never smokers, followed by self-reported ex-smokers and current smokers (P(trend) < 0.001). Cobalamin and its functional marker methylmalonic acid were not associated with smoking status. Based on their low cotinine concentrations, we were able to identify a group of smokers that had abstained from smoking for 3 days or more. Compared with smokers with high plasma cotinine, smokers with low cotinine had significantly higher circulating concentrations of folate, PLP, and riboflavin (all P < 0.005), and this trend continued for ex-smokers, with increasing time since smoking cessation.

CONCLUSIONS:
Smoking lowered circulating concentrations of folate, PLP, and riboflavin, but concentrations increased significantly after a few days of smoking cessation. We propose that short-term effects may be related to acute smoking-induced oxidative stress, whereas the longer-lasting effects among ex-smokers may reflect changes in diet and/or restoration of vitamin concentrations in tissue during the first few months to years after smoking cessation.

Vitamin B-6

Am J Clin Nutr. 1990 Jun;51(6):1058-61.

Vitamin B-6 nutrition status and cigarette smoking.

Vermaak WJ, Ubbink JB, Barnard HC, Potgieter GM, van Jaarsveld H, Groenewald AJ.

Source

Department of Chemical Pathology, Institute of Pathology, Pretoria, South Africa.

Abstract

We investigated the vitamin B-6 status in smokers, nonsmokers, and exsmokers by measuring both B-6 aldehyde vitamers, pyridoxal-5'-phosphate (PLP) and pyridoxal (PL), in the plasma as well as in the erythrocyte compartment. Two hundred eighty-six healthy, sedentary male workers from a middle-income group were investigated. There were 159 smokers, 59 exsmokers, and 68 nonsmokers. Plasma PLP and PL concentrations were significantly lower in smokers than in the nonsmokers and exsmokers whereas erythrocyte PLP and PL did not differ significantly between groups. Because PLP mainly functions as an intracellular coenzyme, the clinical significance of a depressed plasma PLP concentration alone is uncertain. It is concluded that circulating plasma PLP is labile and not necessarily indicative of intracellular PLP concentrations. The measurement of erythrocyte PLP and/or PL may be more informative about vitamin B-6 status than is plasma PLP alone.

Przegl Lek. 2008;65(10):486-90.

[Hiperhomocysteinemia in active and passive smokers and the levels of folate and vitamin B6 in plasma].

[Article in Polish]

Marszałł ML[1], Makarowski R, Hinc S, Kłos M, Czarnowski W.

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Abstract

The increased plasma level of homocysteine have been shown to be the sensitive marker for the folate, vitamin B6 and cobalamins deficiency and an independent risk factor for the cardiovascular disease, neutral tube defects and a potential causal risk factor for neuropsychiatric disorders. The blood and plasma homocysteine levels except for genetic defects are influenced by age, gender, efficiency of detoxication systems, one or more unhealthy lifestyle factors, such as high alcohol consumption, low nutritional intake of vitamins, high coffee consumption, acquired disorders and lack of physical exercise. Many studies confirm that active tobacco smoking and environmental tobacco smoke (ETS) have been significantly associated with hiperhomocysteinemia. In metabolic pathway of homocysteine the important role played folic acid, as a donor of methyl group in re-methylated reaction to methionine and vitamin B6. It acts as the cofactor in transsuphuration reactions of homocysteine to cystathionine and cysteine. Hence, the aim of this work was to compare the plasma folate and vitamin B6 concentrations in smokers and passive smokers with a hiperhomocysteinemia (> 15 micromol/L). It was observed that the plasma folate levels in active (n = 30) and passive smokers (n = 29) groups decrease statistically significant (P < 0.001) in comparison to non-smokers (n = 37). The calculated Spaermann's correlations coefficient of total plasma homocysteine level and plasma folate concentrations in the non-smoker group indicated a weak, statistically insignificant correlation (r = -0.103, P = 0.542). However, the above relationship in passive and active smokers were statistically significant (r = -0.495, P 0 0.01; r = -0.672, P < 0.001, respectively). The decrease of vitamin in B6 plasma was observed in all active smokers group (P < 0.01) and men smokers comparing to non-smokers (P < 0.001). There was no observed significant correlations between hiperhomocysteinemia and vitamin B6 in all studied groups. The results indicated that hiperhomocysteinemia have strong negative impact on folate levels in active and passive smokers. The tobacco smoke exposure have negative influence on the status of vitamin B6. The lack of significant correlation between increased homocysteine levels and vitamin B6 status confirmed hypothesis that hiperhomocysteinemia is not depended on vitamin B6 concentrations in plasma.

Eur Heart J. 2002 Oct;23(20):1580-6.

Smoking and plasma homocysteine.

O'Callaghan P, Meleady R, Fitzgerald T, Graham I; European COMAC group.

Source

The Adelaide and Meath Hospital Dublin, Dublin, Ireland.

Abstract

BACKGROUND:
Smoking is known to be associated with an increased plasma homocysteine level. Both are associated with an increased risk of cardiovascular disease. B-vitamins modulate plasma homocysteine levels.

AIMS:
To investigate the relationships between smoking, plasma homocysteine, nutrient levels and risk of cardiovascular disease.

METHODS:
The European Concerted Action Project case control study of 750 cases and 800 age- and sex-matched controls aged less than 60 years from 19 centres in 10 European countries.

RESULTS:
Smokers were at increased risk of vascular disease. This risk was greatly increased in the presence of a raised plasma homocysteine; cigarette smokers with a plasma homocysteine above 12 micromol.l(-1) had a 12-fold increased risk of cardiovascular disease (OR 12.4 95% CI 7.3 to 21.2) compared with non-smokers with a normal plasma homocysteine. In both cases and controls the current smokers had a higher plasma homocysteine level than the never smokers (11.7 micromol.l(-1) vs 10.07 micromol.l(-1), P<0.05 cases; 9.90 micromol.l(-1) vs 9.53 micromol.l(-1)P value non significant controls). Current smokers tended to have lower levels of folate, and vitamin B6 and vitamin B12 than never smokers. The risk of cardiovascular disease associated with smoking was not significantly altered by adjustment for levels of B-vitamins using a conditional regression model (OR for current smoker >20.day(-1) 8.19, after adjustment for B6, B12, folate OR 7.09).

CONCLUSIONS:
This case control study suggests that smokers with high plasma homocysteine are at greatly increased risk of cardiovascular disease and should therefore be offered intensive advice to help them cease smoking. They also have reduced levels of those B-vitamins (folate, vitamin B6 and vitamin B12) that modulate homocysteine metabolism. While this finding may reflect a direct effect of smoking or reduced B-vitamin intake, supplementation of these nutrients may be appropriate in smokers with high homocysteine levels.

Comment on

- Eur Heart J. 2002 Oct;23(20):1559-60.

Clin Chim Acta. 2001 Apr;306(1-2):103-9.

Effect of smoking on serum concentrations of total homocysteine and B vitamins in mid-pregnancy.

Pagán K, Hou J, Goldenberg RL, Cliver SP, Tamura T.

Source

Department of Nutrition Sciences, 218 Webb Building., University of Alabama at Birmingham, Birmingham, AL 35294-3360, USA.

Abstract

There are conflicting findings in the literature on the effect of smoking on total homocysteine (tHcy) concentrations in non-pregnant subjects. We evaluated the effect of smoking on serum concentrations of tHcy, folate, vitamin B-12 pyridoxal 5'-phosphate (PLP, a coenzyme form of vitamin B-6) in 196 women at 18 and 30 weeks' gestation. The smokers were defined as those who self-reported cigarette smoking and had serum concentrations of thiocyanate, a biomaker of smoking, in the highest quartiles of the population. Mid-pregnancy serum tHcy concentrations were not significantly different between smokers and non-smokers. Folate, vitamin B-12 and PLP concentrations were generally lower in smokers than non-smokers. In smokers, tHcy concentrations had significant negative correlations with folate at both time points. The multiple regression analyses indicated that serum folate concentration was the most significant factor associated with tHcy concentrations among smokers, whereas thiocyanate concentrations showed no such effect. We conclude that serum tHcy concentrations were most strongly associated with the nutritional status of folate among the B vitamins tested during mid-pregnancy in our subjects. We suggest that it is essential to consider the nutritional status of folate, vitamin B-12 and vitamin B-6 in evaluating the effect of smoking on homocysteine metabolism.

Vitamin B-12

Am J Clin Nutr. 1994 Oct;60(4):559-66.

Local and systemic effects of cigarette smoking on folate and vitamin B-12.

Piyathilake CJ, Macaluso M, Hine RJ, Richards EW, Krumdieck CL.

Source

Department of Nutrition Sciences, University of Alabama at Birmingham 35294.

Abstract

A cross-sectional study was carried out among 39 current smokers (CS) and 60 noncurrent smokers (NCS) to evaluate the effects of cigarette smoking on folate and vitamin B-12 concentrations in the circulation and in tissues directly exposed to cigarette smoke. Univariate analysis showed significantly lower plasma, red blood cell (RBC), and buccal mucosa (BM) folate and BM vitamin B-12 concentrations in CS compared with NCS. The association between smoking and folate and vitamin B-12 concentrations in plasma, RBCs, and BM cells was reduced after other variables were controlled for. Total folate intake and plasma vitamin C concentrations were significant predictors of plasma and RBC folate concentrations. The plasma and RBC concentrations of folate were significantly lower in subjects who had last smoked < 1 h before the blood sample was drawn than in subjects who had smoked earlier. At the current recommended dietary allowance (RDA) for folate, CS had 42% lower plasma folate concentrations than NCS, whereas at an intake three times the RDA, the plasma folate concentration was the same for CS and NCS. The results also suggested that CS have BM folate and vitamin B-12 concentrations that are lower than those of NCS.

Eur Heart J. 2002 Oct;23(20):1580-6.

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Comment on

- Eur Heart J. 2002 Oct;23(20):1559-60.

Am J Clin Nutr. 2006 Apr;83(4):835-41.

Chronic cigarette smoking is associated with diminished folate status, altered folate form distribution, and increased genetic damage in the buccal mucosa of healthy adults.

Gabriel HE, Crott JW, Ghandour H, Dallal GE, Choi SW, Keyes MK, Jang H, Liu Z, Nadeau M, Johnston A, Mager D, Mason JB.

Source

Vitamins and Carcinogenesis Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, 711 Washington Street, Boston, MA 02111, USA.

Erratum in

Am J Clin Nutr. 2006 Jul;84(1):263.

Abstract

BACKGROUND:
Smoking causes genetic damage in buccal cells and increases the risk of oral cancer. Because folate is instrumental in DNA synthesis and repair, it is a determinant of genetic stability and therefore might attenuate the genotoxic effects of smoking.

OBJECTIVE:
Our aim was to compare the presence of folate metabolites and select indicators of genetic damage in the mouths of chronic smokers and nonsmokers.

DESIGN:
Dietary, biochemical, and molecular correlates of folate status were measured in healthy smoker (n = 35) and nonsmoker (n = 21) groups of comparable age, sex, and body mass indexes.

RESULTS:
After correction for dietary intake, the smokers displayed lower plasma, erythrocyte, and buccal mucosal cell (BMC) folate (20%, 32%, and 50% lower, respectively; P < 0.05) and lower plasma vitamin B-12 and pyridoxal 5-phosphate (P < 0.05) than did nonsmokers. Folate in the BMCs of smokers comprised significantly greater proportions of pteroylmonoglutamate, formyltetrahydrofolate, and 5,10-methenyltetrahyrofolate than did folate in the BMCs of nonsmokers. Although the degree of genomic methylation and uracil incorporation in the buccal cells of the 2 groups were not significantly different, the BMC micronucleus index, a cytologic indicator of genetic damage, in the smokers

was 2-fold that of the nonsmokers (9.57 compared with 4.44 micronuclei/1000 cells; P < 0.0001). Neither systemic nor oral folate status was an independent predictor of micronuclei.

CONCLUSIONS:
Chronic smoking is associated with a lower systemic status of several B vitamins, reduced oral folate, and changes in folate form distribution in the mouth. However, the cytologic damage that is evident in the mouths of smokers does not correlate with oral folate status.

Comment in

Am J Clin Nutr. 2006 Oct;84(4):946-7; author reply 947-8.

Clin Chim Acta. 2001 Apr;306(1-2):103-9.

Effect of smoking on serum concentrations of total homocysteine and B vitamins in mid-pregnancy.

Pagán K, Hou J, Goldenberg RL, Cliver SP, Tamura T.

Source

Department of Nutrition Sciences, 218 Webb Building., University of Alabama at Birmingham, Birmingham, AL 35294-3360, USA.

Abstract

There are conflicting findings in the literature on the effect of smoking on total homocysteine (tHcy) concentrations in non-pregnant subjects. We evaluated the effect of smoking on serum concentrations of tHcy, folate, vitamin B-12 pyridoxal 5'-phosphate (PLP, a coenzyme form of vitamin B-6) in 196 women at 18 and 30 weeks' gestation. The smokers were defined as those who self-reported cigarette smoking and had serum concentrations of thiocyanate, a biomaker of smoking, in the highest quartiles of the population. Mid-pregnancy serum tHcy concentrations were not significantly different between smokers and non-smokers. Folate, vitamin B-12 and PLP concentrations were generally lower in smokers than non-smokers. In smokers, tHcy concentrations had significant negative correlations with folate at both time points. The multiple regression analyses indicated that serum folate concentration was the most significant factor associated with tHcy concentrations among smokers, whereas thiocyanate concentrations showed no such effect. We conclude that serum tHcy concentrations were most strongly associated with the nutritional status of folate among the B vitamins tested during mid-pregnancy in our subjects. We suggest that it is essential to consider the nutritional status of folate, vitamin B-12 and vitamin B-6 in evaluating the effect of smoking on homocysteine metabolism.

Other B-Vitamins: Biotin and Folate

Int J Cancer. 1992 Oct 21;52(4):566-9.

Effect of smoking on folate levels in buccal mucosal cells.

Piyathilake CJ, Hine RJ, Dasanayake AP, Richards EW, Freeberg LE, Vaughn WH, Krumdieck CL.

Source

Department of Nutrition Sciences, University of Alabama, Birmingham 35294.

Abstract

The objective of the study was to document the existence of localized deficiency of folate in a tissue exposed to cigarette smoke, by analysis of oral and circulatory levels of this vitamin in smokers and non-smokers. Buccal mucosal cells and blood samples were collected from 25 smokers and 34 non-smokers. The Health Habits and History Questionnaire was completed by each subject. A 96-well plate L. casei assay, along with preincubation with a folate-free chick pancreas pteroyl-gamma-glutamyl hydrolase, was used to quantitate total buccal mucosal cell folates. The reproducibility (CV 5 to 7%) and recovery (95 to 106%) of the folate assay were satisfactory. Smokers had significantly lower buccal mucosal cell folate levels than did non-smokers. The mean plasma folate level of smokers although within normal limits, was also significantly lower than that of non-smokers. There were no significant differences in mean dietary folate intake or in alcohol consumption between the 2 groups. The strength of the positive association between smoking and plasma and buccal mucosal cell folate deficiency (by any definition) was moderate to strong and statistically significant. Our results indicate that cigarette smoking may result in a localized folate deficiency in buccal mucosal cells, independent of the plasma folate levels.

Am J Clin Nutr. 2004 Oct;80(4):932-5.

Smoking accelerates biotin catabolism in women.

Sealey WM, Teague AM, Stratton SL, Mock DM.

Source

Department of Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences, Little Rock, USA.

Abstract

BACKGROUND:
Smoking accelerates the degradation of many nutrients, including lipids, antioxidants, and certain B vitamins. Accelerated biotin catabolism is of concern in women because marginal biotin deficiency is teratogenic in mammals.

OBJECTIVE:
The objective was to assess the effect of smoking on the biotin status of women.

DESIGN:
A preliminary study of 7 women and 3 men examined the urinary concentrations of biotin and its metabolites biotin sulfoxide and bisnorbiotin in smokers. The interpretation of the results of this study was limited by the lack of a contemporaneous control group; consequently, we conducted a cohort-controlled study. Smoking women (n = 8) and nonsmoking control subjects (n = 15) provided 24-h urine samples; excretion rates of biotin, the biotin metabolites, and 3-hydroxyisovaleric acid were determined. Increased urinary excretion of 3-hydroxyisovaleric acid, which reflects a reduced activity of the biotin-dependent enzyme 3-methylcrotonyl-Co A carboxylase, is a sensitive indicator of biotin depletion at the tissue level.

RESULTS:
Compared with control subjects from previous studies, the smoking women in the preliminary study excreted significantly less urinary biotin (P = 0.02). Moreover, the ratio of urinary biotin sulfoxide to biotin increased (P = 0.04) in these women. In the cohort-controlled study, the urinary excretion of biotin decreased by 30% (P = 0.04), and the ratios of urinary bisnorbiotin and biotin sulfoxide to biotin increased significantly, which indicated accelerated catabolism in smokers. Moreover, the urinary excretion of 3-hydroxyisovaleric acid was greater in the smokers than in the control subjects (P = 0.04), which indicated biotin depletion in the smokers at the tissue level.

CONCLUSION:

These data provide evidence of accelerated biotin metabolism in smoking women, which results in marginal biotin deficiency.

Am J Clin Nutr. 1994 Oct;60(4):559-66.

Local and systemic effects of cigarette smoking on folate and vitamin B-12.

Piyathilake CJ, Macaluso M, Hine RJ, Richards EW, Krumdieck CL.

Source

Department of Nutrition Sciences, University of Alabama at Birmingham 35294.

Abstract

A cross-sectional study was carried out among 39 current smokers (CS) and 60 noncurrent smokers (NCS) to evaluate the effects of cigarette smoking on folate and vitamin B-12 concentrations in the circulation and in tissues directly exposed to cigarette smoke. Univariate analysis showed significantly lower plasma, red blood cell (RBC), and buccal mucosa (BM) folate and BM vitamin B-12 concentrations in CS compared with NCS. The association between smoking and folate and vitamin B-12 concentrations in plasma, RBCs, and BM cells was reduced after other variables were controlled for. Total folate intake and plasma vitamin C concentrations were significant predictors of plasma and RBC folate concentrations. The plasma and RBC concentrations of folate were significantly lower in subjects who had last smoked < 1 h before the blood sample was drawn than in subjects who had smoked earlier. At the current recommended dietary allowance (RDA) for folate, CS had 42% lower plasma folate concentrations than NCS, whereas at an intake three times the RDA, the plasma folate concentration was the same for CS and NCS. The results also suggested that CS have BM folate and vitamin B-12 concentrations that are lower than those of NCS.

Am J Clin Nutr. 2006 Apr;83(4):835-41.

Chronic cigarette smoking is associated with diminished folate status, altered folate form distribution, and increased genetic damage in the buccal mucosa of healthy adults.

Gabriel HE, Crott JW, Ghandour H, Dallal GE, Choi SW, Keyes MK, Jang H, Liu Z, Nadeau M, Johnston A, Mager D, Mason JB.

Source

Vitamins and Carcinogenesis Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, 711 Washington Street, Boston, MA 02111, USA.

Erratum in

Am J Clin Nutr. 2006 Jul;84(1):263.

Abstract

BACKGROUND:
Smoking causes genetic damage in buccal cells and increases the risk of oral cancer. Because folate is instrumental in DNA synthesis and repair, it is a determinant of genetic stability and therefore might attenuate the genotoxic effects of smoking.

OBJECTIVE:
Our aim was to compare the presence of folate metabolites and select indicators of genetic damage in the mouths of chronic smokers and nonsmokers.

DESIGN:
Dietary, biochemical, and molecular correlates of folate status were measured in healthy smoker (n = 35) and nonsmoker (n = 21) groups of comparable age, sex, and body mass indexes.

RESULTS:
After correction for dietary intake, the smokers displayed lower plasma, erythrocyte, and buccal mucosal cell (BMC) folate (20%, 32%, and 50% lower, respectively; P < 0.05) and lower plasma vitamin B-12 and pyridoxal 5-phosphate

(P < 0.05) than did nonsmokers. Folate in the BMCs of smokers comprised significantly greater proportions of pteroylmonoglutamate, formyltetrahydrofolate, and 5,10-methenyltetrahyrofolate than did folate in the BMCs of nonsmokers. Although the degree of genomic methylation and uracil incorporation in the buccal cells of the 2 groups were not significantly different, the BMC micronucleus index, a cytologic indicator of genetic damage, in the smokers was 2-fold that of the nonsmokers (9.57 compared with 4.44 micronuclei/1000 cells; P < 0.0001). Neither systemic nor oral folate status was an independent predictor of micronuclei.

CONCLUSIONS:

Chronic smoking is associated with a lower systemic status of several B vitamins, reduced oral folate, and changes in folate form distribution in the mouth. However, the cytologic damage that is evident in the mouths of smokers does not correlate with oral folate status.

Comment in

Am J Clin Nutr. 2006 Oct;84(4):946-7; author reply 947-8.

Clin Chim Acta. 2001 Apr;306(1-2):103-9.

Effect of smoking on serum concentrations of total homocysteine and B vitamins in mid-pregnancy.

Pagán K, Hou J, Goldenberg RL, Cliver SP, Tamura T.

Source

Department of Nutrition Sciences, 218 Webb Building., University of Alabama at Birmingham, Birmingham, AL 35294-3360, USA.

Abstract

There are conflicting findings in the literature on the effect of smoking on total homocysteine (tHcy) concentrations in non-pregnant subjects. We evaluated the effect of smoking on serum concentrations of tHcy, folate, vitamin B-12 pyridoxal 5'-phosphate (PLP, a coenzyme form of vitamin B-6) in 196 women at 18 and 30 weeks' gestation. The smokers were defined as those who self-reported cigarette smoking and had serum concentrations of thiocyanate, a biomaker of smoking, in the highest quartiles of the population. Mid-pregnancy serum tHcy concentrations were not significantly different between smokers and non-smokers. Folate, vitamin B-12 and PLP concentrations were generally lower in smokers than non-smokers. In smokers, tHcy concentrations had significant negative correlations with folate at both time points. The multiple regression analyses indicated that serum folate concentration was the most significant factor associated with tHcy concentrations among smokers, whereas thiocyanate concentrations showed no such effect. We conclude that serum tHcy concentrations were most strongly associated with the nutritional status of folate among the B vitamins tested during mid-pregnancy in our subjects. We suggest that it is essential to consider the nutritional status of folate, vitamin B-12 and vitamin B-6 in evaluating the effect of smoking on homocysteine metabolism.

Przegl Lek. 2008;65(10):486-90.

[Hiperhomocysteinemia in active and passive smokers and the levels of folate and vitamin B6 in plasma].

[Article in Polish]

Marszałł ML[1], Makarowski R, Hinc S, Kłos M, Czarnowski W.

Author information

1

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Abstract

The increased plasma level of homocysteine have been shown to be the sensitive marker for the folate, vitamin B6 and cobalamins deficiency and an independent risk factor for the cardiovascular disease, neutral tube defects and a potential causal risk factor for neuropsychiatric disorders. The blood and plasma homocysteine levels except for genetic defects are influenced by age, gender, efficiency of detoxication systems, one or more unhealthy lifestyle factors, such as high alcohol consumption, low nutritional intake of vitamins, high coffee consumption, acquired disorders and lack of physical exercise. Many studies confirm that active tobacco smoking and environmental tobacco smoke (ETS) have been significantly associated with hiperhomocysteinemia. In metabolic pathway of homocysteine the important role played folic acid, as a donor of methyl group in re-methylated reaction to methionine and vitamin B6. It acts as the cofactor in transsuphuration reactions of homocysteine to cystathionine and cysteine. Hence, the aim of this work was to compare the plasma folate and vitamin B6 concentrations in smokers and passive smokers with a hiperhomocysteinemia (> 15 micromol/L). It was observed that the plasma folate levels in active (n = 30) and passive smokers (n = 29) groups decrease statistically significant (P < 0.001) in comparison to non-smokers (n = 37). The calculated Spaermann's correlations coefficient of total plasma homocysteine level and plasma folate concentrations in the non-smoker group indicated a weak, statistically insignificant correlation (r = -0.103, P = 0.542). However, the above relationship in passive and active smokers were statistically significant (r = -0.495, P 0 0.01; r = -0.672, P < 0.001, respectively). The decrease of vitamin in B6 plasma was observed in all active smokers group (P < 0.01) and men smokers comparing to non-smokers (P < 0.001). There was no observed significant correlations between hiperhomocysteinemia and vitamin B6 in all studied groups. The results indicated that hiperhomocysteinemia have strong negative impact on folate levels in active and passive smokers. The tobacco smoke exposure have negative influence on the status of vitamin B6. The lack of significant correlation between increased homocysteine levels and vitamin B6 status confirmed hypothesis that hiperhomocysteinemia is not depended on vitamin B6 concentrations in plasma.

Eur Heart J. 2002 Oct;23(20):1580-6.

Smoking and plasma homocysteine.

O'Callaghan P, Meleady R, Fitzgerald T, Graham I; European COMAC group.

Source

The Adelaide and Meath Hospital Dublin, Dublin, Ireland.

Abstract

BACKGROUND:
Smoking is known to be associated with an increased plasma homocysteine level. Both are associated with an increased risk of cardiovascular disease. B-vitamins modulate plasma homocysteine levels.

AIMS:
To investigate the relationships between smoking, plasma homocysteine, nutrient levels and risk of cardiovascular disease.

