**Arsenosis and its management**

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**Introduction**

Arsenic is a metalloid, a known poison as well as carcinogen that occurs naturally in earth’s crust. It is found in most of the environmental media such as air, soil and water. It enters the body through ingestion, inhalation and per cutaneous route. Health hazards of arsenic toxicity can occur as acute and chronic forms. Recently arsenicosis has emerged as a public health problem in many countries of South East Asian region.¹

**Historical background**

As early as 500 B.C. the ancients knew about arsenic, whose name comes from the Greek word for potent. Through the centuries, this "king of poisons" was a common means of homicide. It has been known since ancient times and has been continually used as medicine usually as Traditional Chinese Medicines (TCMs). Inorganic arsenic has been used in medicine for over 2500 years. The most widely used form was Fowler solution containing 1% potassium arsenite, which was used for treatment of psoriasis. Some are used for syphilis as well. Acute arsenic poisoning presenting as acute gastro-enteritis was not very rare in Nepal till 1960s.²³⁴

**Arsenosis**

Arsenosis is defined as a chronic health condition arising from prolonged ingestion of arsenic above the safe dose for at least six months, usually manifested by characteristic skin lesions of melanosis and keratosis, occurring alone or in combination, with or without the involvement of internal organs.¹

**Epidemiology**

There are many countries in the world as Argentina, Australia, Bangladesh, Nepal, Chile, China, Hungary, India, Mexico, Peru, Thailand and the United States of America where arsenic in drinking-water has been detected at concentration greater than the Guideline Value, 0.01 mg/L or the prevailing national standard. Seven of 16 districts of West Bengal have been reported to have ground water arsenic concentrations above 0.05 mg/L. According to a British Geological Survey study in 1998 on shallow tube-wells in 61 of the districts in Bangladesh, 46% of the samples were above 0.01 mg/L and 27% were above 0.05 mg/L. Environment Protection Agency of the United States of America has estimated that some millions of the population of USA, mostly in the western states, are exposed to arsenic in the water at 0.01 mg/L, although concentrations appear to be typically much lower than those encountered in areas such as Bangladesh and West Bengal.⁵⁶

**Arsenic contamination in Nepal**

2.4 million at risk - WHO standard

0.3 million at risk - Nepal standard
Arsenicosis calamity occurred in different countries of the world and in Asia

Etiology

Inorganic arsenic is the main cause of arsenicosis. The lethal dose of arsenic is 1-4 mg/kg body weight.

Sources

Arsenic is widely distributed throughout the earth’s crust. Arsenic is introduced into water through the dissolution of minerals and ores, and concentrations in ground water in some areas are elevated as a result of erosion from local rocks. Industrial effluents also contribute arsenic to water in some areas. Arsenic is also used commercially e.g. in alloying agents and wood preservatives. Combustion of fossil fuels is a source of arsenic in the environment through disperses atmosphere deposition. Exposure at work in mining and industrial emissions may also be significant locally. 5

Chemical and physical properties of Arsenic

Arsenic is an element that can combine with both metals and non-metals to form inorganic and organic compounds. The inorganic forms are toxic to human health and consist mostly of arsenite and arsenate compounds. The organic forms are comparatively non-toxic and one mostly present in sea foods. It has an atomic number 33 and an atomic mass of 74.91. It can exist in four valency states; -3, 0, +3 and +5. Arsenic and its compounds occur in crystalline, powder, amorphous forms. It is odorless and nearly tasteless. Specific gravity is 5.73 and it is non soluble in water. 1, 7

Uses of Arsenic

Arsenic compounds are mainly used in agriculture, forestry and industrial processes. Arsenic trioxide is used in manufacturing of agricultural chemicals (pesticides), glass and glassware, industrial chemicals, copper and lead alloys and pharmaceuticals. Chromated copper arsenite, sodium arsenate and zinc arsenate are used as wood preservatives. Some arsenic compounds such as arsanilic acid are used as food additives for poultry and swine. Small number of arsenic compounds continue to be used as drugs in some countries. Previously arsenic preparations were used for the treatment of skin disorders, tuberculosis, asthma, leprosy, syphilis and amoebic dysentery. 8

Normal values of arsenic in biological samples

Water: 0.01 mg/L (some countries have national standard as 0.05 mg/L)

Urine: <50 μgm/L

Dry Hair: <1 mg/kg

Nail: <1.5 mg/kg

Characteristic cutaneous lesion of arsenicosis

Melanos

Diffuse and generalized hyper pigmentation, Raindrop pigmentation, Leukomelanosis, Localized or patchy pigmentation generally on the body, Pigmentation of mucous membranes.

Keratosis:

Mild – Slight thickening or minute papules (<2 mm) of palms and soles, often associated with a grit
like texture, Moderate – Multiple, raised keratosis (>2 to 5 mm) appearing mainly or exclusively in symmetric distribution of palms and soles, Severe – Large discrete of confluent keratotic elevations (>5 mm) on palms and soles with nodular, wart like or horny appearance. Less commonly, there may also be involvement of the dorsum of the extremities and trunk. Diffused thickening of the palms and soles may occur alone or in combination with the keratotic nodules.

**Bowen’s disease:**

May appear as multiple macules, papule or plaque (1 mm to many cm) in non-sun exposed areas usually a scaly, crusted erythematous plaque. They are usually sharply demarcated and seldom indurated and if the crust is removed, the underlying surface may be red and oozing.

**Squamous Cell and Basal Cell Carcinoma**

Both these cancers have highly variable clinical appearances, depending in part on the stage of the malignancy. Squamous Cell Carcinoma is characterized by ulcerated or fungating growth. Basal Cell Carcinoma is initially characterized by pearly translucent nodules leading to ulceration.

