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Analytical aspects and Management of Antimony poisoning – A review

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ABSTRACT: Antimony poisoning is a metal poisoning, which has no known function in the body of humans and has got a low toxicity. It causes pneumoconiosis and acutely affects skin and the eyes. Cardiovascular effects include blood pressure increase as well as repeated exposure to airborne antimony has been seen to cause abdominal pain, vomiting, ulcers or diarrhoea. Clinical features of antimony poisoning along with differential diagnostic investigations have been presented. The chemical tests for antimony poisoning have been well presented. The pre- hospital and hospital management will help in providing proper care to the patient.

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INTRODUCTIONS:

The present review paper is an accumulation of the facts known till date about the toxicity of antimony and its management. Antimony is a hard, grey lustrous metalloid, found in nature as the sulphide mineral stibnite. It has an atomic weight of 122. Antimony sulphide is being used as early as 3000 B.C. The women of Middle East used to apply this compound as a cosmetic to darken their eyelids and eyebrows. The increased exposure to antimony is said to cause antimony poisoning. Antimony is stable in the presence of oxygen,

but reacts with it, when heated. In the presence of oxygen and heat it produces antimony trioxide. It exists in 4 valence states in which its trivalent state being most stable. Inorganic Antimony is more toxic than organic antimony.

It is used as an alloy with metals to enhance their strength and hardness. Antimony is used in printing presses, bullets, and cable sheathing. It is found in quantities in an around 100 mineral species. Extraction of antimony can be done by roasting the antimony sulphide to its oxide, and then reducing it with carbon.

Antimony's main dietary source is rice, but it is also found in fruits, vegetables, fish, meat and higher level of it can be detected in marine foods. Apart from food it is also found in air, drinking water and beverages. Tolerable Daily Intake (TDI) of Antimony on the basis of NOAEL of 6.0 mg/kg body weight per day on a research conducted on rats, where the rats were administered potassium antimony tartarate in drinking water for a decreased body weight gain and reduced water and food intake in a 90 day study was 6 µg/kg. The workplace exposure limit of antimony is of 8 hour time weighted for average of 0.5 mg/m^3. It has some potentially useful medical applications. It is involved as a tartar emetic against lung tumor cell lines [1-3].

SOURCES:

Antimony is found free in nature, but mostly obtained from the ores, Valentinite (Sb_2O_3) and Stibnite ($Sb_2 S_3$). The early Egyptians used to use antimony stibnite for black eye makeup. Antimony is produced by manmade releases to air and water from waste incineration, metal processing mines and from industrial through burning of coal. The main sources of antimony can be the burning of vehicle exhaust gases and industrial dusts [1-3].

Naturally, Antimony is released from the earth's crust and can be found in soils, rivers and sediments. It is found in concentrations up to a few pg/m^3 in remote areas, while in urban areas to a few mg/m^3, this concentration is found to be more in some contaminated sites.

Antimony concentrations in drinking water is found to be below 1µg/l, except in the case of some bottled waters in which high level of antimony can be found under extended storage conditions. Antimony can be mixed in alloys and is used in lead storage batteries, Solder, Semiconductors etc. Antimony oxide can be added to plastics, adhesives, pigments in order to prevent them from catching fire [1-3].

ENVIRONMENTALEFFECTSOFANTIMONY:

Antimony can enter the environment through both natural and man- made processes. It can enter environment during the mining and processing of antimony ores and during the production of antimony metal, its oxides and other combinations. It pollutes soil, water and air. It pollutes soil mainly through groundwater which reaches to other surface waters pollute. The high levels of antimony kill small animals like rats, rabbits and guinea pigs. It causes severe breathing effects in animals. Even low levels of antimony can cause eye irritation, lung damage and hair loss. When breathed in for a couple of months, it too causes fertility problems in animals [4]. Antimony, when enters water bodies, affects aquatic life. It is considered to be toxic to both aquatic and global environments. It has been found stomach ulcers in animals that are exposed to it while drinking water for months. It damages heart muscles, causes lung cancers as observed in the case studies on laborers and mice, breathing antimony in high concentrations. According to the international agency for research on cancer, the antimony trioxide is carcinogenic in humans (Group 2B) [4].

