Effect of high intake of heavy metals from environmental air and in food in diabetic patients

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Abstract

Diabetes mellitus is an endocrine disorder and affecting millions of people. It remains latent and its secondary obstacles lead to the mortality and morbidity. Various metal such as arsenic, beryllium, cadmium and nickel have been linked with the occurrence of diabetes mellitus in peoples exposed to these elements. Some elements like iron and copper are crucial minerals that are necessary for a variety of molecules to maintain their normal structures, functions of cells to existence, grow, and multiply. The homeostasis of iron and copper is coordinated regulation by different proteins concerned in uptake, excretion and intracellular storage or transferring. This study connected airborne levels of these metals with diabetes mortality. The lowest air levels detected were beryllium and cadmium, with nickel showing the highest levels. This supported diabetes mortality effects of air pollution and correlating arsenic, beryllium, cadmium and nickel with diabetes incidence. Although iron is essential but it can be toxic in high amounts. Iron is a transit mineral can generate various reactive oxygen or nitrogen species so abnormal metabolism of iron can lead to numerous chronic pathogenesis. Oxidative stress is one of the main contributing factors for diabetes and diabetic problems. Iron overload may increases risks of insulin resistance and diabetes.
relationship between high urinary levels of cadmium with impaired glucose tolerance [14]. The evidence supporting the link between cadmium exposure and diabetes, finding that cadmium reduces insulin levels, is directly cytotoxic to the pancreas and may be a factor in development of this disease [15]. Potentially connecting cadmium to diabetes mortality, cadmium is likely toxic to nerve terminals, and thus may exacerbate complications from this disease[16]. The nickel effect on diabetes mellitus has bit inconsistent. Nickel is known to avert the development of streptozotocin-induced diabetes in rats and preventing hyperglycemia [21,22]. Additionally, no relationship between nickel blood levels and humans [22]. Nickel is also found in the cytosol and, in concert with nitric oxide, nickel can induce hyperglycemia in rats [8].