METHODS:
The European Concerted Action Project case control study of 750 cases and 800 age- and sex-matched controls aged less than 60 years from 19 centres in 10 European countries.

RESULTS:
Smokers were at increased risk of vascular disease. This risk was greatly increased in the presence of a raised plasma homocysteine; cigarette smokers with a plasma homocysteine above 12 micromol.l(-1) had a 12-fold increased risk of cardiovascular disease (OR 12.4 95% CI 7.3 to 21.2) compared with non-smokers with a normal plasma homocysteine. In both cases and controls the current smokers had a higher plasma homocysteine level than the never smokers (11.7 micromol.l(-1) vs 10.07 micromol.l(-1), P<0.05 cases; 9.90 micromol.l(-1) vs 9.53 micromol.l(-1)P value non significant controls). Current smokers tended to have lower levels of folate, and vitamin B6 and vitamin B12 than never smokers. The risk of cardiovascular disease associated with smoking was not significantly altered by adjustment for levels of B-vitamins using a conditional regression model (OR for current smoker >20.day(-1) 8.19, after adjustment for B6, B12, folate OR 7.09).

CONCLUSIONS:
This case control study suggests that smokers with high plasma homocysteine are at greatly increased risk of cardiovascular disease and should therefore be offered intensive advice to help them cease smoking. They also have reduced levels of those B-vitamins (folate, vitamin B6 and vitamin B12) that modulate homocysteine metabolism. While this finding may reflect a direct effect of smoking or reduced B-vitamin intake, supplementation of these nutrients may be appropriate in smokers with high homocysteine levels.

Comment on

Eur Heart J. 2002 Oct;23(20):1559-60.

Vitamin C

Toxicology. 2002 Nov 15;180(2):121-37.

The influence of cigarette smoking on circulating concentrations of antioxidant micronutrients.

Alberg A.

Source

Department of Epidemiology, Room E6132B, The Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Baltimore, MD 21205, USA. aalberg@jhph.edu

Abstract

Cigarette smoke is a significant source of oxidative stress, one potential mechanism for its untoward health effects. The antioxidant defense system is partly comprised of antioxidant micronutrients, making it important to understand the relationship between cigarette smoking and circulating concentrations of antioxidant micronutrients. A synthesis of the literature shows that compared with nonsmokers, on average, active smokers have greater than 25% lower circulating concentrations of ascorbic acid, alpha-carotene, beta-carotene, and cryptoxanthin. The differences in blood concentrations of these micronutrients in former smokers is intermediate between never and current smokers, but average circulating concentrations of alpha-carotene, beta-carotene, and cryptoxanthin were 16-22% lower in former smokers compared with never smokers. Differences in dietary habits between smokers and nonsmokers could potentially account for these associations. Dietary micronutrient intake is associated with blood micronutrient concentrations. Furthermore, patterns of micronutrient consumption by smoking status mimic the pattern of associations observed for blood concentrations. For example, when pooled across studies intake of vitamin C was 16% lower in current smokers and 2% lower in former smokers than in never smokers; the corresponding figures for beta-carotene were 17 and 4%, respectively. Despite the strong potential for confounding, the differences observed between current smokers and nonsmokers seem to be due to an acute effect of smoking based on results of studies of smoking and antioxidant micronutrient concentrations that have either adjusted for dietary antioxidant micronutrient intake and other potential confounding factors or documented short term changes in circulating antioxidant micronutrient concentrations in smokers before and after smoking cigarettes. The associations observed with active smoking also appear to hold true for passive smoking, implying that even low-dose exposures to tobacco smoke can result in lowered circulating antioxidant micronutrient concentrations. Smoking was more weakly associated with circulating concentrations of vitamin E and the nonprovitamin A carotenoids lutein/zeaxanthin and lycopene. The combined evidence supports the conclusion that cigarette smoking is independently associated with lowered circulating concentrations of ascorbic acid and provitamin A carotenoids. These associations have implications for the design and interpretation of epidemiologic studies of antioxidant micronutrients in relation to health and disease. To the extent that these micronutrients are associated with health and longevity, this evidence documents yet another deleterious consequence of cigarette smoking on human health.

Toxicology. 2002 Nov 15;180(2):121-37.

The influence of cigarette smoking on circulating concentrations of antioxidant micronutrients.

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Department of Epidemiology, Room E6132B, The Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Baltimore, MD 21205, USA. aalberg@jhph.edu

Abstract

Cigarette smoke is a significant source of oxidative stress, one potential mechanism for its untoward health effects. The antioxidant defense system is partly comprised of antioxidant micronutrients, making it important to understand the relationship between cigarette smoking and circulating concentrations of antioxidant micronutrients. A synthesis of the literature shows that compared with nonsmokers, on average, active smokers have greater than 25% lower circulating concentrations of ascorbic acid, alpha-carotene, beta-carotene, and cryptoxanthin. The differences in blood concentrations of these micronutrients in former smokers is intermediate between never and current smokers, but average circulating concentrations of alpha-carotene, beta-carotene, and cryptoxanthin were 16-22% lower in former smokers compared with never smokers. Differences in dietary habits between smokers and nonsmokers could potentially account for these associations. Dietary micronutrient intake is associated with blood micronutrient concentrations. Furthermore, patterns of micronutrient consumption by smoking status mimic the pattern of associations observed for blood concentrations. For example, when pooled across studies intake of vitamin C was 16% lower in current smokers and 2% lower in former smokers than in never smokers; the corresponding figures for beta-carotene were 17 and 4%, respectively. Despite the strong potential for confounding, the differences observed between current smokers and nonsmokers seem to be due to an acute effect of smoking based on results of studies of smoking and antioxidant micronutrient concentrations that have either adjusted for dietary antioxidant micronutrient intake and other potential confounding factors or documented short term changes in circulating antioxidant micronutrient concentrations in smokers before and after smoking cigarettes. The associations observed with active smoking also appear to hold true for passive smoking, implying that even low-dose exposures to tobacco smoke can result in lowered circulating antioxidant micronutrient concentrations. Smoking was more weakly associated with circulating concentrations of vitamin E and the nonprovitamin A carotenoids lutein/zeaxanthin and lycopene. The combined evidence supports the conclusion that cigarette smoking is independently associated with lowered circulating concentrations of ascorbic acid and provitamin A carotenoids. These associations have implications for the design and interpretation of epidemiologic studies of antioxidant micronutrients in relation to health and disease. To the extent that these micronutrients are associated with health and longevity, this evidence documents yet another deleterious consequence of cigarette smoking on human health.

J Toxicol Environ Health. 1982 Sep;10(3):423-31.

Cadmium and nickel in smoke of cigarettes prepared from tobacco cultured on municipal sludge-amended soil.

Gutenmann WH, Bache CA, Lisk DJ, Hoffmann D, Adams JD, Elfving DC.

Abstract

Cigarettes prepared from tobacco grown on municipal sludge-amended soil were smoked, and the mainstream particulates and gaseous fractions were analyzed for total cadmium and nickel content. Sludge-grown and control (soil-grown) tobaccos contained, respectively, 67.4 and 3.18 ppm of cadmium and 19.4 and 1.29 ppm of nickel. The quantities of cadmium (microgram per cigarette) found in the mainstream particulate and gaseous fractions were, respectively, 6.67 and 0.04 for the sludge-grown and 0.21 and 0.03 for the control treatments. The quantities of nickel (microgram per cigarette) found in the mainstream particulates and gaseous fractions were, respectively, 0.11 and 0.07 for the sludge-grown and 0.01 and 0.01 for the control treatments. The potential public health implications of these results and modifying factors are discussed.

Circulation. 1996 Jul 1;94(1):6-9.

Antioxidant vitamin C improves endothelial dysfunction in chronic smokers.

Heitzer T, Just H, Münzel T.

Source

Medizinische Klinik III, Kardiologie, Universität Freiburg, Germany.

Abstract

BACKGROUND:

Chronic smoking is associated with endothelial dysfunction, an early stage of atherosclerosis. It has been suggested that endothelial dysfunction may be a consequence of enhanced degradation of nitric oxide secondary to formation of oxygen-derived free radicals. To test this hypothesis, we investigated the effects of the antioxidant vitamin C on endothelium-dependent responses in chronic smokers.

METHODS AND RESULTS:

Forearm blood flow responses to the endothelium-dependent vasodilator acetylcholine (7.5, 15, 30, and 60 micrograms/min) and the endothelium-independent vasodilator sodium nitroprusside (1, 3, and 10 micrograms/min) were measured by venous occlusion plethysmography in 10 control subjects and 10 chronic smokers. Drugs were infused into the brachial artery, and forearm blood flow was measured for each drug before and during concomitant intra-arterial infusion of the antioxidant vitamin C (18 mg/min). In control subjects, vitamin C had no effect on forearm blood flow in response to acetylcholine and sodium nitroprusside. In contrast, in chronic smokers the attenuated forearm blood flow responses to acetylcholine were markedly improved by concomitant administration of vitamin C, whereas the vasodilator responses to sodium nitroprusside were not affected.

CONCLUSIONS:

The present studies demonstrate that the antioxidant vitamin C markedly improves endothelium-dependent responses in chronic smokers. This observation supports the concept that endothelial dysfunction in chronic smokers is at least in part mediated by enhanced formation of oxygen-derived free radicals.

Comment in

Circulation. 1999 Mar 9;99(9):1273-4.

J Biol Chem. 2004 Sep 24;279(39):40337-44. Epub 2004 Jul 22.

Depletion of intracellular ascorbate by the carcinogenic metals nickel and cobalt results in the induction of hypoxic stress.

Salnikow K, Donald SP, Bruick RK, Zhitkovich A, Phang JM, Kasprzak KS.

Source

NCI-Frederick, National Institutes of Health, Frederick, Maryland 21702, USA. salnikow@ncifcrf.gov

Abstract

Exposure of cells to carcinogenic compounds of nickel(II) and cobalt(II) causes activation of the HIF-1 transcription factor and up-regulates a battery of hypoxia-inducible genes. However, the mechanism of HIF-1 activation by these metals is not known. It was shown recently that hydroxylation of prolines in the HIFalpha subunit of HIF-1 is required for its binding with the von Hippel-Lindau tumor suppressor protein and the subsequent proteasomal destruction. Here we show that responsible prolyl hydroxylases are targets for both nickel(II) and cobalt(II) because degradation of a reporter protein containing the oxygen-dependent degradation domain (Pro-402/564) of HIFalpha was abolished in a von Hippel-Lindau-dependent manner in cells exposed to nickel(II) or cobalt(II). The enzymatic activity of prolyl hydroxylases depends on iron as the activating metal, 2-oxoglutarate as a co-substrate, and ascorbic acid as a cofactor. Hydroxylase activity can be impaired by the depletion of any of these factors. We found that exposure of cells to nickel(II) or cobalt(II) did not affect the level of intracellular iron. Instead, nickel(II) or cobalt(II) exposure greatly depleted intracellular ascorbate. Co-exposure of cells to metals and ascorbate resulted in the increase of intracellular ascorbate and reversed both metal-induced stabilization of HIF-1alpha and HIF-1-dependent gene transcription. Because ascorbate is essential for maintaining iron in prolyl hydroxylases in the active iron(II) state, we suggest that the observed depletion of ascorbate by nickel(II) or cobalt(II) favors iron oxidation and thus inactivation of the enzyme.

Am J Clin Nutr. 2003 Jan;77(1):160-6.

Smoking and exposure to environmental tobacco smoke decrease some plasma antioxidants and increase gamma-tocopherol in vivo after adjustment for dietary antioxidant intakes.

Dietrich M, Block G, Norkus EP, Hudes M, Traber MG, Cross CE, Packer L.

Source

School of Public Health, University of California, Berkeley 94720-7360, USA. mdietric@uclink.berkeley.edu

Abstract

BACKGROUND:
Free radicals in cigarette smoke may cause oxidative damage to macromolecules, contributing to cardiovascular diseases and cancer. Decreased plasma antioxidant concentrations may indicate cigarette smoke-related oxidative stress.

OBJECTIVE:
We compared the effects on plasma antioxidant concentrations in cotinine-confirmed active and passive smokers with those in nonsmokers, independent of differences in dietary intakes and other covariates.

DESIGN:
Plasma samples from 83 smokers, 40 passive smokers, and 36 nonsmokers were analyzed for total ascorbic acid, alpha- and gamma-tocopherols, 5 carotenoids, retinol, and cotinine. Groups were compared by using analysis of variance with adjustment for sex, age, race, body mass index, alcohol intake, triacylglycerol concentration, fruit and vegetable intakes, and dietary antioxidants.

RESULTS:
After adjustment for dietary antioxidant intakes and other covariates, smokers and passive smokers had significantly lower plasma beta-carotene concentrations than did nonsmokers (0.15, 0.17, and 0.24 micro mol/L, respectively) and significantly higher gamma-tocopherol concentrations (7.8, 7.8, and 6.5 micro mol/L, respectively). Smokers had significantly lower plasma ascorbic acid and beta-cryptoxanthin concentrations than did nonsmokers and passive smokers (ascorbic acid: 43.6, 54.5, and 54.6 micro mol/L, respectively; beta-cryptoxanthin: 0.12, 0.16, and 0.16 micro mol/L, respectively) and significantly lower concentrations of lutein and zeaxanthin than did nonsmokers (0.33 compared with 0.41 micro mol/L). The P values for all the differences described above were < 0.05. No significant differences in plasma concentrations of alpha-tocopherol, alpha-carotene, total carotenoids, lycopene, or retinol were observed.

CONCLUSIONS:
These results indicate that cigarette smokers and nonsmokers exposed to cigarette smoke have a significantly lower plasma antioxidant status than do unexposed nonsmokers, independent of differences in dietary antioxidant intakes. Further research is required to explain why plasma gamma-tocopherol concentrations were significantly higher in smokers and passive smokers than in nonsmokers.

J Nutr Sci Vitaminol (Tokyo). 2005 Oct;51(5):374-6.

Influence of cigarette smoke on the L-ascorbic acid metabolism and the activities of drug-metabolizing enzyme in rats.

Suzuki E, Hayashi M, Kaminao M, Kurata T.

Source

Department of Nutrition and Food Sciences, Ochanomizu University, 2-1-1 Otsuka, Bunkyo-ku, Tokyo, 112-8610, Japan.

Abstract

This study clarified the influence of cigarette smoke on the L-ascorbic acid (AsA) metabolism and the activities of drug-metabolizing enzyme in rats. The test rats (group T) were exposed to weak sidestream smoke from cigarettes for 2 h, everyday for 57 days. AsA concentration in the tissues and excreted amount of AsA in urine of group T tended to be higher than those of control group (group C). The plasma AsA concentration and the activities of aniline hydroxylase and 7-ethoxycoumarin O-deethylase of group T were significantly higher than those of group C. There was no significant difference in the activity of UDP glucuronosyltransferase or in the liver cytochrome P-450 content between these two groups.

Nutrition. 2006 Nov-Dec;22(11-12):1192-201.

Alpha-tocopherol and ascorbic acid supplementation reduced acute lung inflammatory response by cigarette smoke in mouse.

Silva Bezerra F, Valença SS, Lanzetti M, Pimenta WA, Castro P, Gonçalves Koatz VL, Porto LC.

Source

Laboratory of Tissue Repair, Histology and Embryology Department, IBRAG, UERJ, Rio de Janeiro, Brazil.

Abstract

OBJECTIVE:
Short-term cigarette smoke (CS) exposure leads to acute lung inflammation through its influence over oxidants/antioxidants imbalance. Antioxidant vitamins such as ascorbic acid and alpha-tocopherol interact with oxidizing radicals. It is not clear if antioxidant supplementation can reduce inflammatory lung responses. Thus our aim was to analyze the effects of vitamin supplementation on the lungs of mice exposed to six cigarettes per day with histologic, cytological, and biochemical methods.

METHODS:
C57BL/6 mice were exposed to ambient air (control) or CS from 3, 6, 9, 12, or 15 cigarettes daily for up to 5 d. Mice alveolar macrophages and polymorphonuclear cells were counted in the bronchoalveolar lavage. Groups of CS animals received 50 mg/kg of ascorbic acid daily and/or 50 mg/kg of alpha-tocopherol daily as an oral supplementation (CS+C, CS+E, CS+C+E, respectively) 12 h before CS exposure. Thiobarbituric acid-reactive substances were detected and western blot to nuclear factor-kappaB were performed in lung extracts; metalloprotease-12 and tumor necrosis factor-alpha positive alveolar macrophages were quantified in the lungs processed for immunohistochemistry of the animals exposed to the smoke from six cigarettes daily for 5 d.

RESULTS:
The number of alveolar macrophages and polymorphonuclear cells in bronchoalveolar lavage (cells x 10(3)/mL) in mice exposed to CS were increased and CS with vitamin supplementation groups presented bronchoalveolar lavage cells similar to those of control. Thiobarbituric acid-reactive substances values were reduced in vitamin supplementation groups when compared with CS and the lower value was found in the CS+C+E group. Metalloprotease-12 and tumor necrosis factor-alpha were more evident in CS as much as nuclear factor-kappaB activation when compared with control and vitamin supplementation groups.

CONCLUSION:
Our results showed that CS induced acute lung inflammation. The inflammatory process after cigarette exposures was reduced by ascorbic acid, alpha-tocopherol, or more efficiently by both vitamin supplementations.

Am J Clin Nutr. 2000 Feb;71(2):530-6.

Ascorbate is depleted by smoking and repleted by moderate supplementation: a study in male smokers and nonsmokers with matched dietary antioxidant intakes.

Lykkesfeldt J, Christen S, Wallock LM, Chang HH, Jacob RA, Ames BN.

Source

Department of Molecular and Cell Biology, University of California, Berkeley, CA, USA.

Abstract

BACKGROUND:
Lack of reliable dietary data has hampered the ability to effectively distinguish between effects of smoking and diet on plasma antioxidant status. As confirmed by analyses of comprehensive food-frequency questionnaires, the total dietary intakes of fruit and vegetables and of dietary antioxidants were not significantly different between the study groups in the present study, thereby enabling isolation of the effect of smoking.

OBJECTIVE:
Our objective was to investigate the effect of smoking on plasma antioxidant status by measuring ascorbic acid, alpha-tocopherol, gamma-tocopherol, beta-carotene, and lycopene, and subsequently, to test the effect of a 3-mo dietary supplementation with a moderate-dose vitamin cocktail.

DESIGN:
In a double-blind, placebo-controlled design, the effect of a vitamin cocktail containing 272 mg vitamin C, 31 mg all-rac-alpha-tocopheryl acetate, and 400 microg folic acid on plasma antioxidants was determined in a population of smokers (n = 37) and nonsmokers (n = 38). The population was selected for a low intake of fruit and vegetables and recruited from the San Francisco Bay area.

RESULTS:
Only ascorbic acid was significantly depleted by smoking per se ($P < 0.01$). After the 3-mo supplementation period, ascorbic acid was efficiently repleted in smokers ($P < 0.001$). Plasma alpha-tocopherol and the ratio of alpha- to gamma-tocopherol increased significantly in both supplemented groups ($P < 0.05$).

CONCLUSIONS:
Our data suggest that previous reports of lower concentrations of plasma vitamin E and carotenoids in smokers than in nonsmokers may primarily have been caused by differences in dietary habits between study groups. Plasma ascorbic acid was depleted by smoking and repleted by moderate supplementation.

Indian J Public Health. 1998 Jan-Mar;42(1):20-3.

Influence of cigarette smoking on Vitamin C, glutathione and lipid peroxidation status.

Banerjee KK, Marimuthu P, Sarkar A, Chaudhuri RN.

Source

Department of Occupational Health, All India Institute of Hygiene & Public Health, Calcutta.

Abstract

There has been a growing interest during recent years in the role of free radicals and lipid-peroxidation at tissue-level for the causation of cancer and other age-related diseases like atherosclerosis, rheumatoid arthritis, cataract etc. Free radicals and increased lipid peroxidation play a significant role for causation of human diseases by oxidative damage and functional degeneration of the tissues. Vitamin C, a well-known dietary antioxidant, and other enzymatic antioxidants like glutathione can protect the lipids of lipoproteins and other biomembranes against peroxidative damage by intercepting oxidants before they can attack the tissues. But cigarette smoking was found to affect the antioxidant protective action of Vitamin C, glutathione etc. A group of adult male smokers in this study were found to have lowered Vitamin 'C' & glutathione levels, but increased lipid-peroxide levels in their blood. Thus the increased pathogenicity of the smoking may also be due to indirect biochemical effect of enhanced oxidative stress by increased lipid-peroxidation and lowered Vitamin C & other antioxidants at tissue-level.

Am J Clin Nutr. 2005 Jan;81(1):95-103.

{alpha}-Tocopherol disappearance is faster in cigarette smokers and is inversely related to their ascorbic acid status.

Bruno RS, Ramakrishnan R, Montine TJ, Bray TM, Traber MG.

Source

Department of Human Nutrition, The Ohio State University, Columbus, OH, USA.

Abstract

BACKGROUND:
Cigarette smokers have enhanced oxidative stress from cigarette smoke exposure and from their increased inflammatory responses.

OBJECTIVE:
The objective of this study was to determine whether cigarette smoking increases plasma alpha-tocopherol disappearance in otherwise healthy humans.

DESIGN:
Smokers and nonsmokers (n = 10/group) were supplemented with deuterium-labeled alpha-tocopheryl acetates (75 mg each of d(3)-RRR-alpha-tocopheryl acetate and d(6)-all-rac-alpha-tocopherols acetate) for 6 evenings (days -6 to -1). Plasma alpha-tocopherols, ascorbic acid, uric acid, and F(2alpha)-isoprostanes were measured in blood samples collected on days -6 through 17. The urinary alpha-tocopherol metabolite, alpha-carboxy-ethyl-hydroxy-chroman (alpha-CEHC), was measured on days -6, 0, and 17 in 24-h urine samples.

RESULTS:
F(2alpha)-isoprostanes were, on average, approximately 40% higher in smokers than in nonsmokers. On day 0, plasma labeled and unlabeled alpha-tocopherol concentrations were not significantly different between groups. Smoking resulted in faster fractional disappearance of plasma alpha-tocopherol (0.215 +/- 0.011 compared with 0.191 +/- 0.009 pools/d; P < 0.05). Fractional disappearance rates of alpha-tocopherol correlated with plasma ascorbic acid concentrations in smokers (P = 0.021) but not in nonsmokers despite plasma ascorbic acid concentrations that were not significantly different between groups. By day 17, cigarette smoking resulted in lower plasma alpha-tocopherol concentrations and urinary excretion of labeled and unlabeled alpha-CEHC (P < 0.05).

CONCLUSIONS:
Cigarette smoking increased alpha-tocopherol disappearance. Greater rates of alpha-tocopherol disappearance in smokers appear to be related to increased oxidative stress accompanied by lower plasma ascorbic acid concentrations. Thus, smokers have an increased requirement for both alpha-tocopherol and ascorbic acid.

Korean J Lab Med. 2009 Feb;29(1):10-6.

Concentrations of blood vitamin A, C, E, coenzyme Q10 and urine cotinine related to cigarette smoking exposure.

[Article in Korean]

Song SM, Park YS, Lee A, Cho YG, Kim DS, Lee HS, Choi SI, Lee KR.

Source

Seoul Clinical Laboratories, Seoul, Korea. drssm@scllab.co.kr

Abstract

BACKGROUND:

In smokers, smoking causes many disease entities including cancers, chronic pulmonary diseases and cardiovascular diseases. Passive smoking is also accepted as a carcinogen and its adverse health effects are emphasized. We measured blood vitamin A, C, E (alpha-, beta- and gamma-tocopherol), coenzyme Q10 and urine cotinine concentrations in nonsmokers and smokers.

METHODS:

Twenty-one healthy nonsmokers and 24 healthy smokers were included in this study. Smoking status was assessed with a self-reported questionnaire. Plasma was analyzed for coenzyme Q10 and serum for vitamin A, C, E using HPLC (Agilent Technologies Inc., USA) and random urine for cotinine using LC/tandem mass spectrometry (Applied Biosystems Inc., Canada).

RESULTS:

Smokers had significantly lower serum concentrations of vitamin C than nonsmokers (P=0.0005). No significant differences in concentrations of serum vitamin A, E, and plasma coenzyme Q10 were observed. Smokers had highly elevated urine cotinine levels (1,454+/-903 ng/mL). In 16 (76.2%) of 21 nonsmokers, urine cotinine was detected (3.25+/-4.08 ng/mL). The correlations between urine cotinine and blood antioxidants levels were not found. Neither, the correlation between smoking status and blood antioxidants & urine cotinine was found.

CONCLUSIONS:

This study shows that smokers had significantly lower vitamin C levels among nonenzymatic antioxidants, namely, vitamin A, C, E and coenzyme Q10. High detection rate of urine cotinine in nonsmokers show the seriousness of passive smoking exposure, therefore more social efforts should be directed to reduce passive smoking exposure.

Vitamin D-3

J Bone Miner Res. 2003 Mar;18(3):553-60.

Influence of environmental cadmium exposure on forearm bone density.

Wang H, Zhu G, Shi Y, Weng S, Jin T, Kong Q, Nordberg GF.

Source

Department of Bone Metabolism, Institute of Radiation Medicine, Fudan University, Shanghai, China.

