UPDATE HEAVY METAL ATHEROSCLEROSIS 2013

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Int J Occup Med Environ Health. 2009;22(2):135-42. doi: 10.2478/v10001-009-0017-4.

The dependence between urinary mercury concentration and carotid arterial intima-media thickness in workers occupationally exposed to mercury vapour.

Skoczyńska A, Poreba R, Steinmentz-Beck A, Martynowicz H, Affelska-Jercha A, Turczyn B, Wojakowska A, Jedrychowska I.

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Abstract

OBJECTIVES: Mechanisms of the mercury effect on arterial vessel walls include increased free radicals generation, decreased nitric oxide synthesis and increased reactivity to vasoconstrictors, leading to accelerated development of atherosclerosis and arterial hypertension. The aim of this study was to evaluate the correlation between urinary mercury (Hg-U) concentration and carotid intima-media thickness (IMT) or intraventricular septum diastolic diameter (IVSDD) to find the best markers of mercury cardiovascular toxicity.

MATERIALS AND METHODS: The study included 154 workers of a chemical factory using mercury in chlorine production. Urinary mercury concentration was determined by atomic absorption spectrophotometry. Serum lipids were assessed by routine methods using enzymatic assay. Serum total antioxidant status (TAS) was determined by colorimetry. Measurements of IMT and IVSDD were made by ultrasound imaging using MEDISON SA 9900 PRIME system.

RESULTS: The mean Hg-U concentration was 1.9+/-2.7 microg/g creatinine in women (n = 29) and 5.6+/-12.2 microg/g creatinine in men (n = 125). In the group of non-smokers (n = 102) there was a positive linear correlation between Hg-U concentration and IMT ($r = 0.1728$; $p < 0.05$) and a negative dependence between high density cholesterol (HDL-C) and IMT ($r = -0.2109$; $p < 0.01$). The negative linear correlation between serum total antioxidant status (TAS) and carotid IMT ($r = -0.2142$; $p < 0.05$), and the positive correlation between HDL-C and TAS ($r = 0.1953$; $p < 0.05$) were shown to be valid for the total studied group. Serum lipids in women were normal, but in men the mean triglyceride level was higher than normal.

CONCLUSIONS: The occupational exposure to mercury vapour remains in a relationship with early, asymptomatic carotid atherosclerosis. The dependence between urinary mercury elimination and carotid intima-media thickness is evidenced in non-smoking workers. Defensive anti-atherosclerotic mechanisms in these workers are strongly related with HDL. In smokers, these protective mechanisms are disturbed.

PMID: 19617193 [PubMed - indexed for MEDLINE]

Neurotoxicology. 2009 Nov;30(6):876-80. doi: 10.1016/j.neuro.2009.07.004. Epub 2009 Jul 16.

Association of high body lead store with severe intracranial carotid atherosclerosis.

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Abstract

OBJECTIVE: Lead is involved in the pathogenesis of atherosclerosis and hypertensive disease and may be related to cerebrovascular disease. We studied the association of body lead level with stroke subtypes and severity of cerebral atherosclerosis in order to identify the significance of lead exposure to cerebrovascular disease.

METHODS: From April, 2002 to March, 2005, we studied the lead level in all patients receiving digital subtraction angiography. Diameter stenosis at extracranial carotid, intracranial carotid and vertebrobasilar system was calculated according to the NASCET criteria. A blood sample and a mobilization test of 72-h urine sample were collected for lead measurement.

RESULTS: In a total of 213 subjects, 19 were free of stroke (blood lead level=4.62+/-2.41 microg/dL, body lead store=39.04+/-20.91 microg) and 194 were stroke patients (4.89+/-2.75 microg/dL, 45.13+/-29.8 microg; all stroke vs. non-stroke, P>0.05). In the 153 subjects with atherosclerotic origin, body lead store but not blood lead level in the intracranial carotid system was significantly higher in > or =50% group than <50% group (blood lead: 5.61+/-3.02 microg/dL vs. 4.80+/-2.50 microg/dL, Student's t-test, P=0.129; body lead store: 51.7+/-27.0 microg vs. 41.9+/-23.5 microg, Student's t-test, P=0.038, multivariate logistic regression, odds ratio=1.02, 95% CI: 1.00-1.03, P=0.043). However, there was no significant association between lead level and stenotic severity in extracranial and vertebrobasilar systems (P>0.05).

