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Oxidative stress in liver of mice exposed to arsenic-contaminated water

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Background: Oxidative stress has been implicated in the initiation of hepatic damage caused by various agents. Not much data on oxidative stress in liver in chronic arsenic exposure are available in the literature. We therefore studied this aspect in a murine model. **Methods:** BALB/c mice were given arsenic-contaminated (3.2 mg/L) or arsenic-free (<0.01 mg/L, control) drinking water *ad libitum*. Batches of mice were sacrificed after 2 and 4 months, and blood samples and liver tissue were collected. Liver histology was examined and levels of hepatic reduced glutathione (GSH), malondialdehyde, and enzymes of the antioxidant defense system in the liver tissue were determined. Arsenic content in liver tissues obtained at 4 months was estimated. **Results:** Two-month exposure to arsenic caused significant elevation of hepatic GSH (11.4 [0.8] µg/mg protein) compared to control mice (9.3 [0.4]; $p<0.01$). Levels of enzymes related to GSH homeostasis were also elevated. At 4 months, hepatic GSH was significantly reduced (8.4 [0.5] µg /mg protein) when compared to control mice (9.3 [0.4]; $p<0.01$). Arsenic content in the liver tissue after 4 months of exposure was significantly higher (0.40 [0.05] µg /g) as compared to control mice (0.04 [0.04]; $p<0.01$). **Conclusion:** The results suggest that the antioxidant defense system in the liver of mice is activated after exposure to arsenic for 2 months. However, prolonged exposure to arsenic probably causes overuse failure of this system, which might result in initiation of biochemical injury to the liver. [*Indian J Gastroenterol* 2000;19:112-115]

Key words: Antioxidants

Arsenic contamination of subsoil drinking water and consequent chronic arsenic toxicity is a major public health problem in eight districts of West Bengal.[1] Although such an environmental health problem has been reported from various parts of the world,[2,3,4] the largest has involved vast areas of West Bengal and Bangladesh.[5,6] The source of such contamination is geological. The arsenic content of most drinking water sources in these areas exceeds the WHO permissible limit of 50 µg /L.

Prolonged arsenic ingestion leads to hepatic fibrosis and non-cirrhotic portal hypertension.[7,8] Although described for nearly a century, the mechanism of arsenic-induced liver injury remains elusive.

In several animal models, free radical-mediated oxidative stress has been shown to be responsible for hepatocellular injury and hepatic fibrosis, in particular those induced by CCl_4[9] and ethanol.[10] Free radicals have also been proposed to be involved in the liver damage caused by excess deposition of iron[11] and copper.[12] Previously, we have shown that feeding arsenic for prolonged periods in mice caused perturbation of the enzymes involved in the antioxidant defense system, resulting in depletion of hepatic GSH and elevation of lipid peroxidation. This, in turn, produced hepatocellular injury and eventually fibrosis.[13] Based on this information, we hypothesized that oxidative stress may play an important role in the genesis of hepatic damage that results from chronic arsenic exposure.

In the present communication, we present data on the initial biochemical events in relation to oxidative stress following administration of arsenic for short duration.

Methods

Arsenic-contaminated subsoil drinking water was collected from a well that had been used as a drinking water source for many years by a family, several members of which manifested clinical features of arsenic toxicity. Total arsenic content of the water was measured spectrophotometrically using Ag-DDTC in $CHCl_3$ with hexamethylene tetramine[14] and the proportions of arsenite (As III) and arsenate (As V) were determined.[15] The water sample was preserved at -20°C for the study.

Inbred BALB/c mice (7-8 weeks old, weighing 20 - 22 g) were maintained on standard laboratory chow at a constant temperature and humidity environment in 12-hour light-dark cycles. All animal experiments were approved by the institution and were performed in accordance with local institutional guidelines for the care and use of laboratory animals.

The mice were divided into two groups. The experimental group was provided with the arsenic-contaminated water (3.2 mg/L) *ad libitum* while the control group was provided arsenic-free water (<0.01 mg/L). The mice