Abstract

Cadmium may have both direct and indirect effects on bone turnover. It is nephrotoxic and can interfere with vitamin D metabolism. Such perturbation may result in osteoporosis and osteomalacia. In this study, a total of 790 persons (302 males and 488 females) participated; they were all over 35 years old and resided in an area near a cadmium smelter in southeast China. All participants completed a questionnaire, and bone mineral density was measured by SPA-4 single-photon absorptiometry at the radius and ulna. Cadmium content of urine was determined by graphite-furnace atomic absorption spectrophotometry as a measure of dose. The decline in bone mineral density with age in a heavily polluted area was greater than that in a control area for subjects over 60 years of age of both sexes ($p < 0.05$). In single regression, forearm bone densities were negatively correlated with urinary cadmium excretion in both males and females ($p < 0.001$), whereas stepwise regression showed that forearm bone density decreased linearly with age ($p < 0.001$) and urinary cadmium ($p < 0.01$) in both sexes, suggesting a dose-effect relationship between cadmium dose and bone mineral density. Based on the World Health Organization criteria, (bone mineral density < -2.5 SDs below the normal young adult), the prevalence of osteoporosis in women increased from 34.0% in the control area to 51.9% in the heavily polluted area ($p < 0.01$) among subjects over 50 years old, and the odds ratio value was 2.09 (95% CI: 1.08-4.03) for the highly polluted area compared with the control area. A striking observation in the study was the marked increase of the prevalence of fracture in the cadmium-polluted area in both sexes. It was concluded that environmental exposure to cadmium is associated with an increased loss of bone mineral density in both males and females, leading to osteoporosis and increased risk of fractures, especially in the elderly and in females.

Public Health Nutr

. 2020 May;23(7):1273-1277.

doi: 10.1017/S1368980018003932. Epub 2019 Feb 8.

Smoking during pregnancy reduces vitamin D levels in a Finnish birth register cohort

A Inkeri Lokki[1,2], Jenni Heikkinen-Eloranta[3], Hanna Öhman[4,5], Seppo Heinonen[3], Heljä-Marja Surcel[4,5], Henriette Svarre Nielsen[6]

Abstract

Objective: Maternal vitamin D level in pregnancy may have implications for both the mother and fetus. Deficiency of vitamin D has been linked to several pregnancy complications and fetal skeletal health. Smoking has been associated with reduced serum level of the vitamin D metabolite, 25-hydroxyvitamin D (25(OH)D).

Design: A nested case-control study within the Finnish Maternity Cohort, a population-based cohort which includes first-trimester sera from 98 % of pregnancies in Finland since 1987. The selection consisted of women with uncomplicated pregnancies. We studied serum concentration of 25(OH)D in 313 non-smoking and forty-six self-reported smoking pregnant women.

Setting: We hypothesize that pregnant smokers may have an increased risk of low 25(OH)D levels especially during winter months.

Participants: A control group from an unpublished pregnancy complication study consisting of 359 uncomplicated pregnancies. Individuals who reported that they do not smoke were considered 'non-smokers' (n 313) and those who reported continued smoking after the first trimester of pregnancy were considered 'smokers' (n 46).

Results: Smokers had significantly lower levels of 25(OH)D irrespective of sampling time ($P<0{\cdot}0001$). Furthermore, during the low sun-exposure season, only 14 % of smokers met the guideline level of 40 nmol/l for serum 25(OH)D in comparison with 31 % of non-smokers.

Conclusions: Expectant mothers who smoke have an increased risk of vitamin D deficiency during low sun-exposure months in northern regions. Further studies are needed to assess the associated risks for maternal and fetal health as well as possible long-term implications for the infant.

Vitamin E:

As Alpha Tocopherol

or

Alpha and Gamma Tocopherol

Free Radic Res. 2004 Aug;38(8):861-8.

Cigarette smokers have decreased lymphocyte and platelet alpha-tocopherol levels and increased excretion of the gamma-tocopherol metabolite gamma-carboxyethyl-hydroxychroman (gamma-CEHC).

Jeanes YM, Hall WL, Proteggente AR, Lodge JK.

Source

Centre for Nutrition and Food Safety, School of Biomedical and Molecular Sciences, University of Surrey, Guildford, Surrey GU2 7XH, UK.

Abstract

Cigarette smoking is associated with increased oxidative stress and increased risk of degenerative disease. As the major lipophilic antioxidant, requirements for vitamin E may be higher in smokers due to increased utilisation. In this observational study we have compared vitamin E status in smokers and non-smokers using a holistic approach by measuring plasma, erythrocyte, lymphocyte and platelet alpha- and gamma-tocopherol, as well as the specific urinary vitamin E metabolites alpha- and gamma-carboxyethyl-hydroxychroman (CEHC). Fifteen smokers (average age 27 years, smoking time 7.5 years) and non-smokers of comparable age, gender and body mass index (BMI) were recruited. Subjects completed a 7-day food diary and on the final day they provided a 24 h urine collection and a 20 ml blood sample for measurement of urinary vitamin E metabolites and total vitamin E in blood components, respectively. No significant differences were found between plasma and erythrocyte alpha- and gamma-tocopherol in smokers and non-smokers. However, smokers had significantly lower alpha-tocopherol (mean+/-SD, 1.34+/-0.31 micromol/g protein compared with 1.94+/-0.54, P = 0.001) and gamma-tocopherol (0.19+/-0.04 micromol/g protein compared with 0.26+/-0.08, P = 0.026) levels in their lymphocytes, as well as significantly lower alpha-tocopherol levels in platelets (1.09+/-0.49 micromol/g protein compared with 1.60+/-0.55, P = 0.014; gamma-tocopherol levels were similar). Interestingly smokers also had significantly higher excretion of the urinary gamma-tocopherol metabolite, gamma-CEHC (0.49+/-0.25mg/g creatinine compared with 0.32+/-0.16, P = 0.036) compared to non-smokers, while their alpha-CEHC (metabolite of alpha-tocopherol) levels were similar. There was no significant difference between plasma ascorbate, urate and F2-isoprostane levels. Therefore in this population of cigarette

smokers (mean age 27 years, mean smoking duration 7.5 years), alterations to vitamin E status can be observed even without the more characteristic changes to ascorbate and F2-isoprostanes. We suggest that the measurement of lymphocyte and platelet vitamin E may represent a valuable biomarker of vitamin E status in relation to oxidative stress conditions.

Free Radic Biol Med. 2001 Dec 1;31(11):1368-74.

Vitamin E kinetics in smokers and nonsmokers.

Traber MG, Winklhofer-Roob BM, Roob JM, Khoschsorur G, Aigner R, Cross C, Ramakrishnan R, Brigelius-Flohé R.

Source

Department of Internal Medicine, University of California, Davis, School of Medicine, Sacramento, CA, USA.
maret.traber@orst.edu

Abstract

Does cigarette smoking increase vitamin E utilization in vivo? A trial was carried out in 6 smokers and 5 nonsmokers of comparable ages and serum lipids. Subjects consumed 75 mg each d(3)-RRR and d(6)-all rac-alpha-tocopheryl acetates (natural and synthetic vitamin E, respectively) daily for 7 d with a standardized breakfast. Fasting blood samples were drawn on days -7, -6, -5, -4, -3, -2, -1, 0, 1, 2, 3, 4, 5, 6, 7, 9, 14, 21 (negative days indicate supplementation). In both groups, plasma d(3)-alpha-tocopherol concentrations were approximately double of d(6)-alpha-tocopherol. At day 0, the %d(3) alpha-tocopherols (d(3)-alpha-tocopherol/total-alpha-tocopherol x 100) were similar in both smokers and nonsmokers. Subsequently, there was a trend toward a faster exponential disappearance of the plasma %d(3) alpha-tocopherol in smokers compared with nonsmokers (0.30 +/- 0.04 compared with 0.24 +/- 0.05, p =.0565). The calculated %d(3) half-lives were 55.6 +/- 7.4 h in smokers and 72.1 +/- 17.3 h in nonsmokers (p =.0630). By day 21, the %d(3) in smokers had decreased to 1.4% +/- 0.3% while it was 2.2% +/- 0.7% (p =.0418) in the nonsmokers. These data suggest that smoking increases plasma vitamin E disappearance, but further studies are needed to confirm this finding and to assess its cause.

Nutrition. 2006 Nov-Dec;22(11-12):1192-201.

Alpha-tocopherol and ascorbic acid supplementation reduced acute lung inflammatory response by cigarette smoke in mouse.

Silva Bezerra F, Valença SS, Lanzetti M, Pimenta WA, Castro P, Gonçalves Koatz VL, Porto LC.

Source

Laboratory of Tissue Repair, Histology and Embryology Department, IBRAG, UERJ, Rio de Janeiro, Brazil.

Abstract

OBJECTIVE:

Short-term cigarette smoke (CS) exposure leads to acute lung inflammation through its influence over oxidants/antioxidants imbalance. Antioxidant vitamins such as ascorbic acid and alpha-tocopherol interact with oxidizing radicals. It is not clear if antioxidant supplementation can reduce inflammatory lung responses. Thus our aim was to analyze the effects of vitamin supplementation on the lungs of mice exposed to six cigarettes per day with histologic, cytological, and biochemical methods.

METHODS:

C57BL/6 mice were exposed to ambient air (control) or CS from 3, 6, 9, 12, or 15 cigarettes daily for up to 5 d. Mice alveolar macrophages and polymorphonuclear cells were counted in the bronchoalveolar lavage. Groups of CS animals received 50 mg/kg of ascorbic acid daily and/or 50 mg/kg of alpha-tocopherol daily as an oral supplementation (CS+C, CS+E, CS+C+E, respectively) 12 h before CS exposure. Thiobarbituric acid-reactive substances were detected and western blot to nuclear factor-kappaB were performed in lung extracts; metalloprotease-12 and tumor necrosis factor-alpha positive alveolar macrophages were quantified in the lungs processed for immunohistochemistry of the animals exposed to the smoke from six cigarettes daily for 5 d.

RESULTS:

The number of alveolar macrophages and polymorphonuclear cells in bronchoalveolar lavage (cells x 10(3)/mL) in mice exposed to CS were increased and CS with vitamin supplementation groups presented bronchoalveolar lavage cells similar to those of control. Thiobarbituric acid-reactive substances values were reduced in vitamin

supplementation groups when compared with CS and the lower value was found in the CS+C+E group. Metalloprotease-12 and tumor necrosis factor-alpha were more evident in CS as much as nuclear factor-kappaB activation when compared with control and vitamin supplementation groups.

CONCLUSION:
Our results showed that CS induced acute lung inflammation. The inflammatory process after cigarette exposures was reduced by ascorbic acid, alpha-tocopherol, or more efficiently by both vitamin supplementations.

Ann N Y Acad Sci. 2004 Dec;1031:357-60.

Cigarette smoking increases human vitamin E requirements as estimated by plasma deuterium-labeled CEHC.

Leonard SW, Bruno RS, Ramakrishnan R, Bray T, Traber MG.

Source

Linus Pauling Institute, Oregon State University, Corvallis, OR 97331, USA.

Abstract

Cigarette smoking (CS) is a well-described oxidant burden in humans. We hypothesized that CS would accelerate alpha-tocopherol (alpha-T) utilization leaving less for metabolite (CEHC) production. After labeled alpha-T consumption (75 mg each of d(3)-RRR-alpha-TAc and d(6)-all-rac-alpha-TAc) by smokers and nonsmokers (n = 10/group), CS increased alpha-T disappearance and decreased plasma and urinary CEHCs. Plasma d(3)/d(6)-alpha-T ratios were approximately 1.4 during supplementation and approximately 2 from days 5 to 17. d(3)/d(6)-alpha-CEHC ratios were on average 0.29 +/- 0.05, confirming that all-rac-alpha-tocopherol is metabolized more efficiently. CEHC may be a good marker of vitamin E status, and smokers may have an increased vitamin E requirement.

Am J Clin Nutr. 2005 Jan;81(1):95-103.

{alpha}-Tocopherol disappearance is faster in cigarette smokers and is inversely related to their ascorbic acid status.

Bruno RS, Ramakrishnan R, Montine TJ, Bray TM, Traber MG.

Source

Department of Human Nutrition, The Ohio State University, Columbus, OH, USA.

Abstract

BACKGROUND:
Cigarette smokers have enhanced oxidative stress from cigarette smoke exposure and from their increased inflammatory responses.

OBJECTIVE:
The objective of this study was to determine whether cigarette smoking increases plasma alpha-tocopherol disappearance in otherwise healthy humans.

DESIGN:
Smokers and nonsmokers (n = 10/group) were supplemented with deuterium-labeled alpha-tocopheryl acetates (75 mg each of d(3)-RRR-alpha-tocopheryl acetate and d(6)-all-rac-alpha-tocopherols acetate) for 6 evenings (days -6 to -1). Plasma alpha-tocopherols, ascorbic acid, uric acid, and F(2alpha)-isoprostanes were measured in blood samples collected on days -6 through 17. The urinary alpha-tocopherol metabolite, alpha-carboxy-ethyl-hydroxy-chroman (alpha-CEHC), was measured on days -6, 0, and 17 in 24-h urine samples.

RESULTS:

F(2alpha)-isoprostanes were, on average, approximately 40% higher in smokers than in nonsmokers. On day 0, plasma labeled and unlabeled alpha-tocopherol concentrations were not significantly different between groups. Smoking resulted in faster fractional disappearance of plasma alpha-tocopherol (0.215 +/- 0.011 compared with 0.191 +/- 0.009 pools/d; P < 0.05). Fractional disappearance rates of alpha-tocopherol correlated with plasma ascorbic acid concentrations in smokers (P = 0.021) but not in nonsmokers despite plasma ascorbic acid concentrations that were not significantly different between groups. By day 17, cigarette smoking resulted in lower plasma alpha-tocopherol concentrations and urinary excretion of labeled and unlabeled alpha-CEHC (P < 0.05).

CONCLUSIONS:

Cigarette smoking increased alpha-tocopherol disappearance. Greater rates of alpha-tocopherol disappearance in smokers appear to be related to increased oxidative stress accompanied by lower plasma ascorbic acid concentrations. Thus, smokers have an increased requirement for both alpha-tocopherol and ascorbic acid.

J Nutr. 2005 Apr;135(4):671-4.

Cigarette smoke alters human vitamin E requirements.

Bruno RS, Traber MG.

Source

Linus Pauling Institute, Oregon State University, Corvallis, Oregon, USA.

Abstract

Vitamin E is a lipophilic chain-breaking antioxidant that prevents lipid peroxidation. Although cigarette smoke is a potent source of oxidative stress that depletes vitamin E in vitro, it is unclear whether it has a similar effect in vivo, particularly in humans. Therefore, this review will discuss the role of cigarette smoke on gamma-tocopherol (gamma-T) nitration, its effect on alpha-tocopherol (alpha-T) biokinetics in smokers, and the changes in the synthesis, plasma concentrations, and urinary excretion of the vitamin E metabolite (CEHC; carboxy-ethyl-hydroxy-chroman). Last, the possibility of CEHC as a biomarker of vitamin E status will be assessed as will the question whether smokers have increased dietary requirements of vitamin E.

Laryngoscope. 2006 Jan;116(1):97-100.

Effects of vitamin E on cigarette smoke induced oxidative damage in larynx and lung.

Uneri C, Sari M, Bağlam T, Polat S, Yüksel M.

Source

Department of Otorhinolaryngology, Head and Neck Surgery, Marmara University School of Medicine, Istanbul, Turkey. cuneri@superonline.com

Abstract

OBJECTIVES:

Cigarette smoke (CS) contains a large variety of compounds, including many oxidants and free radicals (also known as reactive oxygen species), that are capable of initiating or promoting oxidative damage, which leads to various degenerative pulmonary and cardiovascular diseases as well as cancer. Recent studies have established a strong relationship between CS and development of reactive oxygen species (ROS). The aim of the present study was to detect ROS levels in laryngeal and lung tissues of rats by measuring luminol-amplified chemiluminescence and to determine the changes in ROS levels in lung and laryngeal tissues induced by exposure to CS, with and without concurrent treatment with vitamin E.

STUDY DESIGN:

Prospective controlled animal study.

METHODS:

Male Sprague-Dawley rats were divided into three groups of eight animals each. The first group of rats was exposed to cigarette smoke. The second group of rats was exposed to cigarette smoke and concurrently treated with vitamin E. The third group was used as control. Animals were killed and chemiluminescence measurements were made for laryngeal and lung tissues.

RESULTS:

Reactive oxygen species levels were significantly increased in the first group of rats compared to the levels measured in control animals. ROS levels were statistically significantly decreased in the second group as compared to the first group.

CONCLUSION:

Our results indicate that vitamin E decreases CS induced ROS levels in laryngeal and lung tissues.

Ann N Y Acad Sci. 2004 Dec;1031:357-60.

Cigarette smoking increases human vitamin E requirements as estimated by plasma deuterium-labeled CEHC.

Leonard SW, Bruno RS, Ramakrishnan R, Bray T, Traber MG.

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Linus Pauling Institute, Oregon State University, Corvallis, OR 97331, USA.

Abstract

Cigarette smoking (CS) is a well-described oxidant burden in humans. We hypothesized that CS would accelerate alpha-tocopherol (alpha-T) utilization leaving less for metabolite (CEHC) production. After labeled alpha-T consumption (75 mg each of d(3)-RRR-alpha-TAc and d(6)-all-rac-alpha-TAc) by smokers and nonsmokers (n = 10/group), CS increased alpha-T disappearance and decreased plasma and urinary CEHCs. Plasma d(3)/d(6)-alpha-T ratios were approximately 1.4 during supplementation and approximately 2 from days 5 to 17. d(3)/d(6)-alpha-CEHC ratios were on average 0.29 +/- 0.05, confirming that all-rac-alpha-tocopherol is metabolized more efficiently. CEHC may be a good marker of vitamin E status, and smokers may have an increased vitamin E requirement.

Eur J Obstet Gynecol Reprod Biol. 2011 Apr;155(2):132-6. Epub 2011 Jan 7.

The effect of tobacco smoking during pregnancy on plasma oxidant and antioxidant status in mother and newborn.

Chelchowska M, Ambroszkiewicz J, Gajewska J, Laskowska-Klita T, Leibschang J.

Source

Screening Test Department, Institute of Mother and Child, ul. Kasprzaka 17A, 02-211 Warsaw, Poland.

Abstract

OBJECTIVE:

The aim of the study was to estimate the effect of tobacco smoking during pregnancy on oxidative damage and antioxidant defence in matched samples of maternal blood and cord blood.

STUDY DESIGN:

Healthy, pregnant women (n=140) were divided into non-smoking and smoking groups according to the concentration of cotinine in serum and urine. Oxidative damage was measured through levels of malondialdehyde (MDA) and plasma antioxidant status was evaluated by measuring concentrations of total radical trapping parameters (TRAP) and selected antioxidants (β-carotene, vitamin A, vitamin E, uric acid). Statistical analysis was done using the SAS System for Windows (SAS Institute, Cary, NC).

RESULTS:

In the course of pregnancy the concentration of MDA increased, but to higher values in smoking women than in non-smoking ones. It was accompanied by significantly lower TRAP in the smoking group than in the controls ($p<0.05$). Plasma concentration of uric acid ($p<0.05$) and antioxidant vitamins E ($p<0.01$), A and β-carotene ($p<0.0001$) were all

reduced in smokers as compared with non-smoking pregnant women especially in the third trimester. Concentration of MDA in plasma of cord blood of newborns of smoking mothers was significantly higher ($p<0.01$) but the antioxidant defence was lower ($p<0.0001$) than in non-smoking ones. It was particularly pronounced for β-carotene (32%; $p<0.0001$) and vitamin A (28%; $p<0.001$). A significant negative correlation was found between MDA and TRAP levels of maternal plasma (non-smoking and smoking: $r=-0.50$, $p<0.0001$) and cord plasma (non-smoking: $r=-0.54$, $p=0.0057$; smoking: $r=-0.71$, $p=0.0004$) in all the study subjects. Total antioxidant status positively correlated with concentrations of uric acid and vitamin E in non-smoking and smoking mothers as well as their newborns.

CONCLUSION:
Tobacco smoke enhances lipid peroxidation and depletes antioxidant potential in the plasma of pregnant women and umbilical cord blood. Therefore smoking during pregnancy may stimulate free radical damage in the mother and the growing fetus.

Kaohsiung J Med Sci. 2009 Aug;25(8):423-30.

Comparison of plasma antioxidant levels and related metabolic parameters between smokers and non-smokers.

Chiu YW, Chuang HY, Huang MC, Wu MT, Liu HW, Huang CT.

Source

Department of Family Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan.

Abstract

The relationship between cigarette smoking and cell damage is complicated, particularly considering the role of oxidative stress. The aim of this study was to identify the relationships among plasma nicotine metabolites, lipophilic antioxidants, and metabolic parameters in smokers and nonsmokers. This cross-sectional study recruited 100 subjects who visited the Department of Family Medicine at Kaohsiung Medical University Hospital. Excluding 14 ineligible cases, 46 smokers and 40 non-smokers were enrolled. Plasma nicotine metabolites, lipophilic antioxidants (including retinol, lycopene, alpha-carotene, beta-carotene, delta-tocopherol, gamma-tocopherol and alpha-tocopherol), related metabolic parameters, and body composition (including height, weight, body mass index, body fat, and waist circumference) were examined by comparison of means, correlations and regressions. Significant correlations among nicotine metabolites, age, sex, body composition and plasma lipophilic antioxidants were noted. Nicotine metabolites, age, body height and body weight were closely associated with plasma antioxidant levels ($p < 0.05$) in multiple linear regression. The levels of alpha-carotene, beta-carotene, gamma-tocopherol and lycopene were lower in smokers than in non-smokers ($p < 0.01$). The plasma level of high-sensitivity C-reactive protein (hsCRP), which is a marker for high cardiovascular risk, was higher in smokers than in non-smokers ($p = 0.003$). We

conclude that the lower plasma antioxidant levels and the higher level of hsCRP in smokers may lead to decreased protective efficacy compared with non-smokers. Further studies are warranted to support our hypothesis.

Am J Med Sci. 2007 Jun;333(6):346-53.

Exhaustive exercise modifies oxidative stress in smoking subjects.

Gochman E, Reznick AZ, Avizohar O, Ben-Amotz A, Levy Y.

Source

Department of Anatomy and Cell Biology, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.

Abstract

BACKGROUND:
Exhaustive exercise is associated with increased metabolic rate and accelerated generation of reactive oxygen species. Cigarette smoke also contains oxidants that may participate in the development of atherosclerosis. However, data on the association between exercise and smoking are sparse.

METHODS:
A homogenous group of 30 young men (15 smokers and 15 nonsmokers; mean age, 23.7 +/- 2.6 years), healthy, trained subjects, were assessed before and after a standard maximal exercise test.

RESULTS:
Exercise led to increased protein oxidation (carbonyl assay) in both smokers (+17.7%, P < 0.001) and nonsmokers (+19.1%, P < 0.05), elevation in plasma conjugated dienes (+ 157%, P < 0.04), and plasma lipid peroxides (+14%, P < 0.059) in smokers versus nonsmokers after exercise. Plasma antioxidants levels were significantly lower in the smoking group, with reduction in total carotenoids (-36.5%, P < 0.001), vitamin A (-80%, P < 0.001), and vitamin E (-64%, P < 0.002), compared with nonsmokers. A significant rise in leakage of muscle enzymes (CPK, LDH) and urine

proteins (microalbumin and myoglobin) occurred in all subjects after exercise. CRP levels were higher in smokers compared with nonsmokers before and after exercise.

CONCLUSIONS:
Our results suggest that unnoticed interaction exists between smoking and intense exercise, which indicates that smokers are more susceptible to oxidative insults probably due to lower antioxidant capacity.

Am J Clin Nutr. 1996 Apr;63(4):559-65.

Destruction of tocopherols, carotenoids, and retinol in human plasma by cigarette smoke.

Handelman GJ, Packer L, Cross CE.

Source

Department of Molecular and Cell Biology, University of California, Berkeley, U.S.A.

Abstract

The mechanisms by which exposure to cigarette smoke dramatically increase the incidence and severity of atherosclerosis and the incidence of lung cancer, chronic obstructive airways disease, and emphysema are incompletely understood. Epidemiologic evidence has suggested a modifying role for antioxidant micronutrients, including tocopherols and carotenoids, in these disease processes. It has been suggested that oxidants in cigarette smoke could be involved. We exposed freshly obtained human plasma to the gas phase of cigarette smoke to assess its effects on tocopherols, carotenoids, and retinol. Exposure to cigarette smoke led to the depletion of most of the lipophilic antioxidants in 20 mL human plasma. The order of disappearance was lycopene > alpha-tocopherol > trans-beta-carotene++ > (lutein + zeaxanthin) = cryptoxanthin > gamma-tocopherol = retinol. However, despite a substantial loss of alpha-tocopherol, there was very little peroxidative damage to lipids, and no detectable change in the content of polyunsaturated fatty acid-rich cholesterol esters. We conclude that a wide spectrum of lipophilic micronutrients undergo degradation when exposed to gas-phase cigarette smoke. The relevance of these in vitro findings to possible cigarette smoke-induced depletions of respiratory tract lipophilic antioxidants remains to be clarified.

Vitamin A Carotenoid

Am J Clin Nutr. 2003 Jan;77(1):160-6.

