



Toxicology

Suppression of the brain–pituitary–testicular axis function following acute arsenic and manganese co-exposure and withdrawal in rats



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ARTICLE INFO

Article history:

Received 1 March 2016

Received in revised form 12 May 2016

Accepted 1 July 2016

Keywords:

Arsenic

Manganese

Co-exposure

Reproductive toxicity

Oxidative stress

Rats

ABSTRACT

Despite the fact that most environmental exposures to metals do not occur in isolation, the combined effects of metal mixtures on brain–pituitary–gonadal axis are poorly known. The present study investigated the impacts of co-exposure to arsenic (As) and manganese (Mn) on sperm characteristics, reproductive hormones and selected oxidative stress indices in the brain, testes and epididymis of rats following exposure for 15 consecutive days to 60 mg/L of AsO_2Na and 30 mg/L of MnCl_2 in drinking water. The results showed that while the brain weight remained unaffected, the fluid intake and the weights of testes and epididymis significantly ($p < 0.05$) decreased in all the treatment groups. A significant decrease in the body weight gain when compared with control was noted only in the co-exposed rats. Moreover, the significant decreases in the antioxidant status in brain, testes and epididymis as well as in the circulatory concentrations of follicle-stimulating hormone, luteinizing hormone and testosterone were similar following separate or combined exposure of rats to As and Mn. The marked oxidative damage in the investigated tissues was accompanied by a significant decrease in the sperm quantity and quality in all the treated rats when compared with the control. Interestingly, most of the parameters determined immediately after the exposure period persisted in rats from the withdrawal experiment. Collectively, co-exposure to As and Mn suppressed the brain–pituitary–testicular axis function and the post-testicular events such as sperm function possibly via a mechanism involving persistent oxidative stress and endocrine disruption in the exposed rats.

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1. Introduction

Arsenic (As) is a crystalline “metalloid” with characteristics intermediate between metals and non-metals. It was ranked as the 20th most occurring trace element in the earth’s crust, 14th in seawater, and 12th in the human body [1]. Manganese (Mn) is a ubiquitous, naturally occurring trace metal [2]. There is a growing body of evidence indicating that environmental exposure to As and Mn and their mixtures poses public health threats to animals and humans [3,4]. The enrichment and pollution of surface sediments and groundwater by arsenic (As) and manganese (Mn) in several countries including West Bengal in India, Bangladesh, Italy, China and Nigeria have been reported [5–11]. The elevated levels of As and Mn in sediments and groundwater have been attributed to the intense anthropogenic activities in agriculture and unregulated discharge of industrial wastes into rivers [12]. Both As and Mn co-exist in occupational contexts and the populations living in these

contaminated areas are exposed to higher levels of this mixture through water, soil and food contamination [13,14]. Recent study conducted in Rio Branco, Acre, Brazil revealed higher blood levels of As and Mn in individuals living near industrial facilities, working in a glass factory, a compost plant or in metal mining activities than in other non-occupationally exposed populations [15]. Thus, humans are most often exposed to harmful chemical mixtures than one chemical.

Moreover, since exposure to environmental contaminants elicits different sorts of adverse effects in reproductive systems, no single parameter is reliably the most sensitive indicator to predict reproductive health risks [16]. The male reproduction in vertebrates is tightly regulated by the brain–pituitary–gonadal axis. Generally, the brain secretes the gonadotropin-releasing hormone (GnRH) which stimulates the pituitary to produce follicle-stimulating hormone (FSH) and luteinizing hormone (LH) which, in turn, controls Leydig cells to produce and secrete testosterone necessary for spermatogenesis and regulation of the male phenotype [17,18]. Previous investigations showed that chronic exposure to either As or Mn induced oxidative stress and impaired testicular function of spermatogenesis and steroidogenesis in laboratory

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