CONCLUSION: Our study demonstrated that long-term lead exposure as measured by body lead store might carry a potential risk of intracranial carotid atherosclerosis.

PMID: 19616024 [PubMed - indexed for MEDLINE]

Atherosclerosis. 2012 Jun;222(2):512-8. doi: 10.1016/j.atherosclerosis.2012.03.015. Epub 2012 Mar 22.

Reduced metal ion concentrations in atherosclerotic plaques from subjects with type 2 diabetes mellitus.

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Abstract

AIMS: Transition metal ions have been implicated in atherosclerosis. The goal of this study was to investigate whether metal ion levels were higher in people with diabetes, in view of their increased risk of aggravated atherosclerosis.

METHODS AND RESULTS: Absolute concentrations of iron, copper, zinc and calcium, and products of protein and lipid oxidation were quantified in atherosclerotic lesions from subjects with (T2DM, n=27), without Type 2 diabetes (nonDM, n=22), or hyperglycaemia (HG, n=17). Iron ($P<0.05$), zinc ($P<0.01$) and calcium ($P=0.01$) were lower in T2DM compared to nonDM subjects. Copper levels were comparable. A strong correlation ($r=0.618$; $P<0.001$) between EPR-detectable and total iron in nonDM patients was not seen in T2DM. X-ray fluorescence microscopy revealed "hot spots" of iron in both T2DM and nonDM. Calcium and zinc co-localised and levels correlated strongly. F(2)-isoprostanes ($P<0.05$) and di-Tyr/Tyr ratio ($P<0.025$), oxidative damage markers were decreased in T2DM compared to nonDM, or HG.

CONCLUSION: Advanced atherosclerotic lesions from T2DM subjects unexpectedly contained lower levels of transition metal ions, and protein and lipid oxidation products, compared to nonDM and HG. These data do not support the hypothesis that elevated metal ion levels may be a major causative factor in the aggravated atherosclerosis observed in T2DM patients.

PMID: 22521900 [PubMed - indexed for MEDLINE]

Sci Total Environ. 2012 Feb 1;416:80-8. doi: 10.1016/j.scitotenv.2011.11.064. Epub 2011 Dec 15.

Circulating levels of metals are related to carotid atherosclerosis in elderly.

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Abstract

The aim of this study was to investigate if blood levels of trace and/or heavy metals are related to atherosclerosis in a cross-sectional study in elderly. In the population-based Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study (1016 subjects, all aged 70), the prevalence of carotid artery plaques was recorded by ultrasound. The numbers of carotid arteries with plaques (0, 1 or 2) were recorded. Also the thickness (IMT) and gray scale (IM-GSM) of the intima-media complex were measured together with plaque echogenicity. Eleven heavy metals and trace elements were analyzed in whole blood, using inductively coupled plasma-sector field mass spectrometry. Nickel levels were related to the number of carotid arteries with plaques in an inverted U-shaped manner after multiple adjustment for gender, waist circumference, body mass index, fasting blood glucose, systolic and diastolic blood pressure, HDL and LDL cholesterol, serum triglycerides, smoking, antihypertensive treatment and statin use ($p=0.026$). IM-GSM and plaque echogenicity were both inversely related to chromium in a linear fashion, and to aluminum in an inverted U-shaped manner (both $p<0.0001$ for IM-GSM). The relationships between metals and IMT were modest. Circulating levels of some metals, like nickel, aluminum and chromium, were related to atherosclerotic plaques or the echogenicity of the IM-GSM and overt plaques independently of cardiovascular risk factors, including lipids.

