REVIEW ARTICLE

Role of Toxic Metals such as Arsenic, Lead, Cadmium, Mercury, and Copper in Public Health and Cardiovascular Diseases: A Review

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ABSTRACT

The global nature of the toxic metal contamination, accurate characterization of the associations between toxic metals and cardiovascular disease is important to understand the etiology of cardiovascular disease and also to suggest public health efforts to reduce these toxic metal exposures in more effective manner. The purpose of the review was to find the role of arsenic, lead, cadmium, mercury, and copper in public health and cardiovascular disease. In summary, the arsenic, lead, cadmium, and copper are each associated with cardiovascular disease, while mercury was not significantly associated with cardiovascular disease risk.

Keywords: Arsenic, Cadmium, Cardiovascular disease, Copper, Lead, Mercury, Public health.

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BACKGROUND

Direct or indirect exposures to arsenic, lead, cadmium, mercury, and copper which are few main hydrogeological environmental toxic metals have become a major public health concern in past decade due to their potentially harmful health effects in peoples.[1] Arsenic is the world's second leading water-borne cause of mortality and cadmium is a Group I human carcinogens.[2] Long-term exposure to high levels of toxic metals such as cadmium and arsenic has been associates with higher risk of cancers of the bladder, kidney, liver, lung, and skin.[3] A review suggested that for cardiovascular disease, exposure to arsenic and other toxic metals may be an independent risk factor.[4] However, the correlation between the arsenic, lead, cadmium, mercury, copper, and the risk of cardiovascular disease remains less well characterized in clinical outcomes, despite their well-established role as immune toxicants and carcinogens.[5] Arsenic, lead, cadmium, and mercury have been included in the World Health Organization's list of 10 chemicals of major public health concern and have potential mechanistic links to cardiovascular disease.[6] The review was aim to find the role of arsenic, lead, cadmium, mercury, and copper in public health and cardiovascular diseases.

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METHOD

In this review, the literature search was done regarding the topic like the association between arsenic, lead, cadmium, mercury, and copper with cardiovascular diseases. The literature search was conducted using different electronic databases such as PubMed, MEDLINE, Embase, and EBSCOhost. The keywords were used such as "Arsenic;" "Cadmium;" "Cardiovascular disease;" "Copper;" "Coronary heart disease;" "Lead;" "Mercury;" and "Toxic metals," and the articles published in the different journals were obtained.

Arsenic and Health Effects

Arsenic is a widely distributed metalloid, occurring in water, rock, soil, and air.[7] Smelting of non-ferrous metals and the production of energy from fossil fuel are the two major industrial processes that lead to arsenic contamination of soil, water, and air, smelting activities being the largest single anthropogenic source of atmospheric pollution.[8] Inorganic arsenic is acutely toxic and intake of large quantities leads to gastrointestinal symptoms, severe disturbances of the cardiovascular

and central nervous systems, and eventually death.[9] However, the relevant relationships between arsenic exposure and health effects are not completely clear. There is relatively strong evidence for hypertension and cardiovascular disease, but the evidence is only suggestive for diabetes and reproductive effects and weak for cerebrovascular disease, long-term neurological effects, and cancer at sites other than lung, bladder, kidney, and skin.[9]

Lead and Health Effects

Lead in blood is bound to erythrocytes, and elimination is slow and principally through urine. Lead is accumulated in the skeleton and is only slowly released from this body compartment.[10] Individuals with average blood lead levels under 3 μmol/l may show signs of peripheral nerve symptoms with reduced nerve conduction velocity and reduced dermal sensibility. If the neuropathy is severe, the lesion may be permanent; for distinct example, a dark blue lead sulfide line at the gingival margin.[1] Despite intensive efforts to define the relationship between body burden of lead and blood pressure or other effects on the cardiovascular system, no causal relationship has been demonstrated in patients.[11]

Cadmium and Health Effects

Cigarette smoking is the most important source of cadmium exposure and it may cause significant increases in blood cadmium (B-Cd) levels, the concentrations in smokers being on average 4–5 times higher than those in non-smokers.[12] Despite evidence of exposure from environmental tobacco smoke, however, this is probably contributing little to total cadmium body burden.[13] Food is a major source of cadmium exposure in the general non-smoking population.[14] B-Cd generally reflects current exposure, but partly also lifetime body burden.[15] The high risk of cardiovascular mortality in cadmium-exposed persons with signs of tubular kidney damage compared to persons without kidney damage.[16] The International Agency for Research on Cancer has classified cadmium as a human carcinogen – Group I on the basis of sufficient evidence in both humans and experimental animals.[17]