Smoking and exposure to environmental tobacco smoke decrease some plasma antioxidants and increase gamma-tocopherol in vivo after adjustment for dietary antioxidant intakes.

Dietrich M, Block G, Norkus EP, Hudes M, Traber MG, Cross CE, Packer L.

Source

School of Public Health, University of California, Berkeley 94720-7360, USA. mdietric@uclink.berkeley.edu

Abstract

BACKGROUND:

Free radicals in cigarette smoke may cause oxidative damage to macromolecules, contributing to cardiovascular diseases and cancer. Decreased plasma antioxidant concentrations may indicate cigarette smoke-related oxidative stress.

OBJECTIVE:

We compared the effects on plasma antioxidant concentrations in cotinine-confirmed active and passive smokers with those in nonsmokers, independent of differences in dietary intakes and other covariates.

DESIGN:

Plasma samples from 83 smokers, 40 passive smokers, and 36 nonsmokers were analyzed for total ascorbic acid, alpha- and gamma-tocopherols, 5 carotenoids, retinol, and cotinine. Groups were compared by using analysis of variance with adjustment for sex, age, race, body mass index, alcohol intake, triacylglycerol concentration, fruit and vegetable intakes, and dietary antioxidants.

RESULTS:
After adjustment for dietary antioxidant intakes and other covariates, smokers and passive smokers had significantly lower plasma beta-carotene concentrations than did nonsmokers (0.15, 0.17, and 0.24 micro mol/L, respectively) and significantly higher gamma-tocopherol concentrations (7.8, 7.8, and 6.5 micro mol/L, respectively). Smokers had significantly lower plasma ascorbic acid and beta-cryptoxanthin concentrations than did nonsmokers and passive smokers (ascorbic acid: 43.6, 54.5, and 54.6 micro mol/L, respectively; beta-cryptoxanthin: 0.12, 0.16, and 0.16 micro mol/L, respectively) and significantly lower concentrations of lutein and zeaxanthin than did nonsmokers (0.33 compared with 0.41 micro mol/L). The P values for all the differences described above were < 0.05. No significant differences in plasma concentrations of alpha-tocopherol, alpha-carotene, total carotenoids, lycopene, or retinol were observed.

CONCLUSIONS:
These results indicate that cigarette smokers and nonsmokers exposed to cigarette smoke have a significantly lower plasma antioxidant status than do unexposed nonsmokers, independent of differences in dietary antioxidant intakes. Further research is required to explain why plasma gamma-tocopherol concentrations were significantly higher in smokers and passive smokers than in nonsmokers.

Toxicology. 2002 Nov 15;180(2):121-37.

The influence of cigarette smoking on circulating concentrations of antioxidant micronutrients.

Alberg A.

Source

Department of Epidemiology, Room E6132B, The Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Baltimore, MD 21205, USA. aalberg@jhph.edu

Abstract

Cigarette smoke is a significant source of oxidative stress, one potential mechanism for its untoward health effects. The antioxidant defense system is partly comprised of antioxidant micronutrients, making it important to understand the relationship between cigarette smoking and circulating concentrations of antioxidant micronutrients. A synthesis of the literature shows that compared with nonsmokers, on average, active smokers have greater than 25% lower circulating concentrations of ascorbic acid, alpha-carotene, beta-carotene, and cryptoxanthin. The differences in blood concentrations of these micronutrients in former smokers is intermediate between never and current smokers, but average circulating concentrations of alpha-carotene, beta-carotene, and cryptoxanthin were 16-22% lower in former smokers compared with never smokers. Differences in dietary habits between smokers and nonsmokers could potentially account for these associations. Dietary micronutrient intake is associated with blood micronutrient concentrations. Furthermore, patterns of micronutrient consumption by smoking status mimic the pattern of associations observed for blood concentrations. For example, when pooled across studies intake of vitamin C was 16% lower in current smokers and 2% lower in former smokers than in never smokers; the corresponding figures for beta-carotene were 17 and 4%, respectively. Despite the strong potential for confounding, the differences observed between current smokers and nonsmokers seem to be due to an acute effect of smoking based on results of studies

of smoking and antioxidant micronutrient concentrations that have either adjusted for dietary antioxidant micronutrient intake and other potential confounding factors or documented short term changes in circulating antioxidant micronutrient concentrations in smokers before and after smoking cigarettes. The associations observed with active smoking also appear to hold true for passive smoking, implying that even low-dose exposures to tobacco smoke can result in lowered circulating antioxidant micronutrient concentrations. Smoking was more weakly associated with circulating concentrations of vitamin E and the nonprovitamin A carotenoids lutein/zeaxanthin and lycopene. The combined evidence supports the conclusion that cigarette smoking is independently associated with lowered circulating concentrations of ascorbic acid and provitamin A carotenoids. These associations have implications for the design and interpretation of epidemiologic studies of antioxidant micronutrients in relation to health and disease. To the extent that these micronutrients are associated with health and longevity, this evidence documents yet another deleterious consequence of cigarette smoking on human health.

Eur J Obstet Gynecol Reprod Biol. 2011 Apr;155(2):132-6. Epub 2011 Jan 7.

The effect of tobacco smoking during pregnancy on plasma oxidant and antioxidant status in mother and newborn.

Chelchowska M, Ambroszkiewicz J, Gajewska J, Laskowska-Klita T, Leibschang J.

Source

Screening Test Department, Institute of Mother and Child, ul. Kasprzaka 17A, 02-211 Warsaw, Poland.

Abstract

OBJECTIVE:
The aim of the study was to estimate the effect of tobacco smoking during pregnancy on oxidative damage and antioxidant defence in matched samples of maternal blood and cord blood.

STUDY DESIGN:
Healthy, pregnant women (n=140) were divided into non-smoking and smoking groups according to the concentration of cotinine in serum and urine. Oxidative damage was measured through levels of malondialdehyde (MDA) and plasma antioxidant status was evaluated by measuring concentrations of total radical trapping parameters (TRAP) and selected antioxidants (β-carotene, vitamin A, vitamin E, uric acid). Statistical analysis was done using the SAS System for Windows (SAS Institute, Cary, NC).

RESULTS:
In the course of pregnancy the concentration of MDA increased, but to higher values in smoking women than in non-smoking ones. It was accompanied by significantly lower TRAP in the smoking group than in the controls ($p<0.05$). Plasma concentration of uric acid ($p<0.05$) and antioxidant vitamins E ($p<0.01$), A and β-carotene ($p<0.0001$) were all reduced in smokers as compared with non-smoking pregnant women especially in the third trimester. Concentration of MDA in plasma of cord blood of newborns of smoking mothers was significantly higher ($p<0.01$) but the antioxidant

defence was lower (p<0.0001) than in non-smoking ones. It was particularly pronounced for β-carotene (32%; p<0.0001) and vitamin A (28%; p<0.001). A significant negative correlation was found between MDA and TRAP levels of maternal plasma (non-smoking and smoking: r=-0.50, p<0.0001) and cord plasma (non-smoking: r=-0.54, p=0.0057; smoking: r=-0.71, p=0.0004) in all the study subjects. Total antioxidant status positively correlated with concentrations of uric acid and vitamin E in non-smoking and smoking mothers as well as their newborns.

CONCLUSION:
Tobacco smoke enhances lipid peroxidation and depletes antioxidant potential in the plasma of pregnant women and umbilical cord blood. Therefore smoking during pregnancy may stimulate free radical damage in the mother and the growing fetus.

Kaohsiung J Med Sci. 2009 Aug;25(8):423-30.

Comparison of plasma antioxidant levels and related metabolic parameters between smokers and non-smokers.

Chiu YW, Chuang HY, Huang MC, Wu MT, Liu HW, Huang CT.

Source

Department of Family Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan.

Abstract

The relationship between cigarette smoking and cell damage is complicated, particularly considering the role of oxidative stress. The aim of this study was to identify the relationships among plasma nicotine metabolites, lipophilic antioxidants, and metabolic parameters in smokers and nonsmokers. This cross-sectional study recruited 100 subjects who visited the Department of Family Medicine at Kaohsiung Medical University Hospital. Excluding 14 ineligible cases, 46 smokers and 40 non-smokers were enrolled. Plasma nicotine metabolites, lipophilic antioxidants (including retinol, lycopene, alpha-carotene, beta-carotene, delta-tocopherol, gamma-tocopherol and alpha-tocopherol), related metabolic parameters, and body composition (including height, weight, body mass index, body fat, and waist circumference) were examined by comparison of means, correlations and regressions. Significant correlations among nicotine metabolites, age, sex, body composition and plasma lipophilic antioxidants were noted. Nicotine metabolites, age, body height and body weight were closely associated with plasma antioxidant levels ($p < 0.05$) in multiple linear regression. The levels of alpha-carotene, beta-carotene, gamma-tocopherol and lycopene were lower in smokers than in non-smokers ($p < 0.01$). The plasma level of high-sensitivity C-reactive protein (hsCRP), which is a marker for high cardiovascular risk, was higher in smokers than in non-smokers ($p = 0.003$). We conclude that the lower plasma antioxidant levels and the higher level of hsCRP in smokers may lead to decreased protective efficacy compared with non-smokers. Further studies are warranted to support our hypothesis.

Am J Med Sci. 2007 Jun;333(6):346-53.

Exhaustive exercise modifies oxidative stress in smoking subjects.

Gochman E, Reznick AZ, Avizohar O, Ben-Amotz A, Levy Y.

Source

Department of Anatomy and Cell Biology, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.

Abstract

BACKGROUND:
Exhaustive exercise is associated with increased metabolic rate and accelerated generation of reactive oxygen species. Cigarette smoke also contains oxidants that may participate in the development of atherosclerosis. However, data on the association between exercise and smoking are sparse.

METHODS:
A homogenous group of 30 young men (15 smokers and 15 nonsmokers; mean age, 23.7 +/- 2.6 years), healthy, trained subjects, were assessed before and after a standard maximal exercise test.

RESULTS:
Exercise led to increased protein oxidation (carbonyl assay) in both smokers (+17.7%, P < 0.001) and nonsmokers (+19.1%, P < 0.05), elevation in plasma conjugated dienes (+ 157%, P < 0.04), and plasma lipid peroxides (+14%, P < 0.059) in smokers versus nonsmokers after exercise. Plasma antioxidants levels were significantly lower in the smoking group, with reduction in total carotenoids (-36.5%, P < 0.001), vitamin A (-80%, P < 0.001), and vitamin E (-64%, P < 0.002), compared with nonsmokers. A significant rise in leakage of muscle enzymes (CPK, LDH) and urine proteins (microalbumin and myoglobin) occurred in all subjects after exercise. CRP levels were higher in smokers compared with nonsmokers before and after exercise.

CONCLUSIONS:

Our results suggest that unnoticed interaction exists between smoking and intense exercise, which indicates that smokers are more susceptible to oxidative insults probably due to lower antioxidant capacity.

Non Pro-Vitamin A Carotenoids:

Lutein, Zeaxanthin and Lycopene

Toxicology. 2002 Nov 15;180(2):121-37.

The influence of cigarette smoking on circulating concentrations of antioxidant micronutrients.

Alberg A.

Source

Department of Epidemiology, Room E6132B, The Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Baltimore, MD 21205, USA. aalberg@jhph.edu

Abstract

Cigarette smoke is a significant source of oxidative stress, one potential mechanism for its untoward health effects. The antioxidant defense system is partly comprised of antioxidant micronutrients, making it important to understand the relationship between cigarette smoking and circulating concentrations of antioxidant micronutrients. A synthesis of the literature shows that compared with nonsmokers, on average, active smokers have greater than 25% lower circulating concentrations of ascorbic acid, alpha-carotene, beta-carotene, and cryptoxanthin. The differences in blood concentrations of these micronutrients in former smokers is intermediate between never and current smokers, but average circulating concentrations of alpha-carotene, beta-carotene, and cryptoxanthin were 16-22% lower in former smokers compared with never smokers. Differences in dietary habits between smokers and nonsmokers could potentially account for these associations. Dietary micronutrient intake is associated with blood micronutrient concentrations. Furthermore, patterns of micronutrient consumption by smoking status mimic the pattern of associations observed for blood concentrations. For example, when pooled across studies intake of vitamin C was 16% lower in current smokers and 2% lower in former smokers than in never smokers; the corresponding figures for beta-carotene were 17 and 4%, respectively. Despite the strong potential for confounding, the differences observed between current smokers and nonsmokers seem to be due to an acute effect of smoking based on results of studies of smoking and antioxidant micronutrient concentrations that have either adjusted for dietary antioxidant micronutrient

intake and other potential confounding factors or documented short term changes in circulating antioxidant micronutrient concentrations in smokers before and after smoking cigarettes. The associations observed with active smoking also appear to hold true for passive smoking, implying that even low-dose exposures to tobacco smoke can result in lowered circulating antioxidant micronutrient concentrations. Smoking was more weakly associated with circulating concentrations of vitamin E and the nonprovitamin A carotenoids lutein/zeaxanthin and lycopene. The combined evidence supports the conclusion that cigarette smoking is independently associated with lowered circulating concentrations of ascorbic acid and provitamin A carotenoids. These associations have implications for the design and interpretation of epidemiologic studies of antioxidant micronutrients in relation to health and disease. To the extent that these micronutrients are associated with health and longevity, this evidence documents yet another deleterious consequence of cigarette smoking on human health.

Am J Clin Nutr. 2003 Jan;77(1):160-6.

Smoking and exposure to environmental tobacco smoke decrease some plasma antioxidants and increase gamma-tocopherol in vivo after adjustment for dietary antioxidant intakes.

Dietrich M, Block G, Norkus EP, Hudes M, Traber MG, Cross CE, Packer L.

Source

School of Public Health, University of California, Berkeley 94720-7360, USA. mdietric@uclink.berkeley.edu

Abstract

BACKGROUND:
Free radicals in cigarette smoke may cause oxidative damage to macromolecules, contributing to cardiovascular diseases and cancer. Decreased plasma antioxidant concentrations may indicate cigarette smoke-related oxidative stress.

OBJECTIVE:
We compared the effects on plasma antioxidant concentrations in cotinine-confirmed active and passive smokers with those in nonsmokers, independent of differences in dietary intakes and other covariates.

DESIGN:
Plasma samples from 83 smokers, 40 passive smokers, and 36 nonsmokers were analyzed for total ascorbic acid, alpha- and gamma-tocopherols, 5 carotenoids, retinol, and cotinine. Groups were compared by using analysis of variance with adjustment for sex, age, race, body mass index, alcohol intake, triacylglycerol concentration, fruit and vegetable intakes, and dietary antioxidants.

RESULTS:

After adjustment for dietary antioxidant intakes and other covariates, smokers and passive smokers had significantly lower plasma beta-carotene concentrations than did nonsmokers (0.15, 0.17, and 0.24 micro mol/L, respectively) and significantly higher gamma-tocopherol concentrations (7.8, 7.8, and 6.5 micro mol/L, respectively). Smokers had significantly lower plasma ascorbic acid and beta-cryptoxanthin concentrations than did nonsmokers and passive smokers (ascorbic acid: 43.6, 54.5, and 54.6 micro mol/L, respectively; beta-cryptoxanthin: 0.12, 0.16, and 0.16 micro mol/L, respectively) and significantly lower concentrations of lutein and zeaxanthin than did nonsmokers (0.33 compared with 0.41 micro mol/L). The P values for all the differences described above were < 0.05. No significant differences in plasma concentrations of alpha-tocopherol, alpha-carotene, total carotenoids, lycopene, or retinol were observed.

CONCLUSIONS:

These results indicate that cigarette smokers and nonsmokers exposed to cigarette smoke have a significantly lower plasma antioxidant status than do unexposed nonsmokers, independent of differences in dietary antioxidant intakes. Further research is required to explain why plasma gamma-tocopherol concentrations were significantly higher in smokers and passive smokers than in nonsmokers.

Calcium

Przegl Lek. 2006;63(10):1002-6.

[Effect of passive smoking on the level of selected metals in deciduous teeth].

[Article in Polish]

Malara P, Kwapuliński J, Malara B, Drugacz J.

Source

Katedra i Klinika Chirurgii Szczekowo-Twarzowej, Slaskiej Akademii Medycznej, Katowice. malara@netinfo.pl

Abstract

The cigarette smoke is a significant source of heavy metals, which after being absorbed into the human organism, may be accumulated in a calcified tissue. The accumulation process may be also a result of a passive exposure to the cigarette smoke. As the hard tissues of deciduous teeth are relatively stable in chemical composition, they are widely used as the indicators of the exposure to heavy metals in children. This project is aimed to estimate the effect of passive smoke on the levels of selected toxic and essential elements in deciduous teeth. The research material consisted of 386 deciduous teeth. Out of this, 205 teeth were from the children exposed to the cigarette smoke in the apartments. The levels of cadmium, copper, iron, manganese, lead, zinc, calcium and magnesium were determined using atomic absorption spectrometer with flame atomization. It was concluded that the exposure to the cigarette smoke in children is a factor producing the changes in the levels of selected toxic and essential elements in deciduous teeth. This particularly results in the higher levels of cadmium, copper, lead and zinc, which are the permanent constituents of the cigarette smoke, and the lower levels of manganese, calcium and magnesium. Moreover, the disturbed gradient of lead levels dependent on the tooth type is observed in the children exposed to the cigarette smoke in the apartments.

Magnesium

Magnes Res. 2004 Sep;17(3):176-81.

Magnesium influence on nicotine pharmacodependence and smoking.

Nechifor M, Chelarescu D, Mândreci I, Cartas N.

Source

Department of Pharmacology, University of Medicine and Pharmacy Gr. T. Popa Iasi, Universitatii 16, Iasi 700115, Romania. nechifor@umfiasi.ro

Abstract

We followed the magnesium effect (Magne B(6)R, Sanofi-Synthelabo) with internal administration in 53 adult neurotic smoking patients (more than 10 cigarettes/day) of both genders admitted into psychiatric hospital. The nicotine dependence was assessed by the Fagerstrom test, initially and after 28 days of magnesium intake. Plasmatic magnesium level was determined before any therapy and at 28 days. All patients received benzodiazepines during the trial. Our data show that patients that received magnesium therapy showed a significant decrease in the number of cigarettes smoked and Fagerstrom test after 4 weeks [Fagerstrom score 7.93 +/- 0.17 before magnesium therapy versus 6.78 +/- 0.18 ($P < 0.05$) after 28 days of magnesium therapy]. In the group of smokers who did not receive magnesium, the Fagerstrom score did not change significantly [Fagerstrom score 7.48 +/- 0.22 initial versus 7.24 +/- 0.19 after 28 days]. Magnesium supplementation raised plasmatic levels (17.2 +/- 1.2 mg/L before versus 26.1 +/- 1.6 mg/L after 28 days of magnesium intake, $P < 0.01$). The results suggest that this cation might be a useful adjuvant in treatment of nicotine pharmacodependence.

Przegl Lek. 2006;63(10):1002-6.

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[Article in Polish]

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Niger J Physiol Sci. 2008 Jun-Dec;23(1-2):41-9.

High cadmium / zinc ratio in cigarette smokers: potential implications as a biomarker of risk of prostate cancer.

Anetor JI, Ajose F, Anetor GO, Iyanda AA, Babalola OO, Adeniyi FA.

Source

Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan, Nigeria. anetorji@yahoo.com

Abstract

Tobacco smoke may be one of the most common sources of cadmium (Cd) in the general population, particularly in the rising population of smokers in developing countries. Although a relationship between both cigarette smoking and environmental Cd contamination with prostate cancer exist, the mechanisms are unclear. Most prospective cohort studies found a positive association between current smoking and a fatal cancer of the prostate. We investigated the interaction between zinc and cadmium and the potential risk of prostate cancer in smokers. Serum cadmium level was significantly ($P < 0.001$) higher in smokers compared with non-smokers, the level in smokers was three-fold that in non-smokers. In contrast zinc was significantly ($P < 0.001$) reduced in smokers compared with non-smokers. Unlike Zn, Cu was significantly ($P < 0.05$) higher in smokers than in non-smokers. Iron (Fe) though higher in smokers was not significantly different. Zinc: cadmium ratio was very significantly ($P < 0.001$) reduced, implying high cadmium: zinc ratio. This ratio was 4.5-fold the level in non-smokers. Total protein, albumin and total globulin levels were all significantly ($P < 0.001$) reduced in smokers compared with non-smokers respectively. Potassium ($K+$) was significantly ($P < 0.05$) higher in smokers than in non-smokers. Magnesium (Mg) was significantly ($p < 0.01$) reduced in smokers compared to non-smokers. Altered Zn status culminating in high Cd:Zn ratio appears the central factor in

smokers; leading to oxidative stress, DNA damage, mutation, impaired DNA repair, P53 expression, angiogenic effect of Cu and impaired vitamin A metabolism. These converge in the risk of the carcinogenic process, suggesting high Cd: Zn ratio as the critical determinant of the risk of prostate cancer in smokers and possibly a biomarker of susceptibility to this environmental disease.

Biol Trace Elem Res. 2010 Aug;136(2):140-8. Epub 2009 Sep 30.

Effects of vitamins C and E combination on element levels in blood of smoker and nonsmoker radiology X-ray technicians.

Kayan M, Naziroğlu M, Barak C.

Source

Department of Radiology, Medical Faculty, Suleyman Demirel University, Isparta, Turkey.

Abstract

X-ray radiation is detrimental to human cells and may lead to development of life-threatening diseases. Cigarette paper and cigarette smoke contain toxic elements, whereas vitamins C and E (VCE) may have regulator effects on the elements. We investigated effects of VCE administration on X-ray-induced element changes in blood of smoker and nonsmoker X-ray technicians. Twenty technicians and 30 healthy age-matched control subjects were used in the study. Ten of the X-ray technicians and 15 of the control were smokers. Blood serum samples were taken from the control. Oral vitamins C (500 mg) and E (150 mg) were supplemented daily to the smoker and nonsmoker X-ray technicians for 5 weeks. Serum samples were taken from the X-ray technicians before and after 5 weeks. Copper, zinc, selenium, aluminum, iron, magnesium, and calcium levels were investigated in control and X-ray technicians, both smokers and nonsmokers. Copper, zinc, and selenium levels were lower in the total X-ray group and smoker X-ray group than in control and nonsmoker X-ray group, although iron, magnesium, and calcium levels were higher in X-ray group than in control. The copper, zinc, selenium, and aluminum levels were higher in the VCE treatment group than those in X-ray group, although magnesium and calcium levels were decreased by the treatment. The serum zinc, copper, selenium, and magnesium levels were lower in smoker control group when compared to nonsmoker

control group. The serum zinc levels were lower in smoker X-ray group than nonsmoker X-ray group, although iron level was higher in smoker X-ray group than in nonsmoker X-ray group. VCE prevents the smoke and X-ray-induced selenium, zinc, magnesium, and copper decrease to strengthen the antioxidant trace element levels in the serum of the technicians.

Manganese

Przegl Lek. 2006;63(10):1002-6.

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[Article in Polish]

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Katedra i Klinika Chirurgii Szczekowo-Twarzowej, Slaskiej Akademii Medycznej, Katowice. malara@netinfo.pl

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The cigarette smoke is a significant source of heavy metals, which after being absorbed into the human organism, may be accumulated in a calcified tissue. The accumulation process may be also a result of a passive exposure to the cigarette smoke. As the hard tissues of deciduous teeth are relatively stable in chemical composition, they are widely used as the indicators of the exposure to heavy metals in children. This project is aimed to estimate the effect of passive smoke on the levels of selected toxic and essential elements in deciduous teeth. The research material consisted of 386 deciduous teeth. Out of this, 205 teeth were from the children exposed to the cigarette smoke in the apartments. The levels of cadmium, copper, iron, manganese, lead, zinc, calcium and magnesium were determined using atomic absorption spectrometer with flame atomization. It was concluded that the exposure to the cigarette smoke in children is a factor producing the changes in the levels of selected toxic and essential elements in deciduous teeth. This particularly results in the higher levels of cadmium, copper, lead and zinc, which are the permanent constituents of the cigarette smoke, and the lower levels of manganese, calcium and magnesium. Moreover, the disturbed gradient of lead levels dependent on the tooth type is observed in the children exposed to the cigarette smoke in the apartments.

Selenium

Clin Chim Acta. 2007 Feb;377(1-2):14-38. Epub 2006 Sep 1.

Monitoring micronutrients in cigarette smokers.

Northrop-Clewes CA, Thurnham DI.