PMID: 22178028 [PubMed - indexed for MEDLINE]

Ann Biomed Eng. 2012 Mar;40(3):697-706. doi: 10.1007/s10439-011-0434-y. Epub 2011 Oct 19.

Effect of zinc and nitric oxide on monocyte adhesion to endothelial cells under shear stress.

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Abstract

This study describes the effect of zinc on monocyte adhesion to endothelial cells under different shear stress regimens, which may trigger atherogenesis. Human umbilical vein endothelial cells were exposed to steady shear stress (15 dynes/cm(2) or 1 dyne/cm(2)) or reversing shear stress (time average 1 dyne/cm(2)) for 24 h. In all shear stress regimes, zinc deficiency enhanced THP-1 cell adhesion, while heparinase III reduced monocyte adhesion following reversing shear stress exposure. Unlike other shear stress regimes, reversing shear stress alone enhanced monocyte adhesion, which may be associated with increased H(2)O(2) and superoxide together with relatively low levels of nitric oxide (NO) production. L-N(G)-Nitroarginine methyl ester (L-NAME) treatment increased monocyte adhesion under 15 dynes/cm(2) and under reversing shear stress. After reversing shear stress, monocyte adhesion dramatically increased with heparinase III treatment followed by a zinc scavenger. Static culture experiments supported the reduction of monocyte adhesion by zinc following endothelial cell cytokine activation. These results suggest that endothelial cell zinc levels are important for the inhibition of monocyte adhesion to endothelial cells, and may be one of the key factors in the early stages of atherogenesis.

PMID: 22009315 [PubMed - indexed for MEDLINE] PMCID: PMC3288779 **Free PMC Article**

Int Urol Nephrol. 2012 Oct;44(5):1487-92. doi: 10.1007/s11255-011-0055-2. Epub 2011 Sep 9.

Serum cadmium levels are independently associated with endothelial function in hemodialysis patients.

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Abstract

OBJECTIVE: Hemodialysis (HD) patients are at risk of deficiency of essential trace elements and excess of toxic trace elements. The aim of the study was to evaluate the relation between the serum levels of some trace elements and heavy metals (iron, zinc, manganese, copper, magnesium, cobalt, cadmium, and lead) and endothelial function in HD patients.

METHODS: Forty-eight chronic HD patients without known atherosclerotic disease and 42 age- and sex-matched healthy individuals were included in the study. The serum levels of trace elements (iron, zinc, manganese, copper, and magnesium) and heavy metals (cobalt, cadmium, and lead) were measured by Atomic Adsorption Spectrophotometer (UNICAM-929).

RESULTS: The serum levels of iron, zinc, and manganese were lower, and levels of copper, magnesium, cobalt, cadmium, and lead were higher in HD patients compared to controls. Flow-mediated dilatation (FMD %) in HD patients was lower than that in the control group (7.27 ± 0.76 vs. 11.29 ± 0.82, $P < 0.001$). There was a significant negative correlation between FMD % and serum levels of cobalt ($r = -0.313$, $P = 0.03$) and cadmium ($r = -0.524$, $P < 0.01$). A linear regression analysis showed that serum cadmium levels were still significantly and negatively correlated with FMD % (regression coefficient = -0.526, $P < 0.001$).

CONCLUSION: We first demonstrated that serum cadmium levels independently predict endothelial function in HD patients without known atherosclerotic disease.

PMID: 21904850 [PubMed - indexed for MEDLINE]

J Clin Hypertens (Greenwich). 2011 Aug;13(8):621-7. doi: 10.1111/j.1751-7176.2011.00489.x. Epub 2011 Jul 11.

Role of mercury toxicity in hypertension, cardiovascular disease, and stroke.