Mercury and Health Effects

Under particular environmental conditions, inorganic mercury can be transformed into the most toxic form of mercury and methyl mercury.[18] The use of mercury is a cure for syphilis, mercury compounds have also been used as diuretics, and mercury amalgam is still used for filling teeth in many countries all over the world.[19] The general population is primarily exposed to mercury through food, fish a major source of methyl mercury exposure, and dental amalgam.[20] It has shown that mercury vapor is released from amalgam fillings and that the release rate may increase by chewing.[21] However, there is not enough human exposure data to make links between mercury and cancer.[22] Methyl mercury poisoning has a latency of a month or longer after acute exposure, and the main symptoms relate to nervous system damage.[23] Whereas, a high dietary intake of mercury from consumption of fish has been hypothesized to increase the risk of coronary heart disease.[24] Another study investigated the association between mercury levels in toenails and the risk of coronary heart disease among male health professionals. Mercury levels were significantly correlated with fish consumption, and the mean mercury level was higher in dentists than in non-dentists. When other risk factors for coronary heart disease had been controlled for, mercury levels were not significantly associated with the risk of coronary heart disease.[25]

Copper and Health Effects

Copper is an essential trace element, which is an important catalyst for heme synthesis and iron absorption. Chronic copper toxicity is rare and primarily affects the liver. Wilson's disease and Indian childhood cirrhosis are examples of severe chronic liver disease that results from the genetic predisposition to the hepatic accumulation of copper. The serum copper concentration ranges up to approximately 1.5 mg/L in healthy persons, whereas gastrointestinal symptoms occur at whole blood concentrations near 3 mg/L. However, chelating agents are recommended in severe poisoning, but there are little pharmacokinetic data to evaluate the effectiveness of these agents.[26]

Cardiovascular Diseases

The environment is a major determinant of stroke and ischemic heart disease as ambient and household air pollution are estimated to cause 13% and 17% of cardiovascular diseases, respectively; and around 3% of cardiovascular diseases are attributed to second hand smoke and 2% to lead.[27] The other environmental exposures and workplace risks increase the risk of cardiovascular diseases, including arsenic in drinking water, high noise levels, stressful working conditions, and shift work.[28]

DISCUSSION

The studies done by Mitchell *et al*.[29] and Singh *et al*.[30] stated that there was a positive association of arsenic found in large quantities in rice and groundwater in

many parts of the world and associated with the risk of coronary heart disease. The epidemiological study was done by Tseng *et al*.[31] reported striking associations with Blackfoot disease, which is a severe peripheral vascular disease, in people exposed to extremely high cumulative doses of arsenic. A study also observed a positive association between levels of cadmium and cardiovascular disease, which was independent of several potential risks of cardiovascular disease factors.[5] One of the studies showed a positive association of copper with cardiovascular disease.[32] Moreover, the mechanism for the potentially deleterious effects of copper is through a copper-homocysteine complex which has been suggested to induce endothelial dysfunction and vascular injury.[33] Moreover, a study has observed inverse relations between mercury levels and the risk of cardiovascular disease, but there is no accepted biological explanation that supports such a link.[5] More extensive systematic reviews to be needed to better characterize these associations and to assess causality in humans.

Public Health Significance

The different study findings highlighted the importance of environmental toxic metals in enhancing cardiovascular risk, beyond the roles of conventional behavioural risk factors such as tobacco use and unhealthy diet. The global non-communicable disease prevention strategies are focused mainly on tackling behavioral determinants. Although, recognizing environmental factors such as toxic metals, as additional priorities, therefore, will help gain wider sociopolitical support for setting up appropriate legislation, preventive strategies and standards, and investment to tackle these major global determinants of cardiovascular diseases. Primary prevention by developing evidence-based public health guidelines and innovative low cost, scalable interventions to reduce human exposure should be prioritized.

CONCLUSION

The arsenic, lead, cadmium, and copper are each associated with cardiovascular disease. By contrast, mercury was not significantly associated with cardiovascular risk.

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