



ARSENIC: A MAJOR CONCERN OVER PUBLIC HEALTH

PHYSIOLOGY

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ABSTRACT

Human beings are much concerned about the direct effect of pollutants on their own health. Arsenic being a potent environmental toxic agent, leads to development of various hazardous effects on human health. Elevated concentrations of inorganic arsenic, a potent toxicant and carcinogen in drinking water are common worldwide. A large number of reports show associations between arsenic exposure and multiple noncancer health effects, e.g., diabetes, skin diseases, chronic cough, and toxic effects on liver, kidney, cardiovascular system, peripheral and central nervous systems. It has been reported that there are increased incidences of arsenic toxicity even at low and permissible dose limit. The present review discusses some of the health issues related with arsenic toxicity.

KEYWORDS

Arsenic, groundwater, reproductive toxicity

Introduction:

Contamination of the natural environment by thousands of chemicals or xenobiotics to meet the demands of modern era has been considered as an increasing concern over the public health.⁽¹⁾ Although the entire biosphere is affected, it is the water resources that are the most polluted because water is the ultimate sink for many contaminants. One of the most important environmental issues today is groundwater contamination and between the wide diversity of contaminants affecting water resources, heavy metals receive particular concern due to their non biodegradable nature and strong toxicity even at low concentration. Among heavy metals, arsenic receives particular attention as its contamination in groundwater is a severe global environmental problem⁽²⁾ and a matter of utmost concern to public health. Increasing concentration of arsenic in groundwater which is also used for irrigation may result in land degradation in terms of crop production (loss of yield) and food safety (food chain contamination)⁽³⁾

General account

Arsenic: Properties and sources: Arsenic is classified as a metalloid, as it has both the properties of a metal and a non-metal, but frequently referred to as a metal. (4) It derived its name from the Greek word arsenikon, meaning potent. Arsenic ranks as the 20th most occurring trace element and exists mainly in four valency states (0, -3, +3, +5). It occurs in ground water in the form of arsenite, arsenate, methyl arsenic acid and dimethyl arsenic acid and ranks first in the list drafted by the Agency for Toxic Substances and Disease Registry⁽⁴⁾ of the 20 most hazardous compounds in the environment.

The main source of human exposure to inorganic arsenic worldwide occurs through consumption of drinking water drawn from groundwater sources that contain dissolved inorganic arsenic, which has become a serious problem, with considerable impact on public health.⁽⁵⁾ Daily millions of people, mostly in developing countries, consume drinking water with arsenic concentrations several times higher than the permissible limit (10µg/L) set by WHO.

Arsenic enters the environment naturally through ground water, mineral ore and geothermal processes. It is also used in agricultural applications such as insecticides, herbicides, fungicides, algacides, sheep dips and wood preservatives.⁽⁶⁾ Presently, arsenic is widely used in the electronics industry in the form of gallium arsenide and arsine gas as components in semiconductor devices.

Arsenic enters in to organisms through dermal contact, inhalation or through ingestion of contaminated drinking water. Most of the ingested arsenic stored in liver, kidney, heart and lung while lower amount were present in muscle and neural tissues. Arsenic gets incorporated in to the nails, hair and skin by binding to keratin sulphhydryl groups. Transverse white striae (Mee's lines) in nails are indicative of arsenic exposure. The first sign of poisoning is appearance of black spots on the upper chest, back and arms, a condition termed melanosis in medical parlance. The toxicity of

arsenic compounds depends highly on the oxidation state and chemical composition of the arsenicals. The inorganic form of arsenic particularly, arsenite (III) and arsenate (V) compounds are highly toxic to human beings and to animals,⁽⁷⁾ while arsenite has a tendency to readily react with the sulphhydryl groups of proteins which inturn inhibit biochemical pathways and arsenate acts as a phosphate analogue and interferes with phosphorylation reactions.⁽⁸⁾

Kinetics and metabolism

Elemental arsenic (0), when ingested, is considered less toxic as it is poorly absorbed and largely eliminated unchanged from the human body. However, soluble arsenic compounds are mostly absorbed through gastrointestinal tract and eliminated via kidney. After absorption, inorganic arsenic is readily distributed and taken up by cells in tissues. Both trivalent arsenite (AsIII) and pentavalent arsenate (AsV) are actively transported to the cell; the former by aquaglycoporins, which normally transport water and glycerol, and the latter by phosphate transporters.⁽⁹⁾

Mode of action

The different ways by which arsenic causes toxicity are disruption of cellular signaling, generation of apoptosis, oxidative damage, altering DNA repair leading to carcinogenicity but generation of reactive oxygen species (ROS) leading to oxidative damage is the most important one which describes best arsenic's mode of action.