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Abstract

Mercury has a high affinity for sulfhydryl groups, inactivating numerous enzymatic reactions, amino acids, and sulfur-containing antioxidants (N-acetyl-L-cysteine, alpha-lipoic acid, L-glutathione), with subsequent decreased oxidant defense and increased oxidative stress. Mercury binds to metallothionein and substitute for zinc, copper, and other trace metals, reducing the effectiveness of metalloenzymes. Mercury induces mitochondrial dysfunction with reduction in adenosine triphosphate, depletion of glutathione, and increased lipid peroxidation. Increased oxidative stress and reduced oxidative defense are common. Selenium and fish containing omega-3 fatty acids antagonize mercury toxicity. The overall vascular effects of mercury include increased oxidative stress and inflammation, reduced oxidative defense, thrombosis, vascular smooth muscle dysfunction, endothelial dysfunction, dyslipidemia, and immune and mitochondrial dysfunction. The clinical consequences of mercury toxicity include hypertension, coronary heart disease, myocardial infarction, cardiac arrhythmias, reduced heart rate variability, increased carotid intima-media thickness and carotid artery obstruction, cerebrovascular accident, generalized atherosclerosis, and renal dysfunction, insufficiency, and proteinuria. Pathological, biochemical, and functional medicine correlations are significant and logical. Mercury diminishes the protective effect of fish and omega-3 fatty acids. Mercury inactivates catecholaminei-0-methyl transferase, which increases serum and urinary epinephrine, norepinephrine, and dopamine. This effect will increase blood pressure and may be a clinical clue to mercury-induced heavy metal toxicity. Mercury toxicity should be evaluated in any patient with hypertension, coronary heart disease, cerebral vascular disease, cerebrovascular accident, or other vascular disease. Specific testing for acute and chronic toxicity and total body burden using hair, toenail, urine, and serum should be performed.

PMID: 21806773 [PubMed - indexed for MEDLINE]

Circ J. 2011;75(10):2491-5. Epub 2011 Jul 28.

Non-toxic cadmium concentrations induce vascular inflammation and promote atherosclerosis.

Knoflach M, Messner B, Shen YH, Frotschnig S, Liu G, Pfaller K, Wang X, Matosevic B, Willeit J, Kiechl S, Laufer G, Bernhard D.

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Abstract

BACKGROUND: Cadmium is a potential new risk factor for early atherosclerosis and cardiovascular diseases in humans, yet pathogenetic mechanisms are still a matter of debate.

METHODS AND RESULTS: In-depth histological analysis of 18 sections taken from 6 cadmium-fed ApoE-/- mice and 12 sections from 5 littermates not exposed to cadmium by light and scanning electron microscopy was performed. Cadmium-fed mice showed a marked increase in lesion load (plaque area) and severity as classified according to the American Heart Association vascular lesion grading. All inflammatory markers studied (CD68, CD3, CD25, vascular cell adhesion molecule 1 (VCAM-1), and heat shock protein 60 (Hsp60)) yielded a higher expression in cadmium-fed mice. Statistical difference was achieved for VCAM-1 and Hsp60 ($P=0.03$ and $P=0.02$). The shoulder region of atherosclerotic plaques in cadmium-fed mice showed a prominent retraction of endothelial cells on electron microscopy.

CONCLUSIONS: Our data indicate that cadmium exposure amplifies the development of vessel pathology in atherosclerosis susceptible ApoE-/- mice and suggests upregulation of VCAM-1 and Hsp60 and endothelial leakage as potential pathomechanisms.

PMID: 21799275 [PubMed - indexed for MEDLINE] **Free full text**

Biol Trace Elem Res. 2011 Dec;144(1-3):436-44. doi: 10.1007/s12011-011-9123-9. Epub 2011 Jul 1.

The relationship between serum levels of Zn and Cu and severity of coronary atherosclerosis.