EXPOSURE OF ANTIMONY:

People are exposed to antimony both by occupational and non-occupational means.

Occupational:

Antimony being an important metal of world economy is produced at about 50,000 tons per year. Occupational exposures of antimony occur during the mining and processing of antimony ores and during the production of its metal oxides. The people working near antimony mines or in industries that processes antimony ores and metals are exposed to antimony by inhaling its dust or through dermal contact [4].

Non- Occupational:

Non-occupational exposure occurs through air, water and food. Exposure also occurs through dermal contact with soil and water contaminated with antimony. Food may contain certain amounts of antimony. Drinking water containing levels of antimony as high as 9.7 µg/l has been reported some of rural areas [5].

HUMAN INTAKE OF ANTIMONY:

Inhalation:

Inhalation exposure occurs during occupational activities while working with antimony compounds and inhaling antimony dust, or fumes.

Ingestion:

Antimony could be present in vegetables, food which are grown on antimony contaminated soils. The daily average intake of antimony through food varies from about 10 to 25 µg and it could too get dissolved from older cooking utensils. Higher levels of antimony can be reported in water in PET bottles. It has been speculated that antimony could be a natural contaminating agent with arsenic in drinking waters. Daily uptake of antimony through ingestion ranges from 10 to 70 µg, which is significantly higher than uptake through inhalation.

Dermal:

Dermal exposure occurs during working near antimony mines or antimony processing sites. It occurs through skin contact with water, soil and other materials containing antimony.

PHARMACO-KINETICS OF ANTIMONY:

Absorption:

Antimony compounds get absorbed through ingestion and inhalation. Gastrointestinal absorption being poor in man necessitates parental administration of pharmaceuticals of antimony.

Distribution and excretion:

The trivalent as well as pentavalent antimony and its compounds, differ significantly in its distribution. The trivalent antimony has an affinity for the red blood cells, while pentavalent antimony has affinity for the white blood cells and plasma. Significant amount of antimony can be found in the kidney, liver, adrenals, thyroid and bone, pentavalent antimony gets reduced to the trivalent form in the liver [5].

Lauwers and co-workers in a study (1990) estimated the total body pool of antimony [6]. They observed that only 5 % of the ingested dose could be found, in a patient who died of accidental antimony potassium tartarate ingestion, with high antimony concentrations found in the liver, gall bladder and gastrointestinal mucosa.

Antimony compounds get eliminated mainly through urine, with smaller amounts appearing in the faeces, through bile after getting conjugated with glutathione. Reasand co-workers (1980) demonstrated that about 80 to 90 % of the intramuscular dose of sodium stibogluconate is recovered in the urine within about 6 h of administration. Kentner *et al* (1995) estimated renal elimination half life of about four days, upon occupational inhalation of antimony trioxide and stibine among 21 employees of a battery manufacturing plant.

Mechanism of toxicity:

Antimony compounds get slowly absorbed through the gastrointestinal tract. It gets distributed to the liver, bones, kidney and other highly vascularized organs, when ingested or orally administered. The mechanism of toxicity of antimony involves distribution of thiol proteins by binding to sulphydryl groups. It has been found to react with erythrocyte membrane and thus interfering with normal hemoglobin function. It is believed that antimony is toxic due to its combination with several enzymes (the organic catalysts of cells) and thus interfering with cellular metabolism.

Metabolism of antimony:

Inorganic trivalent antimony does not get methylated *in vivo*. It gets excreted in the bile by getting conjugated with glutathione and even gets excreted in urine. The antimony excretion is related to the intensity of its exposure in workers. The excretion of antimony takes place through urination; very less gets secreted into milk. The organs found to show highest concentrations are the Spleen, bone and the liver, which was evident through studies observed in lactating cows. Antimony, unlike arsenic does not get detoxified through methylation.

Susceptibility to antimony by parasites is related to parasite's level of antimony reducing ability. Anion exchange chromatography is indicative of the metabolism of antimony in both promastigotes and amastigotes. Sb (+5) is anti-leishmanial and its anti-leishmanial work is dependent upon its reduction to Sb (+3) as evident in studies observed on leishmanias. The metabolism of antimony is not known much and very less is known about the genes that regulate these processes of metabolism.