Minerals and trace elements may exert protective or scavenging effects, as well as being essential components of several key enzymes in intracellular antioxidant defense [25]. Their deficiency, or excess, may contribute to derangement of the pro-oxidant/anti-oxidant balance, and hence to the progressive appearance of secondary complications as the disease advances. Both type I and II diabetes are accompanied by alterations in micronutrient absorption, tissue uptake, and excretion, some in a time-dependent fashion. A major effect of these changes may be a worsening of the oxidative balance, with declining capability to combat endogenously produced free radicals. Macro and microelements are involved in the complex processes of development of the secondary complications of diabetes mellitus affecting many organs. They may be integral components of antioxidative enzymes (e.g., Cu, in case of superoxide dismutase, and Se for Glutathione peroxidase), cofactors in a variety of enzymatic processes of importance in glucose and lipid metabolism (e.g., Cu), or potential pro-oxidant catalysts (e.g., Cu, Fe). The etiology of diabetes and its complications still is not clear, however several factors as aging, obesity and oxidative damage have been implicated. Several micronutrients have beneficial effects in healthy subjects and also in diabetes [26,27]. Copper, iron and manganese are important components of metalloenzymes such as Se-cys containing glutathione peroxidase, Cu/Fe cytochrome C oxidase and/or different types of superoxide dismutases, all of them imperative in intra- and extra-cellular antioxidant defense [28]. Copper is found in the liver, gallbladder, lungs and heart. It is essential primarily for the absorption and metabolism of iron. A deficiency in copper results in the same effects as an iron deficiency, such as retarded hemoglobin production, general debility, limited growth, etc. Some sources have estimated about 2 milligrams per day. Very few cases of copper depletion have been observed in humans. Copper is needed for synthesis of hemoglobin, proper iron metabolism, and maintenance of blood vessels. Copper is an integral part of the enzyme copper-zinc superoxide dismutase (CuZn SOD); also present in other enzymes, including cytochrome oxidase, ascorbic acid oxidase, and tyrosinasases. It is usually found in the red blood cells, and in blood plasma. The chief supplementary sources of copper are seafood, nuts, legumes, green leafy vegetables. Insufficient copper has been associated with changes in hair colour & texture, and hair loss; disturbances to the nervous system; bone diseases. Serious deficiency is rare but can lead to: Menke's syndrome. Copper has been shown to be elevated in experimentally induced diabetes in rats [29]. Iron status is little affected by diabetes per se; however, because of its role as a catalyst in free radical generation, and the given state of increased oxidant stress in diabetes, it is probably advisable for diabetic individuals to avoid excess iron. Hence, this present research is mainly focused on the role of the following essential trace elements in Type I DM and Type II Diabetes mellitus conditions: iron, selenium, copper, chromium, vanadium and molybdenum. Interactions between these trace elements and hyperglycemia are also briefly considered. Epidemiologic data on the relationship between many of the trace elements and the incidence of diabetes and hypertension are incomplete. Most such studies have focused on cadmium, chromium, and selenium. Furthermore, most of the evidence is not related to dietary exposure but focuses, for example, on inhalation exposure in the workplace. The biochemical role for copper is primarily catalytic, with many copper metalloenzymes acting as oxidases to achieve the reduction of molecular oxygen. Many copper metalloenzymes have been identified in humans [30]. Ferric oxidases are copper enzymes found in plasma, with a function in ferrous iron oxidation (Fe²⁺→Fe³⁺) that is needed to achieve iron's binding to transferring [31]. Ferric oxidase I, also called ceruloplasmin, is the predominant copper protein in plasma and may also have antioxidative functions. Defects in ceruloplasmin function produce metabolites in rats in extract, in concert with nitric oxide, nickel can induce hyperglycemia in rats [8].
Since iron is a reactive metal ion that is known to catalyze damage to cellular macromolecules caused by oxygen radicals, its reduction from Fe$^{3+}$ to the Fe$^{2+}$ state plays a major role in lipid peroxidation process. As the concentration of iron increases, it finally accumulates in the liver. Ferritin, an iron storage protein may function as a source of iron for promotion of superoxide-dependent lipid peroxidation [39]. The small size of O$_{2}^{-}$, which is generated by xanthine oxidase in conjunction with its ability to reduce chelated iron, suggests that it is an excellent candidate for the mobilization of iron from ferritin. All parenterally administered iron in excess of the ferritin storage mechanism accumulates in the liver as hemosiderin. Thus the amount of iron in the serum of the diabetic patients might be either due to increased release of iron from the body storage depot into the systemic circulation or to attenuation in the process of storage related to oxidative stress. Evidence linking iron to diabetic nephropathy includes

1) Animal and epidemiological investigations,  
2) Researches in which an increased amount of iron has been demonstrated in the kidneys of both animals [40,41] and humans [42] with kidney disease,  
3) Evidence for higher urinary iron in patients with diabetic nephropathy, and  
4) The inhibition of progression either by an iron-deficient diet or agents that bind and eliminate iron (chelators) [43-45].

Earlier experimental investigations offer extensive proof for the role of iron and oxidants in the pathogenesis of diabetic nephropathy [46-50]. Oxidative stress from factors such as hyperglycemia, advanced glycation end products, and dyslipidemia contribute to the obtainability of intracellular iron that can produce and viciously worsen oxidative deterioration and renal damage. Iron content in the kidney has been demonstrated to be amplified in an animal model of diabetes [51], and urinary iron excretion is elevated early in the course of diabetic renal disease in humans [50,52]. There is substantial proof that, once renal insufficiency progresses, irrespective of etiology, it inclines to headway over time. This has been interpreted to show certain common pathways for development of kidney disorders. Most notably, the pathogenic part of iron in progression is indicated by the observation that development can be prohibited either by an iron-deficient diet or chelators [43-45].

