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Review Article

HEAVY METAL INTOXICATION, MOBILIZATION AND THERAPY IN CHILDREN AND ADULTS: A REVIEW

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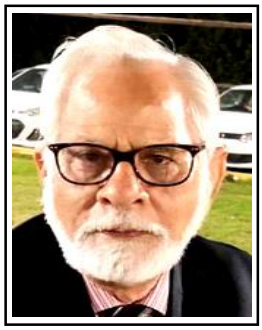
Abstract: The survival of human race depends upon, better environmental management. Therefore, continuous and sincere efforts will have to be carried out by everyone involved in environmental management, protection, monitoring, assessment, research, education, planning, conservation and sustainable development to use the resources. ATSDR toxicological profiles, published in USA have reported a number of hazardous chemicals and characterized the toxicological and adverse health effects. In children heavy metals effect respiratory disorders, cancer, cardiovascular and neurological diseases. Several heavy metals Interact pro-oxidatively with the phagocytic cells of the innate immune system. Nevertheless, these as well as other recent studies are incapable to provide much information about their total removal from body. Therefore, studies on this



Dr. P. P. Sood, is a group leader of scholars investigating heavy metal Toxicology for last 45 years. He received Life time Achievement Award twice, first in Toxicology (New Delhi) in 2002 and second in Neurosciences, University of Calcutta in 2015. He organize symposia on Toxicology in 5 International Conferences held at PARIS, 1991; OTTAWA,1996; JENA GERMANY 2000; POITIERS FRANCE, 2005; and 5th World Congress held at INDORE. He has published about 200 research articles which are well qouted by Research gate and cited by world authors,

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Dedication: . Dr Gupta devoted his entire life to Sciences and to Scientific Edition. He is a Scientific adviser to Journal of Cell and Tissue Research. His scientific and popular articles are appreciated evry where. We are happy to dedicate this research work to him on his 85th Birthday.

subject are regularly carried out by several investigators where the animals were intoxicated with hazardous heavy metals, such as mercury, methyl mercury, lead, chromium, cadmium, aluminium, zink, and other toxicants such as floride and arsanic etc. and thereafter, pre- or post therapies were provided to eliminate the toxicants, to improve their health and to restore the altered conditions caused thereby. The objective of present contribution is to review the toxic effect of some heavy metals and possible therapy provided with antioxidants.

Keywords: Heavy metals, Intoxication, mobilization , Therapy

Any metallic element that has a relatively high density and toxic at low concentrations referred as heavy metals which fall in three categories. viz, those which are inert and rarely effect the living tissues (such as silver, indium and ruthenium), those which are needed in small quantity and essential (such as iron, cobalt, zink and chromium) and finally those which are totally injurious and not required by any living animal cell (such as lead, arsenic, osmium, cadmium, mercury etc.). According to Chang et al. [1] aluminium (Al), antinomy (Sb), arsenic (As), barium (Ba), beryllium (Be), bismuth (Bi), cadmium (Cd), gallium (Ga), germanium (Ge), indium (In), lead (Pb), lithium (Li), mercury (Hg), nickel (Ni), platinum (Pt), silver (Ag), strontium (Sr), tellurium (Te), thallium (Tl), tin (Sn), titanium (Ti), vanadium (V) and uranium (U) have no established biological functions and are considered as non-essential metals. Heavy metals effect different body organs mainly intestine, kidney nervous tissues, skin and vascular damage and immune system and cause oxidative stress. Children are more susceptible to toxic elements due to poorly developed immune system, fast abortion in intestine and quick effect on all developing organs, specially liver, kidney, brain intestine etc. According to one WHO report 90% of world children breath polluted air.

Before entering into any major city of the country a sewage canal, containing wastage from residential and industrial units contaminated with human excreta, insecticides, pesticides, dyes, heavy metals and other pollutants, is a common sight without exception. The use of this water for irrigation of vegetables and crops is also a common feature throughout the country and causing health problems. The emerging advanced technologies offer the promises of higher productivity, increased efficiency and decreased pollution, but may bring risk of new toxic chemicals and wastes. Increasing environment awareness and strict government regulation in toxic waste management, though give some hopes, but illiteracy, poverty, ignorance, greed, competition and mismanagement are neutralizing these efforts.

In the course of modern civilization an improved quality of life has undoubtedly emerged as a desired goal. Rapid urbanization, industrialization and improved agricultural practices are identified as the key factors to achieve this goal, hence came into force, particularly during the last four to five decades. For increasing population the agriculture and industries have to be increased. Until some genetic engineer transfers the nitrogen fixation gene in the roots of crop plant, the fertilizers are to be used. Until there is a biological control of pests, the insecticides and fungicides are needed to increase agricultural products. The excessive use of chemicals is polluting our environment up to the extent that even the mother milk and sperm contain pesticides and heavy metals. Therefore, it is necessary either to reduce the population or to stop industrialization. At present, we are not at a stage of any. Therefore, industrialization and population have to proceed hand in hand. We can at the best help only to reduce the extent of pollution and its various ill effects by finding suitable effective drugs or chelating agents. The author's investigation is a step in this direction.