Source

Division of Nutrition and Physical Activity, Centers for Disease Control and Prevention (CDC), Atlanta, GA 30341, USA. cclewes@cdc.gov

Abstract

Smoking is associated with oxidative stress and increased risks of many chronic diseases that both shorten life and impair its quality. Low concentrations of several micronutrients, especially the antioxidants vitamin C and beta-carotene, are also associated with smoking, and there has been much interest in determining whether deficiencies in micronutrients are involved etiologically in smoking-related diseases. The objective of this review was to bring together reports on dietary intakes, biochemical indicators of micronutrient status, and results of some intervention studies on micronutrients where authors had compared outcomes in smokers and non-smokers. The micronutrients discussed are vitamins A, E, and C; the carotenoids; some of the B-vitamin group; and the minerals selenium, zinc, copper, and iron. The data were then examined to determine whether effects on the biochemical markers of micronutrient status were due to differences in dietary intakes between smokers and non-smokers or to the consequences of inflammatory changes caused by the oxidative stress of smoking. It was concluded that although smoking is associated with reduced dietary intake of vitamin C and carotenoid-containing foods, inflammatory changes increase turnover of these micronutrients so that blood concentrations are still lower in smokers than non-smokers even when there is control for dietary differences. In the case of vitamin E, there is some evidence for

increased turnover of this nutrient in smokers, but this has little to no influence on blood concentrations, and there are no differences in dietary intake of vitamin E between smokers and non-smokers. Serum concentrations of vitamin A, folate, and vitamin B12 and B6 markers do not appear to be influenced by smoking, although there is some influence of dietary intake on concentrations of these nutrients in the body. In the case of the minerals examined, the main effects on biochemical markers of mineral status were attributed to inflammation and were therefore greater in heavy or long-term smokers. Serum concentrations of selenium and erythrocyte GPx activity were lower in smokers. Erythrocyte CuZn-SOD activity and serum ceruloplasmin concentrations were elevated, while serum zinc concentrations were depressed only in heavy smokers. Lastly, smoking appears to affect iron homeostasis mainly by changing hemoglobin concentrations, which were in general increased. Serum iron, TfR, and ferritin were mostly unaffected by smoking, except in pregnancy where there is evidence of increased erythropoiesis causing lower saturation of plasma transferrin and some evidence of lowering of iron stores.

Biol Trace Elem Res. 1989-1990 Winter;23:55-63.

Cadmium-induced alterations in ocular trace elements. Influence of dietary selenium and copper.

Jamall IS, Roque H.

Source

Department of Health Services, Toxic Substances Control Division, Technical Services, Sacramento, CA 94234-7320.

Abstract

The present report demonstrates, for the first time, that feeding rats 50 ppm cadmium for just 7 wk results in detectable levels of cadmium in the eye of rats. Furthermore, these ocular cadmium concentrations affect significant alterations in the levels of the essential trace elements selenium, calcium, iron, and copper in the eye. Rats were fed a low-selenium (less than 0.02 ppm selenium), high-copper basal diet (50 ppm copper) supplemented with 0, 0.1, and 0.5 ppm selenium. The animals were either untreated or treated with 50 ppm cadmium admixed with their feed. Cadmium treatment resulted in significant reductions (up to 50%) in ocular selenium. Furthermore, rats fed the basal diet and given 100 ppm cadmium via their feed for 6 wk exhibited a 69% reduction in the activity of the selenoenzyme, glutathione peroxidase, in the eye. Cadmium treatment also resulted in reductions of up to 50% in ocular calcium, irrespective of dietary selenium supplementation. Iron levels were increased by 30% in rats fed the low-selenium diet and decreased by as much as 40% in rats fed the selenium-supplemented diets, compared to animals fed identical levels of selenium without cadmium. Ocular copper levels were significantly increased only in rats fed the low-selenium diet and treated with cadmium. Ocular zinc levels were not significantly affected by dietary cadmium or selenium.

Biol Trace Elem Res. 2010 Aug;136(2):140-8. Epub 2009 Sep 30.

Effects of vitamins C and E combination on element levels in blood of smoker and nonsmoker radiology X-ray technicians.

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Department of Radiology, Medical Faculty, Suleyman Demirel University, Isparta, Turkey.

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control group. The serum zinc levels were lower in smoker X-ray group than nonsmoker X-ray group, although iron level was higher in smoker X-ray group than in nonsmoker X-ray group. VCE prevents the smoke and X-ray-induced selenium, zinc, magnesium, and copper decrease to strengthen the antioxidant trace element levels in the serum of the technicians.

Life Sci. 2006 Feb 16;78(12):1378-84. Epub 2005 Oct 13.

Effect of bacoside A on brain antioxidant status in cigarette smoke exposed rats.

Anbarasi K, Vani G, Balakrishna K, Devi CS.

Source

Department of Biochemistry, University of Madras, Guindy Campus, Chennai-600 025, India. anbarasii@yahoo.co.in

Abstract

Free radicals mediated oxidative stress has been implicated in the pathogenesis of smoking-related diseases and antioxidant nutrients are reported to prevent the oxidative damage induced by smoking. Therefore, the present study was conducted to evaluate the antioxidant role of bacoside A (triterpenoid saponin isolated from Bacopa monniera) against chronic cigarette smoking induced oxidative damage in rat brain. Adult male albino rats were exposed to cigarette smoke for a period of 12 weeks and simultaneously administered with bacoside A (10 mg/kg b.w./day, p.o.). Antioxidant status of the brain was assessed from the levels of reduced glutathione, vitamin C, vitamin E, and vitamin A and the activities of superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase. The levels of copper, iron, zinc and selenium in brain and serum ceruloplasmin activity were also measured. Oxidative stress was evident from the diminished levels of both enzymatic and non-enzymatic antioxidants. Alterations in the levels of trace elements with accumulation of copper and iron, and depletion of zinc and selenium were also observed. Bacoside A administration improved the antioxidant status and maintained the levels of trace elements. These results suggest that chronic cigarette smoke exposure enhances oxidative stress, thereby disturbing the tissue defense system and bacoside A protects the brain from the oxidative damage through its antioxidant potential.

Zinc

Life Sci. 2006 Feb 16;78(12):1378-84. Epub 2005 Oct 13.

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Sci Total Environ. 1993 Jan 15;128(1):21-35.

Cadmium and lead in the smoke of a filter cigarette.

Kalcher K, Kern W, Pietsch R.

Source

Institut für Analytische Chemie, Karl-Franzens Universität Graz, Austria.

Abstract

Cadmium and lead were determined in the parts of a filter cigarette after fractional smoking. The partitioning of these elements into the main smoke stream, consisting of particulates and gases, also into the side stream, the ash and the butt was determined. Approximately 70% of the lead mobilized by the smoking process was found in the ash; about 50% of the cadmium was transferred into the side stream. The overall trend shows an increase in the amount of the metals in the main stream as the number of puffs is increased. A model for the behavior of the main stream components within the cigarette was developed and showed a high analogy with the Lambert-Beer law describing the absorption of light.

Biol Trace Elem Res. 2005 Jul;106(1):1-28.

Maternal and neonatal scalp hair concentrations of zinc, copper, cadmium, and lead: relationship to some lifestyle factors.

Razagui IB, Ghribi I.

Source

Academic Department of Obstetrics and Gynaecology, Hull Maternity Hospital, Hedon Road, Hull, HU9 5LX, United Kingdom.

Abstract

Postpartum scalp hair samples from 82 term-pregnancy mother/ neonate pairs were analyzed for their concentrations of zinc (Zn), copper (Cu), cadmium (Cd), and lead (Pb), using inductively coupled plasma-mass spectrometry. Maternal and neonatal Zn concentrations had geometric means (and 99% confidence intervals) of 122.5 microg/g (117.9--131.5 microg/g) and 146.9 microg (141.5--156.7 microg/g) respectively. Corresponding Cu values were 18.4 microg/g (17.6--23.8 microg/g) and 6.7 microg/g (6.3--7.6 microg/g). Those of Cd were 0.49 microg/g (0.47--0.69 microg/g) in the mothers and 0.57 microg/g (0.55--0.86 microg/g) in the neonates. For Pb, they were 7.95 microg/g (7.60--9.32 microg/g) and 4.56 microg/g (4.39--5.56 microg/g). Cigarette smoking, despite its relatively low prevalence (19.5%), was associated with lower Zn and higher Cd and Pb concentrations and in lower Zn/Cd and Zn/Pb molar concentration ratios. Smoking also altered interelemental relationships, particularly those of Zn with Cd and Pb and those between Cd and Pb. Smoking frequency appeared to show negative dose-response effects on maternal and neonatal Zn concentrations, Zn/Pb molar concentration ratios, and birth weight. Mothers with a history of oral contraceptive (OC) usage had significantly higher Cu concentrations and lower Zn/Cu molar concentration ratios than non users, with the highest Cu concentrations and lowest Zn/Cu values being associated with third-

generation OCs. No similar effects were elicited in the respective neonatal Cu concentrations. Neither alcohol consumption nor prenatal supplementation with iron and/or folic acid had discernible effects on the maternal or neonatal elemental concentrations. The data from this study suggest that in a given population of term-pregnancy mothers and neonates, significant interindividual variations in hair trace element concentrations can occur, irrespective of commonality of general environment, and that lifestyle factors, including cigarette smoking and OC usage history, can be significant contributory factors to such variations. The data are discussed in relation to the effects of smoking-associated exposure to Cd and Pb exposure on Zn availability for placental transfer, as well as on the quantitative maternal Zn supply levels to the fetus resulting from the known tendency of smokers to have lower dietary intakes of Zn.

Niger J Physiol Sci. 2008 Jun-Dec;23(1-2):41-9.

High cadmium / zinc ratio in cigarette smokers: potential implications as a biomarker of risk of prostate cancer.

Anetor JI, Ajose F, Anetor GO, Iyanda AA, Babalola OO, Adeniyi FA.

Source

Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan, Nigeria. anetorji@yahoo.com

Abstract

Tobacco smoke may be one of the most common sources of cadmium (Cd) in the general population, particularly in the rising population of smokers in developing countries. Although a relationship between both cigarette smoking and environmental Cd contamination with prostate cancer exist, the mechanisms are unclear. Most prospective cohort studies found a positive association between current smoking and a fatal cancer of the prostate. We investigated the interaction between zinc and cadmium and the potential risk of prostate cancer in smokers. Serum cadmium level was significantly ($P < 0.001$) higher in smokers compared with non-smokers, the level in smokers was three-fold that in non-smokers. In contrast zinc was significantly ($P < 0.001$) reduced in smokers compared with non-smokers. Unlike Zn, Cu was significantly ($P < 0.05$) higher in smokers than in non-smokers. Iron (Fe) though higher in smokers was not significantly different. Zinc: cadmium ratio was very significantly ($P < 0.001$) reduced, implying high cadmium: zinc ratio. This ratio was 4.5-fold the level in non-smokers. Total protein, albumin and total globulin levels were all significantly ($P < 0.001$) reduced in smokers compared with non-smokers respectively. Potassium ($K+$) was significantly ($P < 0.05$) higher in smokers than in non-smokers. Magnesium (Mg) was significantly ($p < 0.01$) reduced in smokers compared to non-smokers. Altered Zn status culminating in high Cd:Zn ratio appears the central factor in smokers; leading to oxidative stress, DNA damage, mutation, impaired DNA repair, P53 expression, angiogenic effect

of Cu and impaired vitamin A metabolism. These converge in the risk of the carcinogenic process, suggesting high Cd: Zn ratio as the critical determinant of the risk of prostate cancer in smokers and possibly a biomarker of susceptibility to this environmental disease.

Biol Trace Elem Res. 2010 Aug;136(2):140-8. Epub 2009 Sep 30.

Effects of vitamins C and E combination on element levels in blood of smoker and nonsmoker radiology X-ray technicians.

Kayan M, Naziroğlu M, Barak C.

Source

Department of Radiology, Medical Faculty, Suleyman Demirel University, Isparta, Turkey.

Abstract

X-ray radiation is detrimental to human cells and may lead to development of life-threatening diseases. Cigarette paper and cigarette smoke contain toxic elements, whereas vitamins C and E (VCE) may have regulator effects on the elements. We investigated effects of VCE administration on X-ray-induced element changes in blood of smoker and nonsmoker X-ray technicians. Twenty technicians and 30 healthy age-matched control subjects were used in the study. Ten of the X-ray technicians and 15 of the control were smokers. Blood serum samples were taken from the control. Oral vitamins C (500 mg) and E (150 mg) were supplemented daily to the smoker and nonsmoker X-ray technicians for 5 weeks. Serum samples were taken from the X-ray technicians before and after 5 weeks. Copper, zinc, selenium, aluminum, iron, magnesium, and calcium levels were investigated in control and X-ray technicians, both smokers and nonsmokers. Copper, zinc, and selenium levels were lower in the total X-ray group and smoker X-ray group than in control and nonsmoker X-ray group, although iron, magnesium, and calcium levels were higher in X-ray group than in control. The copper, zinc, selenium, and aluminum levels were higher in the VCE treatment group than those in X-ray group, although magnesium and calcium levels were decreased by the treatment. The serum zinc, copper, selenium, and magnesium levels were lower in smoker control group when compared to nonsmoker control group. The serum zinc levels were lower in smoker X-ray group than nonsmoker X-ray group, although iron

level was higher in smoker X-ray group than in nonsmoker X-ray group. VCE prevents the smoke and X-ray-induced selenium, zinc, magnesium, and copper decrease to strengthen the antioxidant trace element levels in the serum of the technicians.

Ecotoxicol Environ Saf. 1983 Feb;7(1):71-8.

Cadmium concentrations in tobacco and tobacco smoke.

Scherer G, Barkemeyer H.

Abstract

The amount of cadmium in tobacco depends on the variety and origin of the plant as well as on the analytical method used to determine cadmium. In the literature, cadmium concentrations in tobacco of between 0.5 and 5 ppm are reported. Modern German cigarette tobacco contains about 0.5-1.5 micrograms cadmium/cigarette. Of importance for the smoker is the amount of the metal in the mainstream smoke. The cadmium level in the mainstream smoke of modern cigarettes is reduced by means of filters and other construction features. The average Cd value of German filter cigarettes is less than 0.1 microgram/cigarette in mainstream smoke. An average daily intake of about 1 microgram cadmium by smoking 20 cigarettes can be calculated on the basis of an experimentally proved pulmonary retention rate of 50%. Pulmonary resorption rates relevant to uptake rates of cadmium by smoking are discussed. It can be assumed that cadmium uptake by smoking modern cigarettes has been reduced because of modifications in tobacco processing and cigarette construction in the last few decades.

Glutathione and Substances that Make Glutathione (GSH) Such as N-Acetylcysteine (NAC)

J Cell Physiol. 2008 Jan;214(1):27-37.

Impact of tobacco-smoke on key signaling pathways in the innate immune response in lung macrophages.

Birrell MA, Wong S, Catley MC, Belvisi MG.

Source

Respiratory Pharmacology, Airway Disease Section, Imperial College, National Heart and Lung Institute, London, UK.

Abstract

Many of the healthcare consequences of cigarette smoking could be due to its ability to compromise the immune system, and in respiratory diseases like chronic obstructive pulmonary disease (COPD), a constant low level of infection could be responsible for some of the symptoms/pathology. The aim was to assess the impact of cigarette smoke (CS) on the release of innate effector cytokines in THP-1 cells and human lung macrophages, and to determine the molecular mechanism behind the altered response. Cells were exposed to CS with and without endotoxin stimulus, cytokines, glutathione, mitogen-activated protein kinase (MAPK) phosphorylation, IkappaB kinase-2 (IKK-2) activity, nuclear factor kappa B (NF-kappaB), and activator protein-1 (AP-1) pathway activation was measured. Attempts were made to mimic or block the effect of CS by using nicotine, nitric oxide donors/inhibitors, prostanoid inhibitors, and anti-oxidants. Results showed that CS initially delayed the production of "innate" cytokines (e.g., IL-1beta and IL-6) and reduced glutathione levels. This was associated with a reduction in NF-kappaB pathway activation, which suggested a causative link. CS also increased the phosphorylation of MAPK's and the production of IL-8 but interestingly only in stimulated cells. Exogenous glutathione treatment reversed both these effects of CS, which suggests that this molecule may play a central role. In conclusion, this data provides a novel mechanistic explanation for why smokers have increased prevalence/severity of respiratory infections. In addition, the suppression of the innate response is accompanied by an increase in the neutrophil chemoattractant, IL-8, which may suggest a link to the pathogenesis of smoking-related inflammatory disease.

Eur J Respir Dis Suppl. 1985;139:113-6.

Pharmacoprevention of tobacco smoke effects on macrophage cells.

Green GM.

Abstract

Cigarette smoke components produce a variety of morphologic, physiologic, biochemical, and enzymatic changes in pulmonary alveolar macrophages, cells which are important in pulmonary antibacterial defenses, cellular regulatory activity, and tissue pathogenesis of inflammation, proteolysis and fibrogenesis. A common denominator of enzymes found to be inhibited by cigarette smoke components is a sulfhydryl moiety which is critical to the functioning of the enzyme and highly susceptible to oxidant activity of substances with the properties of agents in cigarette smoke. The inhibitory effect of cigarette smoke components on glyceraldehyde 3-phosphate dehydrogenase, calcium and magnesium ATPase, and endoperoxide E-isomerase is quantitatively prevented by the addition of sulfhydryl agents such as glutathione and cysteine. Furthermore, critical functions of whole cell activity such as phagocytosis, energy metabolism, and prostaglandin synthesis and release, functions which are dependent on sulfhydryl enzymes and are inhibited by cigarette smoke components, are protected when glutathione or cysteine are provided in advance of the exposure. These sulfhydryl agents also protect adhesion and cellular morphology from derangement by cigarette smoke components. These in vitro studies suggest a role for sulfhydryl-containing agents in the prevention of environmentally-induced injuries to alveolar macrophages.

Chem Biol Interact. 2007 Dec 15;170(3):209-20. Epub 2007 Aug 12.

Response of lead-induced oxidative stress and alterations in biogenic amines in different rat brain regions to combined administration of DMSA and MiADMSA.

Flora SJ, Saxena G, Gautam P, Kaur P, Gill KD.

Source

Division of Pharmacology and Toxicology, Defence Research and Development Establishment, Jhansi Road, Gwalior 474002, India. sjsflora@hotmail.com

Abstract

The present study was planned to investigate if combined administration of meso-2,3-dimercaptosuccinic acid (DMSA) and monoisoamyl DMSA (MiADMSA) could achieve better recovery in the altered biochemical parameters suggestive of brain oxidative stress and depletion of lead from blood and brain following acute lead exposure. Male Wistar rats were exposed to lead nitrate (50 mg/kg, i.p., once daily for 5 days) followed by treatment with the above chelating agents using two different doses of 25 or 50 mg/kg (orally) either alone and in combination once daily for five consecutive days. Lead exposure resulted in the significant inhibition of delta-aminolevulinic acid dehydratase activity and depletion of glutathione (GSH) in blood. These changes were accompanied by significant reduction in blood hemoglobin, RBC levels and superoxide dismutase and catalase activities. Significant increase in blood reactive oxygen species (ROS) and thiobarbituric acid reactive substances (TBARS) levels were noted. We observed marked increase in brain ROS level while GSH/oxidized glutathione ratio showed significant decrease accompanied by a significant increase in blood and brain lead concentration. The levels of norepinephrine, dopamine and serotonin in different brain regions were also altered on lead exposure. Co-administration of DMSA and MiADMSA particularly at the lower dose was most effective in the recovery of lead-induced changes in the hematological variables and oxidative stress and resulted in more pronounced depletion of lead from blood and brain compared to monotherapy with these chelators. On the other hand, combined administration of MiADMSA (50 mg/kg) in combination with DMSA

(25 mg/kg each) had additional beneficial effect over the individual effect of chelating agent in the recovery of altered levels of brain biogenic amines. The study suggests that administration of MiADMSA is generally a better lead chelator than DMSA while combined administration of DMSA and MiADMSA might be a better treatment option compared to monotherapy at least in the removal of lead from the target tissues.

Biol Trace Elem Res. 2007 Winter;120(1-3):82-91.

High levels of cadmium and lead in seminal fluid and blood of smoking men are associated with high oxidative stress and damage in infertile subjects.

Kiziler AR, Aydemir B, Onaran I, Alici B, Ozkara H, Gulyasar T, Akyolcu MC.

Source

Department of Biophysics, Cerrahpaşa Faculty of Medicine, Istanbul University, 34098 Istanbul, Turkey. ark@istanbul.edu.tr

Abstract

We measured the levels of malondialdehyde (MDA), protein carbonyls, glutathione S-transferase (GST) and reducte glutathione (GSH) in seminal plasma and spermatozoa from 95 subjects including 50 infertile patients to evaluate the association between oxidative stress and damage and the components of the anti-oxidant defenses in seminal plasma and spermatozoa of infertile subjects and concentrations of cadmium (Cd) and lead (Pb) in the blood and seminal plasma because of tobacco smoke exposure. The reactive oxygen species (ROS) in spermatozoa were also evaluated by luminol (5-amino-2,3-dihydro-1,4-phthalazinedione)-enhanced chemiluminescence assay. The sperm count, motility, and morphology in the smokers infertile group were found to be lower than those in the fertile male group and nonsmokers infertile group ($p < 0.001$). Concentrations of Cd, Pb, MDA, protein carbonyls, and ROS levels in the smokers infertile group were significantly higher than those in the fertile male and nonsmokers infertile male groups ($p < 0.001$). However, GSH levels and GST activities were decreased in the smokers infertile male group than those in the fertile male and nonsmokers infertile male groups ($p < 0.001$). The results indicate that smoking could affect semen quality and oxidative lipid and protein damage in human spermatozoa. From Pearson correlation analysis, positive correlations were demonstrated between the seminal plasma Cd and seminal plasma protein carbonyls and between seminal plasma Pb and spermatozoa ROS levels in smokers of the subfertile group, while there was a significant positive correlation between blood Cd and ROS levels in smokers of the fertile group. There

was also a significant negative correlation of the Cd level of the blood and GSH levels of the sperm and seminal plasma. These findings suggest that cigarette smoking enhances the levels of Cd and Pb in seminal plasma and blood and the extent of oxidative damage associated with a decrease in components of the anti-oxidant defenses in the sperm of infertile males.

Przegl Lek. 2004;61(10):1104-8.

[Tobacco smoke effects the activity of superoxide dismutase, glutathione peroxidase and total antioxidant status in pregnant and non-pregnant animals].

[Article in Polish]

Florek E, Ignatowicz E, Piekoszewski W, Wachowiak A, Wrzosek J, Moczko J, Czekaj P, Slusarska E.

Source

Laboratorium Badań Srodowiskowych Katedry i Zakładu Toksykologii Akademii Medycznej w Poznaniu. eflorek@amp.edu.pl

Abstract

Total antioxidant status was measured as the reduction of the ABTS radical cation as well as the activities of SOD and GPx in female rats exposed and non-exposed to the cigarette smoke, pregnant and non-pregnant. The assessment was done in lungs, plasma, kidneys, liver and placenta of Wistar rats exposed to the cigarette smoke (1500 mg CO/m3 air) for 21 days. Total antioxidant status was significantly elevated in lungs and plasma of smoke-exposed animals, pregnant and non-pregnant, when compared to the matched controls. In other examined tissues antioxidant capacity was diminished in all tested groups of animals. Activities of SOD and GPx were markedly decreased in tissues of all examined animals. Exposition to the cigarette smoke, despite some changes due to the adaptation to stress, diminishes the antioxidant capacities of the body and in the pregnant animals it may effect the pregnancy outcome.

Indian J Public Health. 1998 Jan-Mar;42(1):20-3.

Influence of cigarette smoking on Vitamin C, glutathione and lipid peroxidation status.

Banerjee KK, Marimuthu P, Sarkar A, Chaudhuri RN.

Source

Department of Occupational Health, All India Institute of Hygiene & Public Health, Calcutta.

Abstract

There has been a growing interest during recent years in the role of free radicals and lipid-peroxidation at tissue-level for the causation of cancer and other age-related diseases like atherosclerosis, rheumatoid arthritis, cataract etc. Free radicals and increased lipid peroxidation play a significant role for causation of human diseases by oxidative damage and functional degeneration of the tissues. Vitamin C, a well-known dietary antioxidant, and other enzymatic antioxidants like glutathione can protect the lipids of lipoproteins and other biomembranes against peroxidative damage by intercepting oxidants before they can attack the tissues. But cigarette smoking was found to affect the antioxidant protective action of Vitamin C, glutathione etc. A group of adult male smokers in this study were found to have lowered Vitamin 'C' & glutathione levels, but increased lipid-peroxide levels in their blood. Thus the increased pathogenicity of the smoking may also be due to indirect biochemical effect of enhanced oxidative stress by increased lipid-peroxidation and lowered Vitamin C & other antioxidants at tissue-level.

Toxicol Appl Pharmacol. 1988 Nov;96(2):324-35.

Glutathione metabolism and utilization of external thiols by cigarette smoke-challenged, isolated rat and rabbit lungs.

Joshi UM, Kodavanti PR, Mehendale HM.

Source

Department of Pharmacology and Toxicology, University of Mississippi Medical Center, Jackson 39216-4505.