ONSETAND DURATIONOFACTION:

Antimony in the lungs enters the bloodstream after several days or weeks depending on the nature of its compound. Even a small amount of antimony that is taken orally enters the bloodstream only after a few hours. Exposure to antimony at chronic levels of about 9 mg/m^3 may cause irritation of the skin, lungs and eyes while long time of its exposure and inhalation can initiate pneumoconiosis, changed electrocardiograms, diarrhoea, which is evident among laboratory animals. Stomach ulcers have been found among animals exposed to

antimony containing drinking water for about several months.

FATAL DOSE AND FATAL PERIOD:

The fatal dose of antimony is 90 to180 mg in terms of tartarum, while 8 to 12 ml in terms of trichloride. The fatal period is around 24 h.

NORMAL/ REFERENCE VALUES:

The antimony levels can be found in blood, hair, faeces and urine. High levels of antimony found in the blood or urine can be indicative of exposure to higher than normal exposure levels of antimony [6,7]. The Environmental Protection Agency (EPA) has determined that the exposure to drinking water containing antimony about 0.01 mg/l is not likely to cause harmful effects to children, exposed for a period of 1 to 10 days. Even lifetime exposure of drinking water, containing 0.006 mg/l of antimony is not going to cause adverse effects on health. The detail is given in the Table 1.

Table 1. Various level of Antimony in Human body.

Matrix	Normal Level	Toxic Level
Blood-plasma/serum	0.7-2 µg/l	9mg/l
Urine	0.06-0.01 µg/l	0.26-0.39 µg/l
Hair	<0.066 µg/g	0.088 µg/g

EFFECT OF ANTIMONY POISONING:

Chronic effect of antimony:

Chronic exposure to antimony in form of antimony trioxide or pentaoxide dust is said to cause pneumoconiosis. Other respiratory effects like chronic bronchitis, pleural adhesions, chronic coughing, wheezing are also reported to occur in exposure to antimony. The other effects include cardiovascular effects and gastrointestinal disorders. The animal studies have reported effects on blood, central nervous system, liver and gastrointestinal due to oral exposure to antimony.

Acute effect:

Acute effects involve effects on the skin and eyes. It can also produce skin effects called antimony spots, which produces rashes containing pustules around sweat and sebaceous glands. This dermatitis is commonly seen in hot weather conditions and among workers, working in high temperatures, which can result in rashes getting cleared within 3 to 14 days. The effects on eyes include ocular conjunction, while oral exposure results in gastrointestinal effects. Studies on animals have reported effects on lungs, liver and cardiovascular system.

Effect on cardiovascular system:

Cardiovascular effects include blood pressure increase and changed electrocardiography readings, mostly in the T waves among workers exposed to 2.15 mg/m^3 in the form of antimony trisulphide in addition to phenol for about 8 months to 2 years. More effects could be seen on inhalational exposure to antimony trisulphide dust which results in degenerative changes in the myocardium and some related abnormalities in electrocardiogram in a variety of animal species.

Effect on gastro-intestinal system:

Repeated exposure to airborne antimony compounds such as antimony trichloride, antimony oxide or antimony trisulphide has been seen to cause abdominal pain, vomiting, ulcers, or diarrhoea.

Reproductive effects:

Reproductive effects involve higher incidences of spontaneous abortions and irregular menstruations in women. Animal studies reported failure in the ability to conceive among rats, as evident among two thirds of rats exposed to 209 mg of antimony trioxide for a period of 63 days.

Gene toxicity and mutagenicity effect:

Trivalent and pentavalent antimony compounds are negative among non mammalian gene toxicity tests, while systems involving mammals, give positive results for Sb (+3), while negative results for Sb (+5) compounds. No adequate evidence for carcinogenicity of antimony is seen among humans, but antimony trisulphide and antimony trioxide has been seen to cause lung tumors among rats. Antimony trioxide is considered possibly carcinogenic to humans by the International Agency for research on cancer.