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Abstract

The essential trace elements play important roles in the maintainance of the normal structure and physiology of cells. Several research groups have demonstrated that they also play important roles in states of cardiovascular diseases. Our aim is to investigate whether there is a relationship between trace elements (Zn and Cu) and the degree of atherosclerosis. The sample consisted of 67 patients with coronary artery disease and 26 clinically healthy individuals. Ninety-three subjects were separated into four groups according to their Gensini scores, the number of diseased vessels, the presence of acute coronary syndrome, and ejection fraction. Each group was divided into three subgroups, and serum zinc and copper levels were measured for each individual. The serum levels of zinc and copper were found to be significantly lower in patients with atherosclerosis than in the control group, but there were no significant differences in the serum levels of Cu and Zn between severe atherosclerosis and mild atherosclerosis. In Spearman's rank correlation, the zinc and copper levels were correlated with the Gensini score and the number of diseased vessels. The present study revealed a relationship between the serum levels of zinc and copper and atherosclerosis, but not between these levels and the severity of the disease.

PMID: 21720784 [PubMed - indexed for MEDLINE]

Biol Trace Elem Res. 2011 Dec;144(1-3):351-9. doi: 10.1007/s12011-011-9103-0. Epub 2011 Jun 7.

The correlation of serum trace elements and heavy metals with carotid artery atherosclerosis in maintenance hemodialysis patients.

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Abstract

Changes in essential trace elements and heavy metals may affect the atherosclerotic state of patients on maintenance hemodialysis (HD). The aim of the study was to evaluate the relation between the serum levels of some trace elements and heavy metals (iron, zinc, manganese, copper, magnesium, cobalt, cadmium, lead, and copper/zinc ratio) and carotid artery intima-media thickness (CIMT) in HD patients. Fifty chronic HD patients without known atherosclerotic disease and 48 age- and sex-matched healthy individuals were included in the study. The serum levels of trace elements (iron, zinc, manganese, copper, and magnesium) and heavy metals (cobalt, cadmium, and lead) were measured by Atomic Adsorption Spectrophotometer (UNICAM-929). CIMT was assessed by carotid artery ultrasonography. The serum levels of iron, zinc, and manganese were lower; levels of copper, magnesium, cobalt, cadmium, lead, and copper/zinc ratio were higher in HD patients compared to controls. CIMT in HD patients were higher than the control group (0.64 ± 0.11 vs 0.42 ± 0.05, $p < 0.001$). There was a significant negative correlation between CIMT and serum levels of zinc ($r = -0.70$, $p < 0.01$), iron ($r = -0.71$, $p < 0.01$), and manganese ($r = -0.47$, $p < 0.01$), while there was a significant positive correlation between CIMT and serum levels of copper ($r = 0.63$, $p < 0.01$), magnesium ($r = 0.77$, $p < 0.01$), cobalt ($r = 0.63$, $p < 0.01$), cadmium ($r = 0.48$, $p < 0.01$), lead ($r = 0.38$, $p < 0.01$), and copper/zinc ratio ($r = 0.68$, $p < 0.01$). A linear regression analysis showed that serum levels of magnesium, cadmium, lead, and copper/zinc ratio were still significantly and positively correlated with CIMT. We propose that copper/zinc ratio, magnesium and toxic metals cadmium and lead are independent determinants of CIMT in maintenance HD patients without known atherosclerotic disease.

PMID: 21647752 [PubMed - indexed for MEDLINE]

Am J Pathol. 2011 Jun;178(6):2879-87. doi: 10.1016/j.ajpath.2011.02.004. Epub 2011 Apr 30.

Microcalcifications in early intimal lesions of atherosclerotic human coronary arteries.