Abstract

The purpose of the present investigation was to understand the acute effects of cigarette smoke on glutathione (GSH) metabolism and on utilization of external thiols by cigarette smoke-exposed, perfused rat and rabbit lungs. Most of the experiments were carried out using freshly drawn cigarette smoke. However, cigarette smoke condensate was used in some perfusions for the comparison of the effects between the types of exposures on utilization of external thiols. Cigarette smoke decreased GSH levels significantly (50%) without any increase in glutathione disulfide (GSSG) in both rabbit and rat lungs. In smoke-exposed rabbit lungs, protein thiol groups (protein-SH) decreased significantly (17%) without a significant change in protein-GSH mixed disulfides. However, in the rat lungs, cigarette smoke did not decrease protein-SH and protein-GSH mixed disulfides, indicating species variation in the effect of cigarette smoke. Cigarette smoke inhibited selenium-dependent and -independent GSH peroxidase activities in the rat lung (33%), but not in the rabbit lung. GSH S-transferase and GSSG reductase activities were not altered in cigarette smoke-challenged rabbit and rat lungs. gamma-Glutamylcysteine synthetase and glucose-6-phosphate dehydrogenase activities were significantly lower in smoke-exposed rat lungs as against control lungs, indicating that rat lung enzymes were more susceptible to the effects of cigarette smoke when compared to those of rabbits. N-

Acetylcysteine, but not GSH, added to the perfusate significantly protected rabbit lung from smoke-induced GSH depletion. Smoke condensate added to the perfusate also caused GSH depletion in rabbit lung, and GSH or N-acetylcysteine added to the perfusion medium protected the lung indicating that GSH in the media directly interacts with condensate in the media before coming in contact with cellular GSH. These results indicate that acute smoke inhalation decreases pulmonary GSH and that the decreased GSH was not related to disulfide formation. Inhibited GSH synthesis in rat lung could account for the loss of GSH in part after exposure to cigarette smoke. The alternative pathway of GSH utilization could be conjugation with electrophilic smoke components. Thiols, like N-acetylcysteine, were protective against cigarette smoke-induced damage to the rabbit lung. The mechanism could be either by the increased GSH synthesis or by the direct delivery of sulfhydryls from N-acetylcysteine.

Eur J Respir Dis Suppl. 1985;139:123-9.

N-acetylcysteine protection against the toxicity of cigarette smoke and cigarette smoke condensates in various tissues and cells in vitro.

Moldéus P, Berggren M, Grafström R.

Abstract

The protective effect of N-acetylcysteine on the toxicity of tobacco smoke condensates was investigated using different cellular in vitro systems. Cigarette smoke condensates, and the non-volatile and semi-volatile fractions separated from the condensate were used. All three smoke condensate fractions were toxic to isolated rat hepatocytes and lung cells and caused a loss of cell membrane integrity. A rapid depletion of cellular reduced glutathione (GSH) preceded the toxicity. The loss of GSH was due to conjugation of reactive compounds in the condensate fractions and not to oxidation since no increase in oxidized glutathione (GSSG) could be observed. N-acetylcysteine at a concentration of 1 mM protected both from the GSH loss and cell toxicity caused by the condensate fractions. The effect of the tobacco smoke condensate on the colony forming efficiency (CFE) of cultured human bronchial cells was also investigated. Already at concentrations of 50 micrograms/ml the survival decreased to 40% of control and at 100 micrograms/ml almost no cells formed colonies. N-acetylcysteine substantially increased survival when added at 10 mM concentration.

Hum Exp Toxicol. 2002 Jan;21(1):17-23.

Effects of cigarette smoke with different tar contents on hepatic and pulmonary xenobiotic metabolizing enzymes in rats.

Eke BC, Işcan M.

Source

Department of Toxicology, Faculty of Pharmacy, Ankara University, Tandoğan, Turkey. eke@pharmacy.ankara.edu.tr

Abstract

The effects of smoke from cigarettes with two different tar contents (32 mg/cigarette, high tar, and 15 mg/cigarette, low tar) on hepatic and pulmonary monooxygenase (MO) activities (aniline 4-hydroxylase [AH]; aminopyrine N-demethylase [AMND]; 7-ethoxyresorufin O-deethylase [EROD]; p-nitroanisole O-demethylase [p-NAOD]), lipid peroxidation (LP) and reduced glutathione (GSH) levels and glutathione S-transferase (GST) activities toward several substrates (1-chloro-2,4-dinitrobenzene [CDNBI; 1,2-dichloro-4-nitrobenzene [DCNB]; ethacrynic acid [EAA]; 1,2-epoxy-3-(p-nitrophenoxy)-propane [ENPP]) were determined in adult male rats. Adult male rats were exposed to smoke of high- or low-tar cigarettes five times a day, with 1-hour intervals, for 3 days in a chamber where smoke and fresh air lead alternatively and were killed 16 hours after the last treatment. Smoke of both high- and low-tar cigarettes (SHTCC and SLTCC) significantly increased hepatic and pulmonary EROD and p-NAOD activities compared to controls. However, the increase noted by SHTCC on pulmonary EROD activity was higher than that of

SLTCC. Hepatic AMND and pulmonary AH activities were significantly increased only by SHTCC. LP level was significantly decreased and increased by SHTCC in liver and lung, respectively, whereas it remained unaltered by SLTCC. Only SHTCC significantly increased GSH level in liver. In the lungs, both SHTCC and SLTCC significantly increased GSH level to the same extent. Hepatic GST activity toward EAA was significantly increased by SHTCC but was significantly decreased by SLTCC. ENPP GST activity was significantly decreased by SHTCC and SLTCC in the livers. In the lungs, all the GST activities examined were significantly depressed by SHTCC whereas only GST activity toward DCNB was reduced significantly by SLTCC. These results reveal that the hepatic and pulmonary MOs and GSTs are differentially influenced by SHTCC and SLTCC in rats.

Mutagenesis. 1992 Jul;7(4):295-301.

Metabolic alterations produced by cigarette smoke in rat lung and liver, and their modulation by oral N-acetylcysteine.

Bagnasco M, Bennicelli C, Camoirano A, Balansky RM, De Flora S.

Source

Institute of Hygiene and Preventive Medicine, University of Genoa, Italy.

Abstract

Male Sprague-Dawley rats were exposed whole-body to the mainstream smoke produced by a commercial filter cigarette for 8 consecutive days, accounting for a cumulative exposure to the smoke of 75 cigarettes. Liver and lung S12 fractions were used in the Salmonella mutagenicity test in order to assess either the decrease of potency of a direct-acting mutagen (sodium dichromate) or the metabolic activation of promutagens, including cigarette smoke itself and its condensate, benzo[a]pyrene and its 7,8-diol, the aromatic amine 2-aminofluorene, and the heterocyclic amine 3-amino-1-methyl-5H-pyrido(4,3)indole. Moreover, individual biochemical parameters were measured in the liver and lung of the same rats and, in the case of cytochrome P-450-dependent monooxygenases, also in the heart of untreated or Aroclor-treated rats. The monitored biochemical parameters included aryl hydrocarbon (benzo[a]pyrene) hydroxylase and ethoxyresorufin deethylase in microsomal fractions, epoxide (benzo[a]pyrene-4,5-oxide) hydrolase in both microsomal and cytosolic fractions, glutathione (GSH) and GSH S-transferase in the cytosol.

Exposure to cigarette smoke resulted in a number of significant metabolic changes, as compared to sham-exposed rats. The most pronounced alterations consisted in a 2.6-fold induction of aryl hydrocarbon hydroxylase in the lung and 8-fold induction of ethoxyresorufin deethylase in the liver, and in a marked stimulation of the liver metabolic activation of all promutagens. The last effect was inhibited by the oral administration of the chemopreventive agent N-acetylcysteine. On the whole, there was a poor correlation between the monitored biochemical and mutagenicity endpoints.(ABSTRACT TRUNCATED AT 250 WORDS)

PLoS One. 2009 Dec 9;4(12):e8225.

Cigarette smoking blocks the protective expression of Nrf2/ARE pathway in peripheral mononuclear cells of young heavy smokers favouring inflammation.

Garbin U, Fratta Pasini A, Stranieri C, Cominacini M, Pasini A, Manfro S, Lugoboni F, Mozzini C, Guidi G, Faccini G, Cominacini L.

Source

Department of Biomedical and Surgical Sciences, Section of Internal Medicine, University of Verona, Verona, Italy.

Abstract

Cigarette smoking is an important risk factor for atherosclerosis, a chronic inflammatory disease. However the underlying factors of this effect are unclear. It has been hypothesized that water-soluble components of cigarette smoke can directly promote oxidative stress in vasculature and blood cells. Aim of this study was to study the relationship between oxidative stress and inflammation in a group of young smokers. To do this we evaluated: 1) the oxidation products of phospholipids (oxPAPC) in peripheral blood mononuclear cells (PBMC); 2) their role in causing PBMC reactive oxygen species (ROS) generation and changes in GSH; 3) the expression of the transcription factor NF-E2-related factor 2 (Nrf2) and of related antioxidant genes (ARE); 4) the activation of NF-kB and C-reactive protein (CRP) values. We studied 90 healthy volunteers: 32 non-smokers, 32 moderate smokers (5-10 cigarettes/day) and 26 heavy smokers (25-40 cigarettes/day). OxPAPC and p47phox expression, that reasonably

reflects NADPH oxidase activity, were higher in moderate smokers and heavy smokers than in non-smokers ($p<0.01$), the highest values being in heavy smokers ($p<0.01$). In in vitro studies oxPAPC increased ROS generation via NADPH oxidase activation. GSH in PBMC and plasma was lower in moderate smokers and heavy smokers than in non-smokers ($p<0.01$), the lowest values being in heavy smokers ($p<0.01$). Nrf2 expression in PBMC was higher in moderate smokers than in non-smokers ($p<0.01$), but not in heavy smokers, who had the highest levels of NF-kB and CRP ($p<0.01$). In in vitro studies oxPAPC dose-dependently increased NF-kB activation, whereas at the highest concentrations Nrf2 expression was repressed. The small interference (si) RNA-mediated knockdown of NF-kappaB/p65 increased about three times the expression of Nrf2 stimulated with oxPAPC. Cigarette smoke promotes oxPAPC formation and oxidative stress in PBMC. This may cause the activation of NF-kB that in turn may participate in the negative regulation of Nrf2/ARE pathway favouring inflammation.

Superoxide Dismutase (SOD)

Przegl Lek. 2004;61(10):1104-8.

[Tobacco smoke effects the activity of superoxide dismutase, glutathione peroxidase and total antioxidant status in pregnant and non-pregnant animals].

[Article in Polish]

Florek E, Ignatowicz E, Piekoszewski W, Wachowiak A, Wrzosek J, Moczko J, Czekaj P, Slusarska E.

Source

Laboratorium Badań Srodowiskowych Katedry i Zakładu Toksykologii Akademii Medycznej w Poznaniu. eflorek@amp.edu.pl

Abstract

Total antioxidant status was measured as the reduction of the ABTS radical cation as well as the activities of SOD and GPx in female rats exposed and non-exposed to the cigarette smoke, pregnant and non-pregnant. The assessment was done in lungs, plasma, kidneys, liver and placenta of Wistar rats exposed to the cigarette smoke (1500 mg CO/m3 air) for 21 days. Total antioxidant status was significantly elevated in lungs and plasma of smoke-exposed animals, pregnant and non-pregnant, when compared to the matched controls. In other examined tissues antioxidant capacity was diminished in all tested groups of animals. Activities of SOD and GPx were markedly decreased in tissues of all examined animals. Exposition to the cigarette smoke, despite some changes due to the adaptation to stress, diminishes the antioxidant capacities of the body and in the pregnant animals it may effect the pregnancy outcome.

Melatonin

Toxicol Ind Health. 2005 Mar;21(1-2):21-6.

Active smoking causes oxidative stress and decreases blood melatonin levels.

Ozguner F, Koyu A, Cesur G.

Source

Department of Physiology, Suleyman Demirel University, School of Medicine, 32260 Isparta, Turkey. drmfehmi@yahoo.com

Abstract

Oxidative effects via free radical generation in smokers have been widely investigated. They cause lipid peroxidation, oxidation of proteins and damage to mainly lung and other tissues. In humans, antioxidative capacity of serum is related to antioxidant enzymes superoxide dismutase (SOD), glutathione peroxidase (GSH-Px) and melatonin. The effect of cigarette smoking on plasma levels of melatonin and antioxidant enzymes has not been established together yet. Also, it may not be clear if melatonin levels are affected by smoking and melatonin has a protective effect on cigarette smoking-induced free radical damage. The aim of this study is to investigate the relationship between smoking and antioxidant capacity including melatonin, a powerful endogenous antioxidant, and antioxidant enzymes in teenage girls who are active smokers. Additionally, malondialdehyde (MDA) levels were determined in those who have smoked at least one packet a day for three or more years. MDA levels have been used as a convenient index of the lipid peroxidation-related oxidative damage of tissues. Twenty-one young female active smokers who study at the School of Nursing and 21 nonsmoking students (as controls) at the same school were included in the study. The

activities of two principal antioxidant enzymes SOD, GSH-Px and plasma levels of MDA were significantly increased but melatonin content of the blood was significantly decreased as compared to nonsmokers. In spite of an increase in antioxidant enzyme activities, MDA levels were slightly increased in smokers. This indicates that antioxidant self-defence mechanisms may not sufficiently protect the respiratory system from smoke-mediated oxidative injury. This result may be related to low melatonin levels in teenage female smokers. It seems that melatonin can reduce free radical damage to the respiratory system induced by cigarette smoke. Further experimental investigations with exogenous melatonin treatments will be needed.

Choline

In the form of Phosphatidylcholine

PLoS One. 2009 Dec 9;4(12):e8225.

Cigarette smoking blocks the protective expression of Nrf2/ARE pathway in peripheral mononuclear cells of young heavy smokers favouring inflammation.

Garbin U, Fratta Pasini A, Stranieri C, Cominacini M, Pasini A, Manfro S, Lugoboni F, Mozzini C, Guidi G, Faccini G, Cominacini L.

Source

Department of Biomedical and Surgical Sciences, Section of Internal Medicine, University of Verona, Verona, Italy.

Abstract

Cigarette smoking is an important risk factor for atherosclerosis, a chronic inflammatory disease. However the underlying factors of this effect are unclear. It has been hypothesized that water-soluble components of cigarette smoke can directly promote oxidative stress in vasculature and blood cells. Aim of this study was to study the relationship between oxidative stress and inflammation in a group of young smokers. To do this we evaluated: 1) the oxidation products of phospholipids (oxPAPC) in peripheral blood mononuclear cells (PBMC); 2) their role in causing PBMC reactive oxygen species (ROS) generation and changes in GSH; 3) the expression of the transcription factor NF-E2-related factor 2 (Nrf2) and of related antioxidant genes (ARE); 4) the activation of NF-kB and C-reactive protein (CRP) values. We studied 90 healthy volunteers: 32 non-smokers, 32 moderate smokers (5-10 cigarettes/day) and 26 heavy smokers (25-40 cigarettes/day). OxPAPC and p47phox expression, that reasonably reflects NADPH oxidase activity, were higher in moderate smokers and heavy smokers than in non-smokers

(p<0.01), the highest values being in heavy smokers (p<0.01). In in vitro studies oxPAPC increased ROS generation via NADPH oxidase activation. GSH in PBMC and plasma was lower in moderate smokers and heavy smokers than in non-smokers (p<0.01), the lowest values being in heavy smokers (p<0.01). Nrf2 expression in PBMC was higher in moderate smokers than in non-smokers (p<0.01), but not in heavy smokers, who had the highest levels of NF-kB and CRP (p<0.01). In in vitro studies oxPAPC dose-dependently increased NF-kB activation, whereas at the highest concentrations Nrf2 expression was repressed. The small interference (si) RNA-mediated knockdown of NF-kappaB/p65 increased about three times the expression of Nrf2 stimulated with oxPAPC. Cigarette smoke promotes oxPAPC formation and oxidative stress in PBMC. This may cause the activation of NF-kB that in turn may participate in the negative regulation of Nrf2/ARE pathway favouring inflammation.

Pediatr Pulmonol. 2005 Feb;39(2):97-102.

Effects of maternal nicotine exposure on lung surfactant system in rats.

Chen CM, Wang LF, Yeh TF.

Source

Department of Pediatrics, Taipei Medical University Hospital, Taipei, Taiwan. cmchen@tmu.edu.tw

Abstract

Maternal smoking during pregnancy may impair pulmonary function in infants and children, but the exact mechanisms underlying these changes remain to be determined. Timed pregnant Sprague-Dawley rats were injected subcutaneously with nicotine at a dose of 2 mg/kg/day from days 3-21 of gestation. A control group was injected with saline. Nicotine-treated dams had lower body weights than control dams from gestational days 5-21, and the values reached statistical significance on gestational days 17, 20, and 21. Total lung saturated phosphatidylcholine contents tended to be lower in nicotine-exposed rats than in control rats from postnatal day 21, and the values reached statistical significance on postnatal days 35 and 42. Maternal nicotine exposure significantly increased surfactant protein (SP)-A, SP-B, SP-C, and SP-D mRNA expression on postnatal day 7, and decreased SP-A, SP-B, SP-C, and SP-D mRNA expression on postnatal day 14. In conclusion, maternal nicotine exposure during pregnancy reduces lung surfactant lipids and produces variable changes in surfactant protein gene expression during the late postnatal period. As good surface activity of pulmonary surfactant is essential for normal lung function, these results suggest

that derangement of the pulmonary surfactant system may be important in the pathogenesis of impaired pulmonary function in children exposed in utero to nicotine.

J Lipid Res. 2000 Jul;41(7):1145-53.

Increase in fragmented phosphatidylcholine in blood plasma by oxidative stress.

Frey B, Haupt R, Alms S, Holzmann G, König T, Kern H, Kox W, Rüstow B, Schlame M.

Source

Department of Anesthesiology and Intensive Care Medicine, University Hospital Charité, Humboldt University, Berlin, Germany.

Abstract

Oxidatively modified phospholipids with fragmented acyl chains have attracted much interest because of their proinflammatory activity and their potential involvement in atherosclerosis. They can be formed in vitro by free radical treatment of unsaturated phospholipids but it is not known under which conditions they accumulate in vivo. We assayed one species of fragmented phosphatidylcholine (PC) in human blood plasma by high performance liquid chromatography after precolumn derivatization with chloromethylanthracene. Structural analysis suggested that fragmented PC was a diacyl species with a palmitoyl group and a short oxidized residue, which most likely had four carbons. The concentration of fragmented PC was higher in elderly individuals with coronary heart disease than in young healthy controls. Smoking one cigarette acutely increased the concentration of fragmented PC in healthy adults. Fragmented PC also increased in the reperfusion period after treatment with cardiopulmonary bypass. The increase coincided with a surge of circulating neutrophils. In rats, the plasma concentration of fragmented PC was

elevated by vitamin E deficiency and exposure to high oxygen. The data demonstrate that fragmented PC increases in blood plasma in response to various forms of oxidative stress.

Lung. 1993;171(5):277-91.

Early effects of short-time cigarette smoking on the human lung: a study of bronchoalveolar lavage fluids.

Mancini NM, Béné MC, Gérard H, Chabot F, Faure G, Polu JM, Lesur O.

Source

Service des Maladies Respiratoires et Réanimation Respiratoire, CHRU Nancy-Brabois, Vandoeuvre Les Nancy, France.

Abstract

We investigated the early effects of cigarette smoking in healthy subjects by means of lung lavage, looking at markers of alveolar permeability, the alveolar cell profile, the immunophenotyping of macrophages and lymphocytes, and the level and profile of surfactant phospholipids. Bronchoalveolar lavages (BAL) were performed in 33 healthy subjects [20 nonsmokers (nS), 13 moderate and short-time smokers (S)]. In the acellular supernatants we measured the markers of alveolar permeability (i.e., total proteins, albumin, albumin/urea), the alveolar epithelial lining fluid (AELF), the surfactant amounts and profile, and explored the blood lymphocytes by in vitro exposure. The cell pellet established the alveolar formula and a membrane mapping of macrophages (LFA-1 and HLA-DRII expression) and lymphocytes (CD4, CD8, LFA-1, HLA-DRII expression). We found no significant increase of alveolar permeability in our smokers, but an increased alveolar cellularity (more than 3-fold vs nS, $P < 0.05$) evenly distributed between sub-populations except for an enhanced number of eosinophils in smokers ($P < 0.05$ vs nS). Smokers' alveolar

macrophages had an overloaded cytoplasm, a decreased percentage of antigen-handling cell expression (HLA DRII: P < 0.05 vs nS) and a low percentage of cell to cell adhesion molecule expression (LFA-1: P < 0.05 vs nS). Smoking history and LFA-1 expression on alveolar macrophages were interrelated. Smokers' alveolar lymphocyte subsets were more often T suppressor cells (CD8+) and had an increased percentage of antigen-presenting cell expression (HLA DRII: P < 0.05 vs nS). Smokers' BAL fluid did not show the inhibitory control of phytohemagglutinin-induced lymphocyte proliferation present in nonsmokers' fluids. Surfactant phospholipid amounts were similar, but phosphatidylethanolamine was raised and the ratio of phosphatidylcholine to sphingomyelin decreased in smokers (P < 0.05 vs nS). We observed specific cellular and biochemical alterations in the lung lavage of short-time smokers. Alveolar macrophage and lymphocyte expression of LFA-1 and HLA-DR II molecules was altered. Smokers' alveolar fluids lost the physiologic regulatory control of T mitogen-induced lymphocyte proliferation. Membrane phospholipids released by cellular damage increased early in tobacco-exposed lung fluids. This profile of alterations may be an early and sensitive marker of smoking-induced lung damage.

Int J Biochem. 1988;20(3):285-9.

Altered Na+-K+-ATPase, cell Na+ and lipid profiles in canine arterial wall with chronic cigarette smoking.

Tulenko TN, Rabinowitz JL, Cox RH, Santamore WP.

Source

Department of Physiology and Biochemistry, Medical College of Pennsylvania, Philadelphia 19129.

Abstract

1. We evaluated the influence of cigarette smoking on arterial wall membranes, using Na+-K+-ATPase activity, free cholesterol (FC) and phospholipid (PL) contents as indices of membrane structural and functional integrity. 2. Segments of aorta, carotid and femoral arteries were obtained from normal dogs (controls) and dogs subjected to chronic cigarette smoking for 2 yr (12 cigarettes a day). 3. Na+-K+-ATPase activity was assessed in segments of carotid and femoral arteries using a ouabain-sensitive 86Rb uptake procedure for intact tissues. 4. Free cholesterol and phospholipids were separated, identified, and quantitated from extracts of aortic samples by means of two dimensional thin-layer chromatography. 5. Na+-K+-ATPase activity was reduced in the smoker group in both carotid and femoral arteries. This reduced enzyme activity was accompanied by a rise in cell Na+ levels at both arterial sites. 6. Aortic FC was elevated and the PL profile was altered in the smoker group; as a result, phosphatidylcholine was

reduced, whereas lysophosphatidylcholine, phosphatidic acid, and cardiolipin were elevated. 7. Phosphatidylethanolamine, phosphatidylinositol, phosphatidylserine and sphingolipid levels were unchanged. In addition, the FC/PL ratio was increased in the smokers. 8. Taken together, the changes in Na+-K+-ATPase activity, FC/PL ratio and phospholipid profiles observed are consistent with the hypothesis that chronic cigarette smoking causes a reorganization of the phospholipid bilayer in the smooth-muscle cell membrane of the arterial wall.

Serotonin Precursor 5-HTP

And other Serotonin Agonists

Brain Res. 2006 Sep 21;1111(1):30-5. Epub 2006 Jul 31.

Alterations of serotonin synaptic proteins in brain regions of neonatal Rhesus monkeys exposed to perinatal environmental tobacco smoke.

Slotkin TA, Pinkerton KE, Tate CA, Seidler FJ.

Source

Department of Pharmacology and Cancer Biology, Duke University Medical Center, Durham, NC 27710, USA. t.slotkin@duke.edu

Abstract

Serotonin (5HT) systems play important roles in brain development, and early perturbations of 5HT receptor expression produce permanent changes in 5HT synaptic function and associated behaviors. We exposed pregnant Rhesus monkeys to environmental tobacco smoke (ETS) during gestation and for up to 3 months postnatally and examined the expression of 5HT(1A) and 5HT(2) receptors, and of the presynaptic 5HT transporter in brain regions containing 5HT projections (frontal, temporal and occipital cortex) and cell bodies (midbrain). Perinatal ETS exposure elicited upregulation of 5HT(1A) receptor expression without parallel changes in the other two proteins, a pattern consistent with specific 5HT receptor dysregulation, rather than universal disruption of 5HT synaptic development. The effects seen here for ETS in a primate model are virtually identical in direction, magnitude and regional selectivity to those obtained previously for prenatal nicotine administration in rats. Specifically, early 5HT(1A) overexpression

alters the program for future synaptic and behavioral 5HT responses, thus providing a mechanistic link for the shared effects of ETS and nicotine on a specific pathway responsible for behavioral anomalies associated with perinatal tobacco exposure. These results reinforce the need to reduce ETS exposure of pregnant women and young children.

Chest. 1992 Apr;101(4):976-80.

Relationship of urinary serotonin excretion to cigarette smoking and respiratory symptoms. The Normative Aging Study.

Sparrow D, O'Connor GT, Young JB, Rosner B, Weiss ST.

Source

Department of Veterans Affairs Outpatient Clinic, Boston.

Abstract

The relationship of 2-h urinary excretion of serotonin and 5-hydroxyindoleacetic acid (5-HIAA) to cigarette smoking and respiratory symptoms was examined among 631 male participants in the Normative Aging Study (age range, 44 to 85 years). The amount of serotonin excreted in urine was inversely related to age (p less than 0.001). Mean 2-h excretion of serotonin varied from 8.01 micrograms for men 40 to 49 years of age to 5.84 micrograms for those 70 years of age or over. No clear relationship was evident between the amount of 5-HIAA excreted in urine and age. After adjustment for age, current smokers were found to excrete more serotonin (p less than 0.001) and 5-HIAA (p = 0.001) than never smokers. Former smokers did not differ significantly from never smokers in these respects. After adjustment for age and smoking status in a multivariate model, chronic cough was a significant predictor of serotonin excretion (p = 0.005); chronic cough was less predictive of 5-HIAA excretion (p = 0.07). Other respiratory symptoms

were unrelated to urinary excretion of serotonin and 5-HIAA. The mechanisms underlying the observed relationships of urinary serotonin and 5-HIAA excretion to smoking and to chronic cough and their potential relevance to chronic bronchitis remain to be determined.