CLINICAL APPEARANCE/ SYMPTOMS OF ANTIMONY POISONING:

Upon moderate ingestions, symptoms are usually seen after 30 min to 2 h, which includes nausea, vomiting, metallic taste, abdominal pain or diarrhoea. A garlic odor too can be felt on the breath. While upon substantial ingestions, severe vomiting as well as diarrhoea containing blood, hemorrhagic gastritis can be seen. Cerebral oedema, convulsion, coma occur and chronic ingestion results in anorexia, diarrhoea, weight loss, peripheral neuropathy, skin rash and palmar keratosis.

Inhaling antimony is irritant to the respiratory tract as well as the mucous membranes. Laryngitis, conjunctivitis, pharyngitis, rhinitis, tracheitis and bronchitis may result too. Pneumonitis can be seen too, while chronic inhalation, by occupational means causes pneumoconiosis with cough, wheeze and diffuse as well as punctate opacities can be seen too in the middle and lower zones.

DIAGNOSTIC INVESTIGATION IN CASE OF ANTIMONY POISONING:

The antimony concentration in blood is indicative of any recent exposure of it and is most useful in the diagnosis of acute antimony poisoning. The antimony concentration in blood among unexposed individuals rarely exceeds 10 µg/l. The trivalent form of antimony readily enters the red blood cells, has got an extended half- life of weeks to months, and gets predominantly eliminated through bile. However pentavalent antimony resides in plasma, has got a relatively short half life of about hours to days, and gets predominantly eliminated through the kidneys. The symptoms of toxic antimony exposure vary based on the route of exposure, duration and the source of antimony and includes abdominal pain, dyspnea, vomiting, eye irritation and dermatitis [8,9].

CHEMICALTESTSFORANTIMONYPOISONING:

Qualitative Tests [10]:

Reinsch test:

This test is applicable to urine sample, stomach sample and other scene residues. The test solution amounting to about 5 ml is taken in a China crucible, few drops of hydrochloric acid as well as small pieces of copper strips are added and the mixture is heated on a water bath. A purplish black deposit appears on the copper strip, indicating the presence of antimony.

Micro test:

Small amount of the black deposit obtained from the Reinsch test is taken onto a tile and few drops of dilute hydrochloric acid is added on it in order to dissolve the black deposit. The solution is spotted on a piece of filter paper, which after drying is exposed to hydrogen sulphide. The appearance of an orange spot indicates the presence of antimony.

Rhodamine B Reagent Test:

The about 1 ml of sample is first digested and is taken in test tube which is then acidified by means of hydrochloric acid. The mixture is further mixed with solid sodium nitrite and further addition of 1 ml of aqueous solution of Rhodamine B reagent leads in changing the bright red colour of the reagent to blue, indicating the presence of antimony.

***Phosphomolybdic Reagent test*:**

In this about 1 ml of the extract is taken in a micro test tube. About 1 ml of phosphomolybdic acid is further added and the solution is heated for a short time. The reduction of reagent into a blue compound occurs, which is further extracted by means of amyl alcohol.

Quantitative analysis:

Quantitative analysis of antimony is done using gas liquid chromatography. The sample gets converted into corresponding volatile chlorides, upon reaction with carbon tetrachloride at an elevated temperature. The chlorinated product is transferred directly into a carrier gas stream.

MANAGEMENT/ TREATMENT OF ANTIMONY POISONING [11]:

First aid/Pre-hospital management:

First of all, if someone is suspected of suffering from the effects of antimony poisoning, he should immediately be removed from the toxic environment, and if the person has received it from air, he should be made to breathe fresh air and if the exposure is through skin, clothes containing traces of the element should be removed and the skin is washed with soap and water. Gastric lavage could also be administered and chelating drugs could be given in order to get rid of traces of poisonous elements remaining in the patient's body. Medical help should be seeked immediately.

Hospital management:

Hospital management involves supportive and symptomatic measures as per the patient's conditions:

- Upon ingestion of an antimony compound, gastric lavage could be considered if presentation is within the first hour.
- The administration of 50 g activated charcoal within first hour of substantial ingestion could adsorb antimony.
- ECG could be performed and haematological and biochemical profiles are monitored.

CONCLUSION:

The work place area being the main source of exposure to antimony, work place precaution must be taken foremost. Bottled waters should be used to prevent consuming antimony in tap water. Children should be

prevented from playing or eating dirt, if staying near a waste site that is contaminated with antimony.

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