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Abstract

Although calcium (Ca) precipitation may play a pathogenic role in atherosclerosis, information on temporal patterns of microcalcifications in human coronary arteries, their relation to expression of calcification-regulating proteins, and colocalization with iron (Fe) and zinc (Zn) is scarce. Human coronary arteries were analyzed post mortem with a proton microprobe for element concentrations and stained (immuno)histochemically for morphological and calcification-regulating proteins. Microcalcifications were occasionally observed in preatheroma type I atherosclerotic intimal lesions. Their abundance increased in type II, III, and IV lesions. Moreover, their appearance preceded increased expression of calcification-regulating proteins, such as osteocalcin and bone morphogenetic protein-2. In contrast, their presence coincided with increased expression of uncarboxylated matrix Gla protein (MGP), whereas the content of carboxylated MGP was increased in type III and IV lesions, indicating delayed posttranslational conversion of biologically inactive into active MGP. Ca/phosphorus ratios of the microcalcifications varied from 1.6 to 3.0, including amorphous Ca phosphates. Approximately 75% of microcalcifications colocalized with the accumulation of Fe and Zn. We conclude that Ca microprecipitation occurs in the early stages of atherosclerosis, inferring a pathogenic role in the sequel of events, resulting in overt atherosclerotic lesions. Microcalcifications may be caused by local events triggering the precipitation of Ca rather than by increased expression of calcification-regulating proteins. The high degree of colocalization with Fe and Zn suggests a mutual relationship between these trace elements and early deposition of Ca salts.

PMID: 21531376 [PubMed - indexed for MEDLINE] PMCID: PMC3124018 **Free PMC Article**

Inhal Toxicol. 2010 Dec;22 Suppl 2:95-9. doi: 10.3109/08958378.2010.515269. Epub 2010 Oct 11.

Exposure to inhaled nickel nanoparticles causes a reduction in number and function of bone marrow endothelial progenitor cells.

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Erratum in
Inhal Toxicol. 2013 Mar;25(4):233.

Abstract

INTRODUCTION: Particulate matter (PM), specifically nickel (Ni) found on or in PM, has been associated with an increased risk of mortality in human population studies and significant increases in vascular inflammation, generation of reactive oxygen species, altered vasomotor tone, and potentiated atherosclerosis in murine exposures. Recently, murine inhalation of Ni nanoparticles have been shown to cause pulmonary inflammation that affects cardiovascular tissue and potentiates atherosclerosis. These adverse cardiovascular outcomes may be due to the effects of Ni on endothelial progenitor cells (EPCs), endogenous semi-pluripotent stem cells that aid in endothelial repair. Thus, we hypothesize that Ni nanoparticle exposures decrease cell count and cause impairments in function that may ultimately have significant effects on various cardiovascular diseases, such as, atherosclerosis.

METHODS: Experiments involving inhaled Ni nanoparticle exposures (2 days/5 h/day at ~1200 μg/m(3), 3 days/5 h/day at ~700 μg/m(3), and 5 days/5 h/day at ~100 μg/m(3)), were performed in order to quantify bone marrow resident EPCs using flow cytometry in C57BL/6 mice. Plasma levels of human stromal cell-derived factor 1α (SDF-1α) and vascular endothelial growth factor (VEGF) were assessed by enzyme-linked immunosorbent assay and in vitro functional assessments of cultured EPCs were conducted.

RESULTS AND CONCLUSIONS: Significant EPC count differences between exposure and control groups for Ni nanoparticle exposures were observed. Differences in EPC tube formation and chemotaxis were also observed for the Ni nanoparticle exposed group. Plasma VEGF and SDF-1α differences were not statistically significant. In conclusion, this study shows that inhalation of Ni nanoparticles results in functionally impaired EPCs and reduced number in the bone marrow, which may lead to enhanced progression of atherosclerosis.

PMID: 20936915 [PubMed - indexed for MEDLINE]

Inhal Toxicol. 2010 Dec;22 Suppl 2:95-9. doi: 10.3109/08958378.2010.515269. Epub 2010 Oct 11.

Exposure to inhaled nickel nanoparticles causes a reduction in number and function of bone marrow endothelial progenitor cells.

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PMID: 20936915 [PubMed - indexed for MEDLINE]

Exp Biol Med (Maywood). 2010 May;235(5):633-41. doi: 10.1258/ebm.2009.009229.

The iron chelator, desferrioxamine, reduces inflammation and atherosclerotic lesion development in experimental mice.