Psychopharmacology (Berl). 2005 Nov;182(4):562-9. Epub 2005 Oct 19.

Harmane inhibits serotonergic dorsal raphe neurons in the rat.

Touiki K, Rat P, Molimard R, Chait A, de Beaurepaire R.

Source

Laboratoire de Psychopharmacologie, Centre Hospitalier Paul Guiraud, 54 avenue de la République, Villejuif, 94806, France.

Abstract

RATIONALE:
Harmane and norharmane (two beta-carbolines) are tobacco components or products. The effects of harmane and norharmane on serotonergic raphe neurons remain unknown. Harmane and norharmane are inhibitors of the monoamine oxidases A (MAO-A) and B (MAO-B), respectively.

OBJECTIVES:
To study the effects of harmane, norharmane, befloxatone (MAOI-A), and selegiline (MAOI-B) on the firing of serotonergic neurons. To compare the effects of these compounds to those of nicotine (whose inhibitory action on serotonergic neurons has been previously described). The effects of cotinine, a metabolite of nicotine known to interact with serotonergic systems, are also tested.

METHODS:
In vivo electrophysiological recordings of serotonergic dorsal raphe neurons in the anaesthetized rat.

RESULTS:
Nicotine, harmane, and befloxatone inhibited serotonergic dorsal raphe neurons. The other compounds had no effects. The inhibitory effect of harmane (rapid and long-lasting inhibition) differed from that of nicotine (short and rapidly reversed inhibition) and from that of befloxatone (slow, progressive, and long-lasting inhibition). The inhibitory effects of harmane and befloxatone were reversed by the 5-HT1A antagonist WAY 100 635. Pretreatment of animals with p-chlorophenylalanine abolished the inhibitory effect of befloxatone, but not that of harmane.

CONCLUSIONS:
Nicotine, harmane, and befloxatone inhibit the activity of raphe serotonergic neurons. Therefore, at least two tobacco compounds, nicotine and harmane, inhibit the activity of serotonergic neurons. The mechanism by which harmane inhibits serotonergic dorsal raphe neurons is likely unrelated to a MAO-A inhibitory effect.

Neuroreport. 2007 Jun 11;18(9):925-9.

Effects of tobacco and cigarette smoke extracts on serotonergic raphe neurons in the rat.

Touiki K, Rat P, Molimard R, Chait A, de Beaurepaire R.

Source

Laboratoire de Psychopharmacologie, Centre Hospitalier Paul Guiraud, 54 avenue de la République, Villejuif bINSERM U513, 94010 Créteil, France.

Abstract

Tobacco components other than nicotine might participate in the behavioural effects of smoking. In this study, in-vivo recordings of serotonergic dorsal raphe neurons were performed in the anesthetized rat, whereas tobacco extracts, cigarette smoke extracts, nicotine, nornicotine or anabasine were intravenously injected. All substances inhibited the neurons, and all inhibitions were completely blocked by the nicotine receptor antagonist mecamylamine. The effects of the extracts were much more potent than those of individual substances. These results support the hypothesis that the acute inhibition of serotonin neurons by tobacco compounds is completely related to an effect on nicotine

receptors. Tobacco extracts and tobacco smoke extracts may be useful tools for the study of the effects of central effects of smoking.

Am J Psychiatry. 2003 Apr;160(4):773-9.

Cigarette smoking, suicidal behavior, and serotonin function in major psychiatric disorders.

Malone KM, Waternaux C, Haas GL, Cooper TB, Li S, Mann JJ.

Source

Department of Psychiatry, College of Physicians and Surgeons of Columbia University, New York, USA. kmalone@st-vincents.ie

Abstract

OBJECTIVE:

Cigarette smoking is associated with a higher risk for suicide and attempted suicide, but psychopathological or biological explanations for this association have not been explored. Lower serotonin function and impulsive/aggressive traits are associated with suicidal acts, including completed suicide. The authors hypothesized that the relationship that may exist between cigarette smoking and suicidal behavior may be associated with lower serotonin function and the presence of impulsive/aggressive traits.

METHOD:
Study subjects were 347 patients with a psychiatric disorder (175 with depression, 127 with schizophrenia, and 45 with other disorders). Fifty-three percent of the subjects (N=184) had a lifetime history of suicide attempt, and 47% (N=163) had never attempted suicide. Smoking behavior, lifetime suicidal behavior, and psychopathology were assessed. Serotonin function was assessed in a subgroup of patients with depression (N=162) by using a fenfluramine challenge test and/or measurement of CSF levels of 5-hydroxyindoleacetic acid.

RESULTS:
Among all patients, smokers were more likely to have made a suicide attempt (adjusted odds ratio=2.60, 95% confidence interval=1.60-4.23) and had higher suicidal ideation and lifetime aggression scores, compared with nonsmokers. An inverse relationship was observed between amount of cigarette smoking and both indices of serotonin function.

CONCLUSIONS:
The association between cigarette smoking and the presence and severity of suicidal behavior across major psychiatric disorders may be related to lower brain serotonin function in smokers with depression. Further investigation is required to replicate these findings, to measure serotonin function in patients with disorders other than depression, and to test potential therapeutic effects of serotonin-enhancing treatments on both smoking behavior and suicide risk.

Alcohol Clin Exp Res. 2003 Aug;27(8):1257-61.

Tobacco use is associated with reduced central serotonergic neurotransmission in type 1 alcohol-dependent individuals.

Berggren U, Fahlke C, Eriksson M, Balldin J.

Source

Department of Psychiatry and Neurochemistry, Sahlgrenska Academy at Göteborg University, Göteborg, Sweden.

Abstract

BACKGROUND:
Reduced central serotonergic neurotransmission in alcohol dependence may be attributed to the effects of cigarette smoking (and possibly more specifically to nicotine) rather than to alcoholism or its subtypes. The aim of the present study was therefore to compare central serotonergic neurotransmission in tobacco-using (cigarette smokers and users of smokeless tobacco, i.e., snuffers) alcohol-dependent individuals to that of tobacco-nonusing alcohol-dependent individuals.

METHODS:
The central serotonergic neurotransmission was assessed by the prolactin (PRL) response to the serotonin-releasing agent D-fenfluramine (30 mg orally). Male subjects (n = 37) aged 20-65 years were recruited for this purpose. They were all type 1 alcohol-dependent individuals and had ended their alcohol intake the day before the D-fenfluramine challenge test.

RESULTS:
There was no difference in baseline PRL concentrations between tobacco-using (n = 18) and tobacco-nonusing (n = 19) alcohol-dependent individuals. On the other hand, the maximum PRL response after D-fenfluramine was significantly lower in the tobacco-using group as compared to the tobacco-nonusing individuals.

CONCLUSION:
Whether the reduction in central serotonergic neurotransmission in tobacco-using alcohol-dependent individuals is pre-existing or a result of tobacco use remains to be elucidated.

J Neurochem. 1996 Oct;67(4):1540-50.

Preferential vulnerability of nucleus accumbens dopamine binding sites to low-level lead exposure: time course of effects and interactions with chronic dopamine agonist treatments.

Pokora MJ, Richfield EK, Cory-Slechta DA.

Source

Department of Neurobiology and Anatomy, University of Rochester School of Medicine and Dentistry, New York 14642, USA.

Abstract

This study examined the hypotheses that low-level lead (Pb) exposure would increase dopamine (DA) binding sites, would do so preferentially in nucleus accumbens, and that such effects would be modified by concurrent DA agonist treatment. D1-like and D2-like binding sites and the dopamine transporter (DT) were measured autoradiographically

in caudate-putamen and nucleus accumbens of rats exposed from weaning to 0, 50, or 150 ppm Pb acetate drinking solutions with or without concurrent chronic intermittent intraperitoneal injections of the D1-like agonist SKF 82958 or the DA agonist apomorphine after 2 weeks (no injections), 8 months, or 12 months of Pb exposure. Pb selectively decreased DA binding in nucleus accumbens. Decreases in D2-like and DT sites were sustained across the 12-month exposure, whereas D1-like sites evidenced recovery at 12 months. Chronic intermittent DA agonist treatments reversed these effects of Pb in nucleus accumbens, restoring receptor and DT binding levels to normal, despite decreasing binding sites of non-Pb-treated rats. These studies implicate increased DA availability as a mechanism of Pb-induced DA system changes. They also raise the possibility that Pb exposure could serve as a predisposing factor in neurodegenerative diseases associated with DA system dysfunction or could alter the course of DA-based therapeutic treatments.

Annu Rev Pharmacol Toxicol. 1995;35:391-415.

Relationships between lead-induced learning impairments and changes in dopaminergic, cholinergic, and glutamatergic neurotransmitter system functions.

Cory-Slechta DA.

Source

Department of Environmental Medicine, University of Rochester School of Medicine & Dentistry, New York 14642, USA.

Abstract

Behavioral consequences of low-level lead (Pb) exposure include impairments in learning processes and in Fixed-Interval schedule-controlled operant behavior. Although the neurobiological bases of these effects remain undetermined, current evidence suggests that inhibitory effects of Pb on the NMDA receptor complex may play a preferential role in the learning deficits. In contrast, alterations in dopaminergic systems, consistent with a decrease in dopamine availability, appear to be related to the changes in Fixed-Interval performance. Hypocholinergic function has also been described, but its relationship to the behavioral changes is not yet known. Explication of these

relationships will require more efforts involving direct rather than correlative methods. The answers are critical for understanding risks associated with exposure and for the development of behavioral or chemical therapeutic strategies for dealing with lead neurotoxicity.

Brain Res. 2001 Sep 28;914(1-2):166-78.

Fetal and adolescent nicotine administration: effects on CNS serotonergic systems.

Xu Z, Seidler FJ, Ali SF, Slikker W Jr, Slotkin TA.

Source

Department of Pharmacology and Cancer Biology, Duke University Medical Center, Durham, NC 27710, USA.

Abstract

Nicotine is a neuroteratogen that targets synaptic function during critical developmental stages and recent studies indicate that CNS vulnerability extends into adolescence, the time that smoking typically commences. We administered nicotine to pregnant or adolescent rats via continuous minipump infusions, using dose rates that replicate the plasma nicotine levels found in smokers. Fetal nicotine exposure (gestational days 4-21) decreased the cerebrocortical binding of paroxetine (PXT), a marker for the serotonin (5HT) transporter, likely indicative of a decrease in nerve terminals in that region; the effect lasted into adulthood. There was a corresponding increase in

PXT binding in the midbrain/brainstem, the region containing the 5HT cell bodies that project to the cerebral cortex, a pattern typical of reactive sprouting in response to nerve terminal damage. After adolescent nicotine treatment (postnatal days 30-47), PXT binding was reduced in the hippocampus and striatum instead of the cerebral cortex, again accompanied by increased binding in the midbrain and brainstem; the patterns of effects within each region were gender-selective, although both males and females displayed abnormalities. Superimposed on this overall effect, there were transient increases in PXT binding, likely due to acute stimulant effects of nicotine. We also assessed 5HT presynaptic activity (5HIAA/5HT ratio). Withdrawal from adolescent nicotine treatment led to suppression of activity in the cerebral cortex and activation in the midbrain. These results indicate that both fetal and adolescent nicotine exposure elicit apparent damage to 5HT projections with reactive increases in regions containing 5HT cell bodies. Long-term changes in 5HT innervation and/or synaptic activity may play a role in the subsequent development of depression in the offspring of women who smoke during pregnancy or in adolescent smokers.

Dopamine

Pharmacol Biochem Behav. 2005 Apr;80(4):557-66.

Dietary cadmium exposure attenuates D-amphetamine-evoked [3H]dopamine release from striatal slices and methamphetamine-induced hyperactivity.

Miller DK, Dopheide MM, Smith SM, Casteel SW.

Source

Department of Psychological Sciences, 208 McAlester Hall, University of Missouri, Columbia MO 65211, USA. millerden@missouri.edu

Abstract

Prolonged exposure to environmentally relevant amounts of CdCl2 results in cadmium accumulation in dopamine-rich brain regions, such as striatum. Exposure to these low levels of cadmium also diminishes cocaine-induced hyperactivity and conditioned reinforcement. The goal of the present study was to assess the effect of cadmium on amphetamine pharmacology. Direct application of cadmium (0.1-100 microM), within the concentrations reported in brain after chronic exposure, to preloaded rat striatal slices did not alter D-amphetamine-evoked [3H]dopamine release. To determine the effect of dietary cadmium exposure on amphetamines, rats received ad libitum access to

diet containing CdCl2 (10 or 100 ppm) or to control diet for 30 days and then D-amphetamine-evoked [3H]dopamine release and methamphetamine-induced hyperactivity were measured. Dietary CdCl2 exposure produced a marked increase in cadmium blood and brain levels, approximate to environmental metal exposure. Dietary cadmium exposure was associated with decreased potency of D-amphetamine to evoke [3H]dopamine release. Cadmium-exposed rats were also less sensitive to the locomotor-activating effect of acute methamphetamine (0.3 or 1.0 mg/kg) injection. The present findings demonstrate that the presence of cadmium in brain is not sufficient for the inhibition of D-amphetamine-evoked dopamine release. This suggests that cadmium does not directly interfere with the mechanism of action for amphetamine pharmacology; rather, it suggests that long-term cadmium exposure induces a change in the number and/or function of striatal neurons.

Toxicol Sci. 2007 Aug;98(2):488-94. Epub 2007 May 5.

Cadmium-induced toxicity in rat primary mid-brain neuroglia cultures: role of oxidative stress from microglia.

Yang Z, Yang S, Qian SY, Hong JS, Kadiiska MB, Tennant RW, Waalkes MP, Liu J.

Source

Laboratory of Molecular Toxicology, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina 27709, USA.

Abstract

This study examined the role of oxidative stress in neurotoxic effects of cadmium chloride (Cd) in rat primary mid-brain neuron-glia cultures. Cd accumulated in neuron-glia cultures and produced cytotoxicity in a dose-dependent manner, with IC(50) of 2.5microM 24 h after exposure. (3)H-dopamine uptake into neuron-glia cultures was decreased 7 days after Cd exposure, with IC(50) of 0.9microM, indicative of the sensitivity of dopaminergic neurons to Cd toxicity. To investigate the role of microglia in Cd-induced toxicity to neurons, microglia-enriched cultures were prepared. Cd significantly increased intracellular reactive oxygen species production in microglia-enriched cultures,

as evidenced by threefold increases in 2',7'-dichlorofluorescein signals. Using 5,5-dimethyl-1-pyrroline N-oxide as a spin-trapping agent, Cd increased electron spin resonance signals by 3.5-fold in microglia-enriched cultures. Cd-induced oxidative stress to microglia-enriched cultures was further evidenced by activation of redox-sensitive transcription factor nuclear factor kappa B and activator protein-1 (AP-1), and the increased expression of oxidative stress-related genes, such as metallothionein, heme oxygenase-1, glutathione S-transferase pi, and metal transport protein-1, as determined by gel-shift assays and real-time reverse transcription-PCR, respectively, in microglia-enriched cultures. In conclusion, Cd is toxic to neuron-glia cultures, and the oxidative stress from microglia may play important roles in Cd-induced damage to dopaminergic neurons.

J Neurochem. 1996 Oct;67(4):1540-50.

Preferential vulnerability of nucleus accumbens dopamine binding sites to low-level lead exposure: time course of effects and interactions with chronic dopamine agonist treatments.

Pokora MJ, Richfield EK, Cory-Slechta DA.

Source

Department of Neurobiology and Anatomy, University of Rochester School of Medicine and Dentistry, New York 14642, USA.

Abstract

This study examined the hypotheses that low-level lead (Pb) exposure would increase dopamine (DA) binding sites, would do so preferentially in nucleus accumbens, and that such effects would be modified by concurrent DA agonist treatment. D1-like and D2-like binding sites and the dopamine transporter (DT) were measured autoradiographically in caudate-putamen and nucleus accumbens of rats exposed from weaning to 0, 50, or 150 ppm Pb acetate drinking solutions with or without concurrent chronic intermittent intraperitoneal injections of the D1-like agonist SKF 82958 or

the DA agonist apomorphine after 2 weeks (no injections), 8 months, or 12 months of Pb exposure. Pb selectively decreased DA binding in nucleus accumbens. Decreases in D2-like and DT sites were sustained across the 12-month exposure, whereas D1-like sites evidenced recovery at 12 months. Chronic intermittent DA agonist treatments reversed these effects of Pb in nucleus accumbens, restoring receptor and DT binding levels to normal, despite decreasing binding sites of non-Pb-treated rats. These studies implicate increased DA availability as a mechanism of Pb-induced DA system changes. They also raise the possibility that Pb exposure could serve as a predisposing factor in neurodegenerative diseases associated with DA system dysfunction or could alter the course of DA-based therapeutic treatments.

Annu Rev Pharmacol Toxicol. 1995;35:391-415.

Relationships between lead-induced learning impairments and changes in dopaminergic, cholinergic, and glutamatergic neurotransmitter system functions.

Cory-Slechta DA.

Source

Department of Environmental Medicine, University of Rochester School of Medicine & Dentistry, New York 14642, USA.

Abstract

Behavioral consequences of low-level lead (Pb) exposure include impairments in learning processes and in Fixed-Interval schedule-controlled operant behavior. Although the neurobiological bases of these effects remain undetermined, current evidence suggests that inhibitory effects of Pb on the NMDA receptor complex may play a preferential role in the learning deficits. In contrast, alterations in dopaminergic systems, consistent with a decrease in dopamine availability, appear to be related to the changes in Fixed-Interval performance. Hypocholinergic function has also been described, but its relationship to the behavioral changes is not yet known. Explication of these relationships will require more efforts involving direct rather than correlative methods. The answers are critical for

understanding risks associated with exposure and for the development of behavioral or chemical therapeutic strategies for dealing with lead neurotoxicity.

Neurotoxicol Teratol. 2008 Sep-Oct;30(5):428-32. Epub 2008 Mar 5.

Cortical dopaminergic neurotransmission in rats intoxicated with lead during pregnancy. Nitric oxide and hydroxyl radicals formation involvement.

Nowak P, Szczerbak G, Nitka D, Kostrzewa RM, Jośko J, Brus R.

Source

Department of Pharmacology, Medical University of Silesia, H. Jordana 38, 41-808 Zabrze, Poland. pnowak@sum.edu.pl

Abstract

It is well established that low level Pb-exposure is associated with a wide range of cognitive and neurobehavioral dysfunctions in children. In fact, Pb-induced damage occurs preferentially in the prefrontal cerebral cortex, hippocampus and cerebellum - the anatomical sites which are crucial in modulating emotional response, memory and learning. Previously it was also shown that nitric oxide (NO) signaling pathway as well as glutamatergic neurotransmission are both involved in brain development, neurotoxicity and neurodegeneration processes whereas Pb(2+) interfere with both. For this reason we investigated the effect of ontogenetic Pb(2+) exposure on dopaminergic neurotransmission in the medial prefrontal cortex (mPFC) of rats after amphetamine (AMPH) and/or 7-nitroindazole

(7-NI) administration. Furthermore, the possible role of oxidative stress in Pb(2+)-induced neurotoxicity in prenatally Pb(2+)-treated rats was explored in the content of hydroxyl radical (HO) species in mPFC after AMPH and/or 7-NI injection, assessed by HPLC analysis of 2.3-dihydroxybenzoic acid (2.3-DHBA) - spin trap product of salicylate. As shown, the results of this study suggest that Pb(2+) exposure during intrauterine life did not substantially affect cortical dopaminergic neurotransmission in adult offspring rats evaluated by means of microdialysis of mPFC and the content of the cortical HO. It is likely that striatum, nucleus accumbens or other dopamine rich brain areas are more intricately associated with Pb(2+) precipitated behavioral, dopamine - dependent impairments observed in mammalians.

J Toxicol Environ Health A. 2007 Oct;70(20):1779-82.

Urinary cadmium levels and tobacco smoke exposure in women age 20-69 years in the United States.

McElroy JA, Shafer MM, Trentham-Dietz A, Hampton JM, Newcomb PA.

Source

University of Wisconsin, Paul P. Carbone Comprehensive Cancer Center, Madison, Wisconsin 53726, USA. jamcelroy@wisc.edu

Abstract

Cadmium is a toxic, bioaccumulated heavy metal with a half-life of one to four decades in humans (CDC, 2005). Primary exposure sources include food and tobacco smoke. In our population-based study, a risk-factor interview was conducted as part of a breast cancer study for 251 randomly selected women living in Wisconsin (USA), aged 20-69 yr, and spot-urine specimens were also obtained. Urine collection kits were carefully designed to minimize trace element contamination during specimen collection and handling in each participant's home. Urine cadmium concentrations were quantified using inductively coupled plasma-mass spectrometry, and creatinine levels and

specific gravity were also determined. Statistically significant increasing creatinine-adjusted urinary cadmium mean levels relative to smoking status (never, former, and current respectively) were observed. A difference in mean cadmium levels for nonsmokers who reported environmental tobacco smoke exposure during childhood or the recent past (approximately 2 yr prior to the interview) for exposure at home, at work, or in social settings compared to those who reported no exposure was not found.

Adverse Effects of Second-Hand Tobacco Smoke

Acta Paediatr. 2009 Mar;98(3):531-6. Epub 2008 Oct 29.

The effect of passive smoking and breast feeding on serum antioxidant vitamin (A, C, E) levels in infants.

Yilmaz G, Isik Agras P, Hizli S, Karacan C, Besler HT, Yurdakok K, Coskun T.

Source

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Abstract

AIM:

Toxic substances in tobacco smoke are known to have negative effects on the antioxidant capacity of human body. In order to investigate the effect of passive smoking on serum antioxidant levels in infants, serum vitamin A, E, C levels and urinary cotinine/creatinine levels were measured in 254 infants at the age of 6 months.

METHODS:

The information about infants' nutrition and exposure to tobacco smoke was obtained from the mothers by the help of a questionnaire. The infants were grouped according to both smoking status of mother and urinary cotinine/creatinine levels.

RESULTS:

The mean serum vitamin A, C and E levels of infants of smoking mothers were significantly lower than those of non-smoking mothers ($p < 0.05$). Vitamin A, E and C levels were negatively correlated with urinary cotinine/creatinine levels ($p < 0.05$, r: -0.61, -0.42, -0.53, respectively). Multivariate analysis revealed independent factors determining the serum vitamin A, E and C levels of infants as maternal smoking and breast feeding ($p < 0.05$).

CONCLUSION:

Tobacco smoke exposure of infants significantly decreases their serum antioxidant vitamin A, C and E levels. However, breast feeding may help to prevent the decrement of antioxidant vitamin levels of passive smoking infants.

Eur J Pediatr. 2005 Dec;164(12):775-8. Epub 2005 Jul 16.

Increased oxidative stress in infants exposed to passive smoking.

Aycicek A, Erel O, Kocyigit A.

Source

Paediatrics Department, Children's Hospital of Sanliurfa, Turkey. ayciceka@hotmail.com

Abstract

The purpose of this study was to assess the effect of passive cigarette smoking on the oxidative and anti-oxidative status of plasma in infants. Eighty-four infants aged 6-28 weeks were divided into two groups: the study group included infants who had been exposed to passive smoking via at least five cigarettes per day for at least the past 6 weeks at home, while the control group included infants who had never been exposed to passive smoking. The antioxidative status of plasma was assessed by the measurement of individual antioxidant components: vitamin C, albumin, bilirubin, uric acid, thiol contents and total antioxidant capacity (TAC 1 and TAC 2). Oxidative status was assessed by the determination of total peroxide levels and the oxidative stress index (OSI 1 and OSI 2). Plasma

vitamin C, thiol concentration and TAC 1 and TAC 2 levels were significantly lower, whereas plasma total peroxide levels and OSI 1 and OSI 2 were significantly higher, in passive smoking infants than in the controls (P<0.01). We conclude that passive smoking has a negative impact on numerous parts of the antioxidant defence system in infants, and exposes them to potent oxidative stress.

Ann Nutr Metab. 2010;56(2):113-8. Epub 2010 Jan 29.

Passive smoke exposure and circulating carotenoids in the CARDIA study.

Widome R, Jacobs DR Jr, Hozawa A, Sijtsma F, Gross M, Schreiner PJ, Iribarren C.

Source

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Abstract

Background/Aims: Our objective was to assess associations between passive smoke exposure in various venues and serum carotenoid concentrations. Methods: CARDIA is an ongoing longitudinal study of the risk factors for subclinical and clinical cardiovascular disease. At baseline in 1985/1986, serum carotenoids were assayed and passive smoke exposure inside and outside of the home and diet were assessed by self-report. Our analytic sample consisted of 2,633 black and white non-smoking adults aged 18-30 years. Results: Greater total passive smoke exposure was

associated with lower levels of the sum of the three provitamin A carotenoids, alpha-carotene, beta-carotene, and beta-cryptoxanthin (-0.048 nmol/l per hour of passive smoke exposure, p = 0.001), unassociated with lutein/zeaxanthin, and associated with higher levels of lycopene (0.027 nmol/l per hour of passive smoke exposure, p = 0.010) after adjustment for demographics, diet, lipid profile, and supplement use. Exposure in both home and non-home spaces was also associated with lower levels of the provitamin A carotenoid index. Conclusion: Cross-sectionally, in 1985/86, passive smoke exposure in various venues was associated with reduced levels of provitamin A serum carotenoids.