Toxic effects of arsenic are mediated primarily by triggering the production of reactive oxygen species (ROS), inhibiting the activity of enzymes like superoxide dismutase and catalase, leading to alterations in cells' intrinsic antioxidant defenses; and resulting in oxidative stress or disturbed antioxidant/pro-oxidant ratio.⁽¹⁰⁾ The trivalent arsenic (As III) has the capability to inhibit many enzymes especially those which are involved in cellular glucose uptake, gluconeogenesis, fatty acid oxidation and production of glutathione mainly by interacting with thiol groups and thereby leading to the more production of reactive oxygen species.⁽¹¹⁾

Neurotoxicity

Brain is a soft target for arsenic toxicity as it freely crosses blood-brain barrier. In humans, arsenic exposure is associated with wide range of neurological complications such as impaired memory, poor concentration, Parkinson's disease, Guillain-Barre like neuropathy, verbal comprehension, encephalopathy, and peripheral neuropathy.⁽¹²⁾

Nephrotoxicity and Hepatotoxicity

The kidney and liver are the primary targets for arsenic-induced toxicity. The prospective mechanism for arsenite induced nephrotoxicity and hepatotoxicity involves oxidative stress, apoptosis, and upregulation of transcription factors such as AP-1, ATF-2, and Elk-1. Arsenite increases the generation of ROS, which enhances lipid peroxidation and cellular damage in both hepatic and renal tissue.⁽¹³⁾ Chronic arsenic-mediated oxidative stress activates JNK and p38 MAPK and induces apoptosis in the hepatocytes.⁽¹⁴⁾

Immune system toxicity

It has been demonstrated that arsenic impact adversely on the immune system, which may later predispose to abnormal inflammatory-like immunotoxicity in humans.⁽¹⁵⁾ Several epidemiological study reported that arsenic exposure increased the incidence of autoimmune-mediated diseases, such as diabetes mellitus, cardiovascular disease mediated by arsenic-induced vascular inflammation by increased expression of Tumor Necrosis Factor- α (TNF α) and Interleukin-8 (IL-8). It has been reported that arsenic exposure can cause systemic immunodepression in several animal studies, as well as in humans.

3.4 Reproductive toxicity

Reproductive function is the most important and relevant option in all living organisms. Ovary is a metabolically active organ and, hence, is under a variety of stresses continuously thereby leading to the production of reactive oxygen species (ROS). Physiological ROS levels play an important regulatory role through various signalling and transduction pathways in folliculogenesis, oocyte maturation, corpus luteum, uterine function, embryogenesis, embryonic implantation and fetoplacental development. Imbalances between antioxidants and ROS production are considered to be responsible for the initiation or development of pathological processes affecting female reproductive processes.⁽¹⁶⁾

Exposure of sodium arsenite at the dose of 10mg/kg/BW decreased the reproductive organs weight: testis, epididymis, prostate and seminal vesicle; sperm functions: count, motility and normal morphology.⁽¹⁷⁾ It has been reported that arsenic effects mainly the processes of meiosis and post-meiotic stages of spermatogenesis and acute exposure to arsenic causes rapid and extensive disruption of spermatogenesis in mice.⁽¹⁸⁾

Anthropogenic activities result in contamination of the natural environment by thousands of chemicals or xenobiotics to meet the demands of modern era. Arsenic toxicity is a serious worldwide problem, which adversely affects the growth, health, reproductive performance and life span of all living organism. Reports also point to an increased risk of arsenic toxicity even at low permissible dose limits.

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