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Abstract

Vascular inflammation and monocyte recruitment are initiating events in atherosclerosis that have been suggested to be caused, in part, by iron-mediated oxidative stress and shifts in the intracellular redox environment of vascular cells. Therefore, the objective of this study was to investigate whether the intracellular iron chelator, desferrioxamine (DFO), reduces inflammation and atherosclerosis in experimental mice. Treatment of C57BL/6J mice with DFO (daily intraperitoneal injection of 100 mg/kg body weight for two weeks) strongly inhibited lipopolysaccharide-induced increases of soluble cellular adhesion molecules and monocyte chemoattractant protein-1 (MCP-1) in the serum and activation of the redox-sensitive transcription factors, nuclear factor-kappaB and activator protein-1, in the aorta. Furthermore, treatment of apolipoprotein E-deficient (apoE-/-) mice with DFO (100 mg/kg, intraperitoneal, daily for 10 weeks) attenuated aortic atherosclerotic lesion development by 26% ($P < 0.05$). DFO treatment of apoE-/- mice also lowered serum levels of MCP-1 and gene expression of proinflammatory and macrophage markers in the aorta and heart, in parallel with increased protein expression of the transferrin receptor in the heart and liver. In contrast, DFO treatment had no effect on serum cholesterol and triglyceride levels. These data show that DFO inhibits inflammation and atherosclerosis in experimental mice, providing the proof-of-concept for an important role of iron in atherogenesis. Whether eliminating excess iron is a useful adjunct for the prevention or treatment of atherosclerosis in humans remains to be investigated.

PMID: 20463304 [PubMed - indexed for MEDLINE] PMCID: PMC3057189 **Free PMC Article**

Am J Clin Nutr. 2010 Jun;91(6):1634-41. doi: 10.3945/ajcn.2009.28836. Epub 2010 Apr 28.

Zinc decreases C-reactive protein, lipid peroxidation, and inflammatory cytokines in elderly subjects: a potential implication of zinc as an atheroprotective agent.

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Abstract

BACKGROUND: Chronic inflammation and oxidative stress are common risk factors for atherosclerosis. Zinc is an essential micronutrient that can function as an antiinflammatory and antioxidative agent, and as such, it may have atheroprotective properties.

OBJECTIVE: We hypothesized that zinc down-regulates the production of atherosclerosis-related cytokines/molecules in humans.

DESIGN: To examine these effects, we conducted a randomized, double-blinded, placebo trial of zinc supplementation in elderly subjects. We recruited 40 healthy elderly subjects (aged 56-83 y) and randomly assigned them to 2 groups. One group was given an oral dose of 45 mg zinc/d as a gluconate for 6 mo. The other group was given a placebo. Cell culture models were conducted to study the mechanism of zinc as an atheroprotective agent.

RESULTS: After 6 mo of supplementation, the intake of zinc, compared with intake of placebo, increased the concentrations of plasma zinc and decreased the concentrations of plasma high-sensitivity C-reactive protein (hsCRP), interleukin (IL)-6, macrophage chemoattractant protein 1 (MCP-1), vascular cell adhesion molecule 1 (VCAM-1), secretory phospholipase A2, and malondialdehyde and hydroxyalkenals (MDA+HAE) in elderly subjects. Regression analysis showed that changes in concentrations of plasma zinc were inversely associated with changes in concentrations of plasma hsCRP, MCP-1, VCAM-1, and MDA+HAE after 6 mo of supplementation. In cell culture studies, we showed that zinc decreased the generation of tumor necrosis factor-alpha, IL-1beta, VCAM-1, and MDA+HAE and the activation of nuclear transcription factor kappaB and increased antiinflammatory proteins A20 and peroxisome proliferator-activated receptor-alpha in human monocytic leukemia THP-1 cells and human aortic endothelial cells compared with zinc-deficient cells.

CONCLUSION: These findings suggest that zinc may have a protective effect in atherosclerosis because of its antiinflammatory and antioxidant functions.

PMID: 20427734 [PubMed - indexed for MEDLINE] PMCID: PMC2869512

THANK YOU