Brain Res. 2006 Sep 21;1111(1):30-5. Epub 2006 Jul 31.

Alterations of serotonin synaptic proteins in brain regions of neonatal Rhesus monkeys exposed to perinatal environmental tobacco smoke.

Slotkin TA, Pinkerton KE, Tate CA, Seidler FJ.

Source

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Abstract

Serotonin (5HT) systems play important roles in brain development, and early perturbations of 5HT receptor expression produce permanent changes in 5HT synaptic function and associated behaviors. We exposed pregnant

Rhesus monkeys to environmental tobacco smoke (ETS) during gestation and for up to 3 months postnatally and examined the expression of 5HT(1A) and 5HT(2) receptors, and of the presynaptic 5HT transporter in brain regions containing 5HT projections (frontal, temporal and occipital cortex) and cell bodies (midbrain). Perinatal ETS exposure elicited upregulation of 5HT(1A) receptor expression without parallel changes in the other two proteins, a pattern consistent with specific 5HT receptor dysregulation, rather than universal disruption of 5HT synaptic development. The effects seen here for ETS in a primate model are virtually identical in direction, magnitude and regional selectivity to those obtained previously for prenatal nicotine administration in rats. Specifically, early 5HT(1A) overexpression alters the program for future synaptic and behavioral 5HT responses, thus providing a mechanistic link for the shared effects of ETS and nicotine on a specific pathway responsible for behavioral anomalies associated with perinatal tobacco exposure. These results reinforce the need to reduce ETS exposure of pregnant women and young children.

Brain Res. 2001 Sep 28;914(1-2):166-78.

Fetal and adolescent nicotine administration: effects on CNS serotonergic systems.

Xu Z, Seidler FJ, Ali SF, Slikker W Jr, Slotkin TA.

Source

Department of Pharmacology and Cancer Biology, Duke University Medical Center, Durham, NC 27710, USA.

Abstract

Nicotine is a neuroteratogen that targets synaptic function during critical developmental stages and recent studies indicate that CNS vulnerability extends into adolescence, the time that smoking typically commences. We administered nicotine to pregnant or adolescent rats via continuous minipump infusions, using dose rates that

replicate the plasma nicotine levels found in smokers. Fetal nicotine exposure (gestational days 4-21) decreased the cerebrocortical binding of paroxetine (PXT), a marker for the serotonin (5HT) transporter, likely indicative of a decrease in nerve terminals in that region; the effect lasted into adulthood. There was a corresponding increase in PXT binding in the midbrain/brainstem, the region containing the 5HT cell bodies that project to the cerebral cortex, a pattern typical of reactive sprouting in response to nerve terminal damage. After adolescent nicotine treatment (postnatal days 30-47), PXT binding was reduced in the hippocampus and striatum instead of the cerebral cortex, again accompanied by increased binding in the midbrain and brainstem; the patterns of effects within each region were gender-selective, although both males and females displayed abnormalities. Superimposed on this overall effect, there were transient increases in PXT binding, likely due to acute stimulant effects of nicotine. We also assessed 5HT presynaptic activity (5HIAA/5HT ratio). Withdrawal from adolescent nicotine treatment led to suppression of activity in the cerebral cortex and activation in the midbrain. These results indicate that both fetal and adolescent nicotine exposure elicit apparent damage to 5HT projections with reactive increases in regions containing 5HT cell bodies. Long-term changes in 5HT innervation and/or synaptic activity may play a role in the subsequent development of depression in the offspring of women who smoke during pregnancy or in adolescent smokers.

Mutat Res. 2007 May 18;629(2):140-7. Epub 2007 Feb 20.

Increased DNA damage in children caused by passive smoking as assessed by comet assay and oxidative stress.

Zalata A, Yahia S, El-Bakary A, Elsheikha HM.

Source

Department of Biochemistry, Faculty of Medicine, Mansoura University, Mansoura 35516, Egypt.

Erratum in

Mutat Res. 2007 Aug 15;632(1-2):126.

Abstract

The present study aimed to evaluate the association between the environmental tobacco smoke (ETS) and DNA damage in relation to oxidative stress (OS) in children. Sixty-four children of age 1-8 years, selected from the outpatient clinic of Mansoura University Children Hospital were divided into two groups (23 children/group) based on high (>20 cigarettes/day) or low (<20 cigarettes/day) exposure to ETS at home. Twenty symptom-free children with normal cotinine level and with no exposure to ETS were recruited as controls. The comet assay was used to quantify the level of DNA damage in lymphocytes isolated from all children. Spectrophotometric methods were used to assess the serum level of malondialdehyde (MDA) and activity of glutathione peroxidase (GSH-Px) in erythrocytes. Also, serum level of tocopherol fractions (alpha, gamma, delta) was assessed by high performance liquid chromatography (HPLC). Children exposed to ETS exhibited retarded growth, more chest problems, and gastroenteritis than the control. A significant increase in mean comet tail length indicating DNA damage was observed in ETS-exposed children ($P<0.001$) compared to controls. ETS-exposed children had significantly ($P<0.001$) higher MDA level paralleled with significant ($P<0.001$) decrease in the level of GSH-Px and tocopherol fractions compared with controls. The GSH-Px activity and tocopherol levels were inversely correlated with the increase of ETS exposure. These results show that inhalation of ETS is associated with an increase in the level of oxidants and a simultaneous decrease in the level of antioxidants in the children's blood. This status of oxidant-antioxidant imbalance (OS) may be one of the mechanisms leading to DNA damage detected in lymphocytes of ETS-exposed children. In conclusion, the present study gives an indication of an association between DNA damage and ETS exposure in children.

Acta Paediatr. 2010 Jan;99(1):106-11.

Exposure to secondhand tobacco smoke and child behaviour - results from a cross-sectional study among preschool children in Bavaria.

Twardella D, Bolte G, Fromme H, Wildner M, von Kries R; GME Study Group.

Source

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Abstract

AIM:

To evaluate the association of postnatal exposure to secondhand tobacco smoke on childhood behavioural problems after taking maternal smoking during pregnancy into account.

METHODS:
In a cross-sectional survey of preschool children in Bavaria, exposure to secondhand tobacco smoke in the child's home was assessed via a parent questionnaire. The Strength and Difficulties Questionnaire (SDQ) was applied to assess child's behaviour. The association with secondhand tobacco smoke exposure was assessed for 'probable' outcomes of the problem subscales and of prosocial behaviour.

RESULTS:
Among 5494 children (48% female), the SDQ indicated behavioural problems in up to 11%. After adjustment for socioeconomic factors, low birth weight and maternal smoking before and during pregnancy, a dose-response relationship with exposure to secondhand tobacco smoke was observed regarding hyperactivity/inattention (odds ratio compared to 'none' was 1.35 for 'low/medium' and 2.39 for 'high' exposure, 95% confidence intervals 1.02-1.78 and 1.62-3.53, respectively) as well as for conduct problems (OR 1.68 (1.37-2.06) and 1.93 (1.39-2.68)).

CONCLUSION:
Secondhand tobacco smoke exposure at home appears to be associated with an increased risk of behavioural problems among preschool children. Prevention of behavioural problems may be a further reason to target secondhand tobacco smoke exposure in children.

Mutat Res. 2007 May 18;629(2):140-7. Epub 2007 Feb 20.

Increased DNA damage in children caused by passive smoking as assessed by comet assay and oxidative stress.

Zalata A, Yahia S, El-Bakary A, Elsheikha HM.

Source

Department of Biochemistry, Faculty of Medicine, Mansoura University, Mansoura 35516, Egypt.

Erratum in

Mutat Res. 2007 Aug 15;632(1-2):126.

Abstract

The present study aimed to evaluate the association between the environmental tobacco smoke (ETS) and DNA damage in relation to oxidative stress (OS) in children. Sixty-four children of age 1-8 years, selected from the outpatient clinic of Mansoura University Children Hospital were divided into two groups (23 children/group) based on high (>20 cigarettes/day) or low (<20 cigarettes/day) exposure to ETS at home. Twenty symptom-free children with normal cotinine level and with no exposure to ETS were recruited as controls. The comet assay was used to quantify the level of DNA damage in lymphocytes isolated from all children. Spectrophotometric methods were used to assess the serum level of malondialdehyde (MDA) and activity of glutathione peroxidase (GSH-Px) in erythrocytes. Also, serum level of tocopherol fractions (alpha, gamma, delta) was assessed by high performance liquid chromatography (HPLC). Children exposed to ETS exhibited retarded growth, more chest problems, and gastroenteritis than the control. A significant increase in mean comet tail length indicating DNA damage was observed in ETS-exposed children ($P<0.001$) compared to controls. ETS-exposed children had significantly ($P<0.001$) higher MDA level paralleled with significant ($P<0.001$) decrease in the level of GSH-Px and tocopherol fractions compared with controls. The GSH-Px activity and tocopherol levels were inversely correlated with the increase of ETS exposure. These results show that inhalation of ETS is associated with an increase in the level of oxidants and a simultaneous decrease in the level of antioxidants in the children's blood. This status of oxidant-antioxidant imbalance (OS) may be one of the mechanisms leading to DNA damage detected in lymphocytes of ETS-exposed children. In conclusion, the present study gives an indication of an association between DNA damage and ETS exposure in children.

Int J Cardiol. 2005 Apr 8;100(1):61-4.

Increased oxidative stress in children exposed to passive smoking.

Kosecik M, Erel O, Sevinc E, Selek S.

Source

Department of Pediatric Cardiology, Harran University Faculty of Medicine, Sanliurfa, Turkey. mkosecik@harran.edu.tr

Abstract

BACKGROUND:

Atherogenic process is accelerated with cigarette smoke that contains many oxidants and prooxidants, capable of producing free radical and enhancing the oxidative stress. We investigated oxidative and antioxidative status of children who had been exposed to passive smoking and compared with those of not exposed group.

METHODS:
One hundred forty-three school children aged 9-13 years, 61 of whom had never been exposed to passive smoking, and 82 of whom had been exposed to passive smoking at least 10 cigarette per day for at least last 1 year in their house, were enrolled in this study. Total antioxidative response (TAR) was measured to determine antioxidative status of plasma, and total peroxide concentration was measured to determine oxidative status of plasma. The ratio of TAR to total peroxide was accepted as an indicator of oxidative stress.

RESULTS:
TAR of plasma was significantly lower in children exposed to passive smoking than in those of not exposed group (p=0.018). Mean (S.D.) values were 1.49 (0.07) and 1.52 (0.08) mmol Trolox Equiv./l, respectively. In contrary, the mean (S.D.) total peroxide level of plasma was significantly higher in children exposed to passive smoking [13.06 (2.34) micromol H2O2/l] than in not exposed group [12.24 (1.74) micromol H2O2/l] (p=0.015). The mean (S.D.) oxidative stress index (OSI) value was significantly higher in the children exposed to passive smoking [0.87 (0.15)] than in not exposed group [0.80 (0.10)] (p=0.001).

CONCLUSION:
Children who are exposed to passive smoking are exposed to oxidative stress, which has been implicated in the etiopathogenesis of over 100 disorders including atherosclerosis.

Rev Environ Health. 1984;4(2):161-78.

Genotoxic risk of passive smoking.

Bos RP, Henderson PT.

Abstract

More than 60 chemical components are identified in cigarette smoke which have shown to be carcinogenic. The presence of these chemicals is established in mainstream smoke. However, many of them also appear in sidestream smoke resulting in pollution of indoor air, as is shown by the presence of mutagenic substances. Some rather potent carcinogens like N-nitroso-dimethylamine and benzo(a)pyrene have been established in the air of smoke filled rooms. Only a few studies describe internal exposure of passive smokers. Deposition of sidestream smoke in the human respiratory tract has been established for passive smokers. On the other hand, it was shown that inhalation of air contaminated with sidestream smoke results in an increase in the urinary excretion of products mutagenic in the Salmonella/microsome assay. Three epidemiological studies showed an increased risk of lung cancer for non-

smoking wives having smoking husbands. Since it is generally acknowledged that most of the genotoxic carcinogens can be detected by in vitro mutagenicity tests, mutagenicity in urine of passive smokers can be considered as an indication of exposure to carcinogens. This observation suggests that there is a causality in the association between increased cancer risk and passive smoking as was found in three epidemiological studies. It is generally accepted that genotoxic chemicals exert their effects in direct proportion to the level of exposure, which means that for these agents no safe thresholds can be established. Several studies clearly show the presence of genotoxic substances in indoor air as a consequence of smoking. Therefore, the outcome of the epidemiological studies is not surprising. As long as half of the human population persists in smoking, the problems of involuntary inhalation of genotoxic substances will continue for the other half. Strategies to control the environmental cancer problem can only be successful if the health hazards of passive smoking are taken seriously.

Thorax. 2004 Jul;59(7):569-73.

Glutathione S transferase deficiency and passive smoking increase childhood asthma.

Kabesch M, Hoefler C, Carr D, Leupold W, Weiland SK, von Mutius E.

Source

University Children's Hospital, Ludwig Maxmilians University-Munich, Lindwurmstrasse 4, D-80337 Munich, Germany. Michael.Kabesch@med.uni-muenchen.de

Abstract

BACKGROUND:

It has been suggested that the genetically determined deficiency of glutathione S transferase (GST) enzymes involved in the detoxification of environmental tobacco smoke (ETS) components may contribute to the development of asthma.

METHODS:
A large population of German schoolchildren (n = 3054) was genotyped for deficiencies of the GST isoforms M1 and T1. The association between GSTM1 and GSTT1 genotypes and asthma as well as atopy was investigated with respect to current and in utero ETS exposure.

RESULTS:
In children lacking the GSTM1 allele who were exposed to current ETS the risk for current asthma (OR 5.5, 95% CI 1.6 to 18.6) and asthma symptoms such as wheeze ever (OR 2.8, 95% CI 1.3 to 6.0), current wheezing (OR 4.7, 95% CI 1.8 to 12.6) and shortness of breath (OR 8.9, 95% CI 2.1 to 38.4) was higher than in GSTM1 positive individuals without ETS exposure. Hints of an interaction between ETS exposure and GSTM1 deficiency were identified. In utero smoke exposure in GSTT1 deficient children was associated with significant decrements in lung function compared with GSTT1 positive children not exposed to ETS.

CONCLUSIONS:
GSTM1 and GSTT1 deficiency may increase the adverse health effects of in utero and current smoke exposure.

Rev Environ Health. 1984;4(2):161-78.

Genotoxic risk of passive smoking.

Bos RP, Henderson PT.

Abstract

More than 60 chemical components are identified in cigarette smoke which have shown to be carcinogenic. The presence of these chemicals is established in mainstream smoke. However, many of them also appear in sidestream smoke resulting in pollution of indoor air, as is shown by the presence of mutagenic substances. Some rather potent carcinogens like N-nitroso-dimethylamine and benzo(a)pyrene have been established in the air of smoke filled rooms. Only a few studies describe internal exposure of passive smokers. Deposition of sidestream smoke in the human

respiratory tract has been established for passive smokers. On the other hand, it was shown that inhalation of air contaminated with sidestream smoke results in an increase in the urinary excretion of products mutagenic in the Salmonella/microsome assay. Three epidemiological studies showed an increased risk of lung cancer for non-smoking wives having smoking husbands. Since it is generally acknowledged that most of the genotoxic carcinogens can be detected by in vitro mutagenicity tests, mutagenicity in urine of passive smokers can be considered as an indication of exposure to carcinogens. This observation suggests that there is a causality in the association between increased cancer risk and passive smoking as was found in three epidemiological studies. It is generally accepted that genotoxic chemicals exert their effects in direct proportion to the level of exposure, which means that for these agents no safe thresholds can be established. Several studies clearly show the presence of genotoxic substances in indoor air as a consequence of smoking. Therefore, the outcome of the epidemiological studies is not surprising. As long as half of the human population persists in smoking, the problems of involuntary inhalation of genotoxic substances will continue for the other half. Strategies to control the environmental cancer problem can only be successful if the health hazards of passive smoking are taken seriously.

Women Health. 1986 Fall-Winter;11(3-4):267-77.

Health risks of passive smoking.

Papier CM, Stellman SD.

Abstract

Passive or involuntary smoking is the inhalation of smoke which escapes directly into the air from the lit end of a burning cigarette. This unfiltered smoke contains the same toxic components of the mainstream smoke inhaled directly by the smoker, including numerous carcinogens, many in greater concentrations. It has long been known that exposure to this type of smoke leads to increased respiratory and other adverse health conditions in non-smokers,

especially children. During the past five years, evidence has been accumulating that risk of lung cancer is also higher, particularly in non-smoking women whose husbands smoke. Despite uncertainties and differences in interpretation of various cancer studies, there is ample justification for public health measures now in place or proposed, such as restriction or elimination of smoking in the workplace and in public places.

Am Fam Physician. 1988 May;37(5):212-8.

Passive smoking.

Chesebro MJ.

Source

University of Alabama College of Community Health Services, Tuscaloosa.

Abstract

Absorption of harmful and irritative components of cigarette smoke by nonsmokers may result in both acute and long-term health problems. Persons with asthma or coronary artery disease are at particularly high risk of developing problems. Children living with smokers are at increased risk of persistent middle ear effusions and lower respiratory tract infections. Nonsmokers married to smokers have an increased risk of lung cancer.

Adverse Effects of Second-Hand Tobacco Smoke with Special Consideration to Vitamin B-6 and Methionine

JAMA. 2010 Jun 16;303(23):2377-85.

Serum B vitamin levels and risk of lung cancer.

Johansson M, Relton C, Ueland PM, Vollset SE, Midttun Ø, Nygård O, Slimani N, Boffetta P, Jenab M, Clavel-Chapelon F, Boutron-Ruault MC,Fagherazzi G, Kaaks R, Rohrmann S, Boeing H, Weikert C, Bueno-de-Mesquita HB, Ros MM, van Gils CH, Peeters PH, Agudo A, Barricarte A,Navarro C, Rodríguez L, Sánchez MJ, Larrañaga N, Khaw KT, Wareham N, Allen NE, Crowe F, Gallo V, Norat T, Krogh V, Masala G, Panico S,Sacerdote C, Tumino R, Trichopoulou A, Lagiou P, Trichopoulos D, Rasmuson T, Hallmans G, Riboli E, Vineis P, Brennan P.

Source

International Agency for Research on Cancer, Lyon, France.

Abstract

CONTEXT:

B vitamins and factors related to 1-carbon metabolism help to maintain DNA integrity and regulate gene expression and may affect cancer risk.

OBJECTIVE:

To investigate if 1-carbon metabolism factors are associated with onset of lung cancer.

DESIGN, SETTING, AND PARTICIPANTS:

The European Prospective Investigation into Cancer and Nutrition (EPIC) recruited 519,978 participants from 10 countries between 1992 and 2000, of whom 385,747 donated blood. By 2006, 899 lung cancer cases were identified and 1770 control participants were individually matched by country, sex, date of birth, and date of blood collection. Serum levels were measured for 6 factors of 1-carbon metabolism and cotinine.

MAIN OUTCOME MEASURE:

Odds ratios (ORs) of lung cancer by serum levels of 4 B vitamins (B(2), B(6), folate [B(9)], and B(12)), methionine, and homocysteine.

RESULTS:

Within the entire EPIC cohort, the age-standardized incidence rates of lung cancer (standardized to the world population, aged 35-79 years) were 6.6, 44.9, and 156.1 per 100,000 person-years among never, former, and current smokers for men, respectively. The corresponding incidence rates for women were 7.1, 23.9, and 100.9 per 100,000 person-years, respectively. After accounting for smoking, a lower risk for lung cancer was seen for elevated serum levels of B(6) (fourth vs first quartile OR, 0.44; 95% confidence interval [CI], 0.33-0.60; P for trend <.000001), as well as for serum methionine (fourth vs first quartile OR, 0.52; 95% CI, 0.39-0.69; P for trend <.000001). Similar and consistent decreases in risk were observed in never, former, and current smokers, indicating that results were not due to confounding by smoking. The magnitude of risk was also constant with increasing length of follow-up, indicating that the associations were not explained by preclinical disease. A lower risk was also seen for serum folate (fourth vs first quartile OR, 0.68; 95% CI, 0.51-0.90; P for trend = .001), although this was apparent only for former and current smokers. When participants were classified by median levels of serum methionine and B(6), having above-median levels of both was associated with a lower lung cancer risk overall (OR, 0.41; 95% CI, 0.31-0.54), as well as separately among never (OR, 0.36; 95% CI, 0.18-0.72), former (OR, 0.51; 95% CI, 0.34-0.76), and current smokers (OR, 0.42; 95% CI, 0.27-0.65).

CONCLUSION:

Serum levels of vitamin B(6) and methionine were inversely associated with risk of lung cancer.

Rev Port Cardiol. 2000 Apr;19(4):471-4.

[Influence of smoking on homocysteinemia at baseline and after methionine load].

[Article in Portuguese]

Reis RP, Azinheira J, Reis HP, Pina JE, Correia JM, Luís AS.

Source

Serviço de Cardiologia do Hospital de Pulido Valente.

Abstract

INTRODUCTION AND AIMS:

Homocysteinemia (HC) and smoking are both important risk factors for vascular disease. In the present study, we intend to evaluate the influence of smoking habits on HC values as well as on vitamins B6, B12 and folic acid, co-factors of HC metabolism.

METHODS:

We measured fasting homocysteinemia (basal) and homocysteinemia 6 hours after an overload with 0.1 g methionine/kg body weight in 279 subjects. We also performed the dosage of plasma levels of B6 and B12 vitamins and of red cells folates. Smoking habits were inquired and the subjects were classified as non-smokers, current smokers or ex-smokers (if they had stopped smoking more than 1 month before the study). According to the smoking status, smokers were classified in three groups: less than 20 cigarettes a day, between 20 and 39 and 40 or more cigarettes a day. We studied basal and after methionine load homocysteinemia, B6, B12 and folic acid levels in each group.

RESULTS:

Smokers presented significantly higher levels of basal and after methionine load homocysteinemia then non-smokers (10.6 +/- 4.9 vs 9.4 +/- 2.6, and 26.8 +/- 10.0 vs 24.3 +/- 7.4 mumol/L, respectively, $p < 0.05$ for both and B6 levels (29.2 +/- 12.0 versus 32.6 +/- 12.0 mumol/L, $p < 0.05$). B12 and folic levels were similar in the two groups. These results were quite similar either in the normal subjects or in the subjects with a history of a cardiovascular event. The subjects who smoked 40 or more cigarettes per day, compared with those who smoked less then 20 cigarettes per day, presented higher levels of basal homocysteinemia (12.4 +/- 2.9 vs 10.0 +/- 5.5 mumol/L, $p < 0.05$) and lower levels of B6 (24.7 +/- 8.1 vs 31.7 +/- 12.6 mumol/L, $p < 0.05$).

CONCLUSIONS:

Smoking habits are related with the increase of basal and after methionine load homocysteinemia, probably because of a decrease in B6 vitamin levels. There is a proportional effect between the number of cigarettes smoked, B6 depletion and basal homocysteinemia increase. This study suggests that B6 vitamin supplements for smokers could decrease the vascular risk related with smoking habits.

Adverse Effects of Second-Hand Tobacco Smoke with Special Consideration to Beta Carotene

Free Radic Biol Med. 2009 Jan 15;46(2):299-304. Epub 2008 Oct 31.

Beta-carotene metabolites enhance inflammation-induced oxidative DNA damage in lung epithelial cells.

van Helden YG, Keijer J, Knaapen AM, Heil SG, Briedé JJ, van Schooten FJ, Godschalk RW.

Source

Department of Health Risk Analysis and Toxicology, Research Institute NUTRIM, Maastricht University, 6200MD Maastricht, The Netherlands.

Abstract

beta-Carotene (BC) intake has been shown to enhance lung cancer risk in smokers and asbestos-exposed subjects (according to the ATBC and CARET studies), but the mechanism behind this procarcinogenic effect of BC is unclear. Both smoking and asbestos exposure induce an influx of inflammatory neutrophils into the airways, which results in an increased production of reactive oxygen species and formation of promutagenic DNA lesions. Therefore, the aim of our study was to investigate the effects of BC and its metabolites (BCM) on neutrophil-induced genotoxicity. We observed that the BCM vitamin A (Vit A) and retinoic acid (RA) inhibited the H(2)O(2)-utilizing enzyme myeloperoxidase (MPO), which is released by neutrophils, thereby reducing H(2)O(2) conversion. Moreover, BC and BCM were able to increase (.)OH formation from H(2)O(2) in the Fenton reaction (determined by electron spin resonance spectroscopy). Addition of Vit A and RA to lung epithelial cells that were co-incubated with activated neutrophils resulted in a significant increase in the level of oxidized purines assessed by the formamidopyrimidine DNA glycosylase-modified comet assay. These data indicate that BCM can enhance neutrophil-induced genotoxicity by inhibition of MPO in combination with subsequent increased formation of hydroxyl radicals.