Update Article

Clinical Aspects of Chronic Arsenic Toxicity

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Humans are exposed to arsenic (As) primarily from air, food and water. Drinking water may be contaminated with As from arsenical pesticides, natural mineral deposits or improperly disposed arsenical chemicals. Elevated As levels in drinking water is the major cause of As toxicity in the world. Reports of such contamination are available from Taiwan, Chile, China, Argentina, Mexico, India, Hungary, Bangladesh, USA and Thailand. However, largest number of people in the world affected from chronic As toxicity due to drinking of As contaminated ground water belongs to Bangladesh, India and China. Data derived from various studies show that inorganic As adversely affect multiple organ systems of human body.[1]

Biochemical effect and cellular mechanism of As toxicity have been frequently reviewed. In 1925, Voegtlin demonstrated that the sulfhydryl (SH) groups within cells were receptors for trivalent As. He also showed that glutathione and other sulfhydryl containing chemicals prevented the toxic effects of As. Voegtlin postulated toxic reversible interaction of arsenite (As III) with the SH groups of glutathione in cells or with other SH groups occurring in cell protoplasm.[2] This conclusion has been supporting the concept that the major toxic action of trivalent arsenicals is their interaction with thiol groups.[3] The biologic toxic action of As is due to more functional activity than to any damage to the structural integrity of the tissues. Arsenite inhibits number of thiol dependent enzymes in exerting its toxic effects, arsenite is thought to combine with SH groups and inhibit about 100 different enzymes. It has been shown that the SH groups decrease in whole blood after exposure to arsenite. Arsenic binds to two thiol groups per molecule to form stable ring compounds, in preference to reacting with two thiol groups of two separate molecules.[4] After prolonged feeding of As contaminated water (3.2 mg/l) in mice, increased lipid peroxidation and plasma membrane damage in association with reduction of hepatic glutathion and enzymes of anti oxidant defense system (G6PDH, GPx, GST and GR) were observed by Santra *et al*.[5] According to Casarett and Doul (1986),[6] mitochondria accumulate As. Respiration mediated by NAD linked substrates is particularly sensitive to As. The most As sensitive enzymes are those which are not reactivated by simple monothiol compounds. These sensitive enzymes includes lipoic acid dehydrogenase and the oxidases which use lipoic acid as coenzymes. For these enzyme systems, 2, 3-dimercapto propanol and dithiol compunds are far more effective in reversing the action of As. The As sensitive enzymes have been found to contain vicinal SH groups which can form stable five or six membered rings when bound to monosubstituted As. Disruption of oxidative phosphorylation and concomitant decreases in cellular levels of ATP[7] are thought to be important central events in the onset of cellular injury and death, in arsenic intoxication because ultrastructural morphometric alterations in mitochondrial structure, and disruption of mitochondrial respiratory function, are closely correlated.

Most of the reports of chronic As exposure in man focus attention on skin manifestations because of their diagnostic specificity. Data derived from population based studies, clinical case series and reports relating to intake of inorganic As in drinking water, medications or occupational and environmental exposure show its capacity to adversely affect multiorgan system. The clinical appearance of the non carcinomatous manifestations of As intoxication in humans is dependent on the magnitude of the dose and the time course of its exposure.

Protean clinical manifestations have been described by Guha Mazumder *et al*[8-11] on the basis of detail clinical and relevant investigations (with individual As exposure data) on people drinking As contaminated water in seven affected districts of West Bengal, India.

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