ATSDR toxicological profiles [2-8] published in USA, have reported a number of hazardous chemicals and characterized the toxicological and adverse health effects. Nevertheless, these as well as other recent studies are incapable to provide much information about therapeutic data. Therefore, studies have been carried out by the investigators who intoxicated the animals with hazardous heavy metals and tried natural and synthetic antidotes to mobilise the toxic elements from the body and repair the physiological stress.

Chelation therapy is the only treatment of choice. However, many times the chelators themselves are toxic. Levine [9] claimed the following criteria to consider any compound as an antidote: 1). Antidote

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complexes with the poison rendering it inert. 2). The treatment should start before chronic poisoning. 3). Antidote accelerates metabolic conversion of toxic to a non-toxic product. 4). Antidote blocks metabolic formation of toxicant from less toxic precursor. 5). Antidote specifically accelerates the excretion of toxicant. 6). Antidote competes with the toxicant for essential receptors. 7). Antidote blocks receptors that are responsible for toxic effects and 8). Antidote restores normal functions by repairing or bypassing the effects of toxicants. Nevertheless, it is difficulty to get an antidote, which fulfill all the eight criteria mentioned above except the natural detoxifying system exists in the animal body. The glutathione is one of such cell-generated xenobiotic, which play such role of detoxification.

For the last three decades in the Laboratory of Neurobiology and Toxicology, Department of Biosciences, and Biochemistry, Saurashtra University, Rajkot in association with national and international investigators trying to solve this problems. Our special attention was on mercury and methylmerury, chromium, lead and arsenic. Our findings indicate that various organs have differential capacities to absorb, store, metabolize, and excrete these heavy metals depending upon the dose and duration of metal exposure. For last 30 years we have published a number of papers in different international journal and most of them revealed good citation all over the world. A list of these research articles is presented here for immediate reference:

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From overall studies, it is clear that chelation therapy is the only treatment of choice. However, The glutathione and vitamins are cell-generated xenobiotic, which play important role of detoxification, mobilisation and repairing cellular components [10]. Our studies further conclude that:

- There is a dose and duration dependent toxicity of both most of te heavy metals.
- Chelators accelerate metal elimination from most of the tissues. However some pinch are always left that still effect the tissues.
- Chelators also accelerate metal elimination from brain in methylmercury intoxicated subjects, which was not possible earlier and cellular and myelin generation is fast. Natural chlators like GSH and vitamins B and E in combination mobilize the metal and partly repair the pathological image.
- The reduced food and water intake and body weight of toxicated animals is significantly recovered during therapy.
- The metal creates deficiencies of all macro- and micro-nutrients in all the tissues which are continuously restored during chelation therapy.
- Enzymes of various metabolic pathways, which are inhibited (in some instances increased), are significantly restored.
- Exogenous application of GSH and vitamins restore their levels in tissues.
- Lipid peroxidation, which is increased during intoxication, is reduced.

Inspite of all these studied we feel that more work is required. In recent year several old and new antidotes have been tried and reported to be best to some extant. Chacko and Peter [11] reported that vitamin K, folic acid and pyridoxine are used to antagonise the effects of warfarin, methotrexate and INH respectively in the setting of toxicity or overdose. Many worker reported number of drugs for treatment of metal poisoning such as ba. (dimercaprol), calcium edta (calcium disodium versenate), penicillamine dimercaprol), calcium disodium ethylenediamine tetraacetic acid ($CaNa_2EDTA$) and penicillamine, trimercaptotria-zine, potassium/sodium thiocarbonate, and sodium dimethyl dithiocarbamate. EDTA is FDA-approved for the treatment of lead poisoning in adults and children. Each of these work by binding actions that permit the metals to be eliminated from the body through the urine. Vijayalakshmi and Sood [12] discovered amelirative capacities of vitamins and monothiols post-therapy in the restoration of methylmercury altered glutathione metabolism. we also found that vitamin E, GSH, ashwagandha (*Withania somnifera)*, garlic (*Allium sativum)* in combination with vitamin B complex (B1, B6, and B12) are quite useful as therapeutic agent in heavy metal elimination and recovery of mega- and micro-nutrients, hormonal and neurotransmitter levels. Further some B vitamins have been shown to be protective in nature [13,14], hence repair the pathological changes [15].

RECOMONDATIONS:

Our findings indicate that various organs have differential capacities to absorb, store, metabolize, and excrete different metals, depending upon the dose and duration of intoxication. One way to check the toxicity of the chemicals is their testing on some animals, because no experiments can directly be performed on human beings. To protect the public from harmful effects of toxic chemicals and to find ways to treat people, who are suffering, we we recommend to follow the following:

- Monitored the level of toxic metals in experi-mentally intoxicated animals and effective population. .
- Examined the effect of toxic metals in nutritional deficiency.
- Screened the effect of toxic metals on animal growth in children.
- Checked the metabolic disturbance during toxic metals intoxication.
- Screened the suitability of therapeutic agents for the elimination of toxic metals and neutralizing the toxic effects.

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