**Nail:** Mee’s lines, dystrophy, leukonychia, pitting and Beau’s lines.

**Mucous membrane:** Hyperpigmentation of buccal mucosa, gum, palate and tongue.

**Constitutional symptoms:**

Anaemia, weakness, weight loss, anorexia, asthenia, conjunctivitis and burning sensation of eyes, non-pitting pedal edema, muscular wasting with claw hand, cramps in leg and hyperhidrosis of palms and soles.

**Systemic involvement**

**Neurological:** Paresthesias and numbness.

**Haematological:** Leucopenia and anaemia.

**Gastrointestinal:** Anorexia, vague abdominal pain or chronic diarrhea.

**Respiratory:** Chronic cough and bronchitis.

**Cardiovascular:** Peripheral vascular disease as Black Foot disease (BFD). Hypertension and non-pitting edema of the limbs.

**Urinary:** Proteinuria, Oliguria, haematuria and cast.

**Endocrine:** Diabetes mellitus and goiter.

**Reproductive:** Congenital malformation, miscarriages, spontaneous abortion and still birth.

**Hepatobiliary:** Cirrhosis, liver enlargement with or without non-cirrhotic portal fibrosis and hepatocellular carcinoma.

**Mechanism of arsenic poisoning**

Arsenic (As) has an affinity to bind sulfhydryl group (-SH) of different proteins as different enzymes, keratins, hemoglobin etc and accumulate in different parts of body and produce chronic health effect. It
crosses mitochondrial membrane and impairs oxidative phosphorylation which inhibits ATP and NADH production then reduces energy production causing oxidative stress and \( \text{H}_2\text{O}_2 \) production increase which leads to release of free radicals and causes cell injury. Arsenic also inhibits non competitively alpha ketogluterate dehydrogenase causing decreased succinyl CoA which leads to decrease in porphyrin and heme. Also, it inhibits DNA synthesis and repair in mitochondria which cause malignancy.\(^14,15\)

**Diagnostic criteria of arsenicosis**

**History of exposure**

At least 6 months exposure to arsenic above 0.05 mg/L in water, food or air.

**Clinical manifestations**

Constitutional symptoms as anemia, weakness, weight loss, anorexia, asthenia, conjunctivitis and burning sensation of eyes, non pitting pedal edema, muscular wasting with claw hand, cramps in leg and hyperhidrosis of palms and soles.

Systemic manifestations and complications as chronic lung disease, non cirrhotic portal fibrosis of liver with/without portal hypertension, peripheral neuropathy, vascular disease and cancers: Bowen’s disease, Squamous cell carcinoma, Basal cell carcinoma at multiple sites, occurring in unexposed parts of the body.

**Investigations**

Arsenic level in hair and nail above 1 mg/kg and 1.08 mg/kg respectively and/or arsenic level in urine, above 50 \( \mu \text{g} \)/L.

Presence of arsenic in urine is generally regarded as most reliable indicator of recent or continuing exposure to arsenic.

Skin biopsy and histopathology.\(^{16,17}\)

**Management strategies**

"Prevention is better than cure" is the pillar of success in arsenicosis mitigation.

However there are five key approaches for the management of Arsenicosis.

Cessation of exposure to arsenic

Administration of drugs and nutrients

Supportive care

Prevention of latent effects

Counseling and education

**Cessation of exposure to arsenic**

Make effort to stop drinking arsenic contaminated water or exposure to arsenic from any other sources. Various options of safe drinking water like Deep tube well, Rain water harvesting, Filtration (pond sand filtration, household filtration: Sonofilter), Dug well and Pipe water supply.

**Doses and Schedules for some common drugs use in arsenicosis**

**Chelating agents:**

Dimercaprol (BAL in oil) (British antilewisite): Adult dose: 2.5-3 mg/kg 4 hourly for 2 days, then 6 hourly for 1 day followed by bid for 10 days for arsenic levels over 50.

DMSA (Dimercaptosuccinic acid): 10 mg/kg PO 8 hourly for 7 days followed by 10 mg/kg 12 hourly for 14 days and repeat course 3 weeks later.
Penicillamine: Adult dose: 25 mg/kg PO 6 hourly to maximum 1 g/d.

**Antioxidants, vitamins and minerals:**

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<tr>
<th>Vitamin</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>Vitamin A</td>
<td>50,000 IU every alternate day for 6 months.</td>
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<tr>
<td>Vitamin E</td>
<td>200mg daily for 6 months.</td>
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<tr>
<td>Vitamin C</td>
<td>500 mg daily for 6 months.</td>
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<tr>
<td>Folic acid</td>
<td>1 to 2 capsules daily for prolonged period.</td>
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<tr>
<td>Spirulina</td>
<td>10 gm daily for 4 months.</td>
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<tr>
<td>Selenium</td>
<td>200µg/day for prolonged period.</td>
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**Supportive and symptomatic treatment**

Keratolytic agents: salicylic acid in ointment base or in Vaseline.

Cryosurgery can be done to remove keratosis.

Associated fungal infection should be treated with topical and oral anti-fungal agents.

Surgical excision can be employed in some cases.

Retinoid may be applied topically and systemically to reduce keratosis and to prevent malignancy.

**Prevention of latent effects and counseling:**

Create public awareness about health effects of arsenic toxicity

Avoid drinking arsenic contaminated water.

Avoid excess sunlight exposure and smoking.

Avoid occupational exposure to arsenic.

Avoid risk factors for cardiovascular, neurological, nephrological and other systemic disorders etc.

Avoid social prejudices of the disease.

Periodic examination for early detection and management of cutaneous malignancies.

Steps to promote health and nutrition.\(^{18,19,20}\)

**References**