

# Hepatic manifestations in chronic arsenic toxicity

AMAL SANTRA, J DAS GUPTA, BINAY K DE,\* B ROY, D N GUHA MAZUMDER

Departments of Gastroenterology and \*Medicine, Institute of Post Graduate Medical Education & Research, 244 Acharya JC Bose Road, Calcutta 700 020

**Objective:** The hepatotoxic action of arsenic, when used as a therapeutic agent, has long been recognized. Data on liver involvement following chronic exposure to arsenic-contaminated water are scanty. We report the nature and degree of liver involvement on the basis of hospital-based and cohort follow-up studies in patients who consumed arsenic-contaminated drinking water for 1 to 15 years.) **Methods:** 248 patients with evidence of chronic arsenic toxicity underwent clinical and laboratory examinations including liver function tests and HBsAg status. Liver biopsy was done in 69 cases; in 29 patients, liver arsenic content was estimated by neutron activation analysis. A cohort follow up of 23 patients who took arsenic-free water for 2-12 years was also carried out. **Results:** Hepatomegaly was present in 190 of 248 patients (76.6%). Noncirrhotic portal fibrosis (91.3%) was the predominant lesion in liver histology. The maximum arsenic content in liver was 6 mg/Kg (mean 1.46 [0.42], control value 0.16 [0.04];  $p < 0.001$ ); it was undetected in 6 of 29 samples studied. Cohort follow-up studies showed elevation of globulin in four cases and development of esophageal varices in one case. **Conclusion:** We report the largest number of patients with liver disease due to chronic arsenicosis from drinking arsenic-contaminated water. Noncirrhotic portal fibrosis is the predominant lesion in this population.) [*Indian J Gastroenterol* 1999;18:152-155]

**Key words:** Chronic arsenicosis, hepatomegaly, noncirrhotic portal fibrosis, portal hypertension

See editorial on page 141

Chronic exposure to inorganic arsenic has been reported to be associated with chronic changes in the liver. Development of ascites has been reported in patients taking liquor arsenic in therapeutic doses for prolonged periods.<sup>1,2</sup> Cases of cirrhosis of liver resulting from continued use of Fowler's solution containing potassium arsenite have also been described.<sup>3</sup> However, when liver biopsies of 44 psoriatic patients receiving potassium arsenate and 37 similar patients receiving no drug were compared, no histological differences were found.<sup>4</sup> Portal hypertension without signs of cirrhosis of liver has subsequently been reported following chronic arsenic medication, mostly as Fowler's solution.<sup>5-11</sup> Some of those patients also had typical skin manifestations.

Drinking of arsenic-contaminated water was first sus-

pected to cause noncirrhotic portal hypertension in two patients from Chandigarh.<sup>12</sup> A large number of patients suffering from chronic arsenic toxicity due to drinking of arsenic-contaminated tubewell water have been attending our institute since 1983. This led us to carry out a systematic study on the problem of liver disease caused by chronic intake of arsenic through drinking water. Some results of our study have been published previously.<sup>13,14,15</sup> The current presentation is a compilation of our data between 1985 and 1998.

## Methods

A total of 248 consecutive patients with evidence of chronic arsenic toxicity attending the arsenic clinic and medical out patients department of our hospital were studied. The inclusion criteria were as follows: (1) typical raindrop pigmentation and/or depigmentation of the skin of the body and limbs, (2) thickening of palms and soles with or without nodules in those areas characteristic of chronic arsenic toxicity and (3) arsenic level above the permissible limit set by the WHO ( $>0.05$  mg/L) in the water consumed by these people. The exclusion criteria were (1) past history of malaria or kala-azar, (2) prolonged intake of a hepatotoxic drug or alcohol, (3) hematological disease, and (4) cardiovascular or metabolic disease.

The arsenic-contaminated water (0.05-3.2 mg/L) which the subjects drank was drawn by hand pump from subsoil water at varying depths. The patient population also included 20 cases from southern Calcutta who took water containing high quantities of arsenic (5.05-14.2 mg/L) due to contamination of subsoil water by the waste of a factory manufacturing Paris green (copper acetoarsenite). None of these patients gave any history of taking arsenic-contaminated food. The duration of intake of contaminated water usually varied from 1 to 15 years, but in some cases it was life-long.

In addition to a thorough clinical examination, blood counts, blood biochemistry and examination of urine and stool were performed. Upper gastrointestinal (GI) endoscopy could be done on 73 patients with splenomegaly. Liver biochemistry and viral markers for HBsAg (ELISA) were carried out in 93 cases who could be admitted in the hospital. Liver biopsy was carried out in 69 of these patients who consented. The degree of portal fibrosis was graded<sup>13</sup> as: grade I - mild fibrosis producing expansion of portal zone; grade II - expansion of portal zone with thin fibrous extension producing septae; grade III - moderate fibrosis in the portal zone with thick septae; grade IV -