A current randomized trial involving 191 patients with diabetes, proteinuria, and a decreased glomerular filtration rate exhibited that a low-iron-available, carbohydrate-restricted, polyphenol-enriched diet compared with a standard protein-restricted diet had a renoprotective activity [53]. Epidemiologic investigations [54-56] in explicit iron overload states such as transfusional iron overload and hemochromatosis have indicated that the incidence of coronary heart disease is increased [57] and that dietary intake with iron chelation recovers cardiovascular outcome. Likewise, numerous researches have indicated a direct connotation between higher iron intake, body iron reservoirs, and cardiovascular jeopardy in the general population. Elevated intake of heme iron is related with augmented cardiovascular events [58-60], and increased body iron stores are linked with myocardial ischemia in a prospective epidemiological investigation [62]. Reliable and sensitive methods need to be developed to precisely measure the free/catalytic iron that participates in oxidative injury. Iron chelation therapy may present a novel way to interrupt the cycle of catalytic iron-induced oxidative stress and tissue injury and consequent release of catalytic iron in diabetes and to prevent diabetes-related complications.

Copper has been known to be essential for health for more than three quarters of a century. Copper functions as a component of a number of metalloenzymes acting as oxidases to achieve the reduction of molecular oxygen. The primary criterion used for copper is a combination of indicators, including plasma copper and ceruloplasmin concentrations, erythrocyte superoxide dismutase activity, and platelet copper concentration in controlled human depletion/repletion studies [63]. There was a significant elevation observed in serum copper content in Type I and Type II diabetic patients as compared to normal controls. There is a significant increase in the levels of copper in type 1 DM subjects when compared to healthy control subjects. There is significant increase in the levels of copper in type 2 DM subjects when compared to healthy control subjects. There is significant increase in the levels of copper in type 1 DM subjects when compared to type 2 DM subjects. Elevated level of copper in type I and type II diabetes mellitus is a major risk factor for the incidence of cardiovascular disease [64]. Diabetic patients with vascular complications have higher plasma copper levels than diabetic patients without complications or normal controls [64]. Patients with the amount of iron in the serum of the diabetic patients might be either due to increased release of iron from the body storage depot into the systemic circulation or to attenuation in the process of storage related to oxidative stress. Evidence linking iron to diabetic nephropathy includes

2. Discussion

This study has found an association between heavy metals arsenic, beryllium, cadmium and nickel air contaminants and age adjusted diabetes mellitus mortality rates. Although associations between these heavy metals arsenic, beryllium, cadmium and nickel and diabetes prevalence by the high concentrations of these heavy metals in the diabetic patient and increase in diabetes mortality. Hazardous air pollutants-including arsenic, beryllium, cadmium and nickel-an analysis of these elements’ concentrations based might start to mitigate diabetes death for pollutants [70,71]. It is important to note that these results are subject to a number of limitations. First, although this study con-trolled for many county-level risk factors for
diabetes, it could not control for other confounders. Such factors might include county level obesity and heart disease rates. Additionally this analysis was unable to control for other environmental toxins known to be associated with diabetes (e.g., chromium), nor is it known the sources from which these toxins are released. In addition, since ecological studies compare data at the population level, these results cannot be extrapolated down to the individual level. For example, it could be that no person with diabetes who died in a specific county was ever exposed to these elevated environmental toxins. In spite of the great amount of work that has been done on the relationships between trace elements and diabetes, the evidence is still fragmentary. The nature of the correlations—whether it is a cause-to-effect relationship or simply a statistical association—is still unknown. The mechanisms of action are also poorly understood. Further clinical investigations are needed to elucidate these problems, and hence the present study has been taken as a contribution to the research activities in this field with special emphasis on role of minerals in influencing the metabolic homeostasis in Type I and Type II diabetes [71].

3. Conclusion

There is suggestive evidence that iron and copper plays a pathogenic role in diabetes and its complications such as microangiopathy and atherosclerosis. Reliable and sensitive methods need to be developed to precisely measure the free/catalytic iron and copper that participates in oxidative injury. Hence measures need to be developed to precisely measure the free/catalytic iron and copper levels in early age may help to predict the onset of diabetes and its secondary complications which may postpone the diabetes.

References

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