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Effect of arsenic acid withdrawal on hepatotoxicity and disruption of erythrocyte antioxidant defense system

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ABSTRACT

We investigated the effects of withdrawal from Sodium arsenite ($NaAsO_2$) on the hepatic and antioxidant defense system in male Wistar rats using a before and after toxicant design. Rats were orally gavaged daily with varying doses of $NaAsO_2$ for a period of 4 weeks. One half of the population was sacrificed and the remaining half had the toxicant withdrawn for another further 4 weeks. Biochemical and immunohistochemical techniques were used to assess the impact of withdrawal on the erythrocyte and hepatic systems. Exposure of Wistar rats to $NaASO_2$ led to a significant ($p < 0.05$) increase in hepatic and erythrocyte markers of oxidative stress (malondialdehyde, thiol contents and hydrogen peroxide generation). Concurrently, there was a significant ($p < 0.05$) increase in hepatic and erythrocyte antioxidant enzymes (glutathione-S-transferase, glutathione peroxidase and superoxide dismutase) following exposure. Withdrawal from $NaAsO_2$ exposure led to a decline in both erythrocyte and hepatic markers of oxidative stress and together with a significant improvement in antioxidant defense system. Histopathology and immunohistochemistry revealed varying degrees of recovery in hepatocyte ultrastructure alongside increased expression of the pro-survival protein Kinase B (Akt/PKB) after 4 weeks of $NaAsO_2$ withdrawal. Conclusively, withdrawal from exposure led to a partial recovery from oxidative stress-mediated hepatotoxicity and derangements in erythrocyte antioxidant system through Akt/PKB pathway.

1. Introduction

Of the many naturally occurring elements found abundantly distributed in the earth's crust, arsenic has found its way into prominence as a toxicant of significant public health risk [1]. A heavy metal, specifically classed as a metalloid [2], it is naturally produced during processes such as volcanic eruptions and the biodegradation of other organic minerals and rocks [3]. Increased dependency on arsenic among other heavy metals for anthropogenic causes has resulted in widespread release of arsenic by-products into the environment [4]. Human exposure is then unavoidable, not just from occupational causes, but also from atmospheric pollution, ingestion of contaminated food and water sources and from contact with certain finished industrial products [5].

Of the routes to exposure, the most important source, by far appears to be dietary. Tchounwou et al. [1] report that each individual has an average intake of 50 μg per day. Recent studies show a rise in the levels of inorganic arsenic in food items, especially rice, a staple of third world and underdeveloped countries [6–8]. Arsenic was found to accumulate more in the liver than other tissues after one month of exposure, when administered orally and subcutaneously. However, after 3 months of exposure, was found to accumulate more in the kidney than in the liver or other tissues. [9]. With a high correlation established between exposure and increased health risks, and an uptick in the incidence of health-related conditions among affected populations, it is no wonder arsenic is listed as one of the high malignancy causing elements today [10,11].

Certain heavy metals as cobalt and copper have been classified as essentials due to their absolute requirements in trace quantities for normal biochemical and physiological functions in the human body [12]. Arsenic, on the other hand, has been found to have no beneficial physiologic role in the human body and is classified as a non-essential

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