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Randomized Placebo-Controlled Trial of 2,3-Dimercaptosuccinic Acid in Therapy of Chronic Arsenicosis Due to Drinking Arsenic-Contaminated Subsoil Water

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ABSTRACT

Introduction: Chronic arsenic toxicity producing various clinical manifestations is currently epidemic in West Bengal, India, Bangladesh, and other regions of the world. Animal studies have indicated that 2,3-dimercaptosuccinic acid can be used as an oral chelating agent. A prospective, double-blind, randomized controlled trial was carried out to evaluate the efficacy and safety of 2,3-dimercaptosuccinic acid for chronic arsenicosis due to drinking arsenic-contaminated ($\geq$ 50 μg/L) subsoil water in West Bengal. Method: Twenty-one consecutive patients with chronic arsenicosis were individually randomized (random number; assignment made by individual not evaluating patients) into 2 groups: 11 patients (10 male, age 25.5$\pm$8 years) received 2,3-dimercaptosuccinic acid 1400 mg/d (1000 mg/m^2) in the first week and 1050 mg/d (750 mg/m^2) during the next 2 weeks with a repeat course 3 weeks later. The other 10 patients (all male, age 32.2$\pm$9.7 years) were given placebo capsules for the same schedule. The clinical features were evaluated by an objective scoring system before and after treatment. Routine investigations

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including liver function tests, arsenic concentrations in urine, hair, and nails, and skin biopsy evaluations were also completed. Results: Though there was improvement in the clinical score of 2,3-dimercaptosuccinic acid–treated patients, similar improvement was observed in the placebo-treated group. There were no statistical differences in the clinical scores between the 2 groups at the beginning and at the end of treatment. Similarly, no differences were found for the other investigated parameters. Conclusion: Under the conditions of this study, 2,3-dimercaptosuccinic acid was not effective in producing any clinical or biochemical benefit or any histopathological improvement of skin lesions in patients with chronic arsenicosis.

INTRODUCTION

In West Bengal, India, a large number of people have been affected by chronic arsenicosis due to drinking geologically contaminated subsoil water from tubewells.[1,2] Similar problems have been reported in certain other geographical areas of the world.[3-5] Chronic arsenicosis leads to reversible damage to several vital organs and is established as carcinogenic.[5-7] Despite the magnitude of this potentially fatal toxicity, there is no effective therapy for this disease; patients once affected may not recover even after remediation of the arsenic-contaminated water.[8] The need for an effective therapy for chronic arsenicosis is obvious.

2,3-Dimercaptosuccinic acid (DMSA), a chelating agent, has been used in therapy for lead and mercury poisoning in humans.[10] There are reports of its efficacy in acute arsenic poisoning in mice[11] and in chronic arsenic poisoning in rats.[12] There are no studies on use in chronic arsenic poisoning of humans although mobilization of arsenic from the human body has been shown in acute arsenic poisoning.[13] We undertook this prospective, randomized controlled trial to evaluate the efficacy and safety of DMSA in patients with chronic arsenicosis due to drinking arsenic-contaminated subsoil water.

PATIENTS AND METHODS

Twenty-one consecutive patients with chronic arsenicosis were randomized into 2 groups. Eleven patients (10 males, ages 25.5±8.0 years) received DMSA 1400 mg/d (100 mg/m^2) in 4 divided doses the first week and then 1050 mg/d (750 mg/m^2) in 3 divided doses during the next 2 weeks. The same was repeated after 3 weeks during which no drug was administered. The other 10 patients (all males, ages 32.2±9.7 years) were given placebo capsules (resembling DMSA) in the same schedule. The patients were blinded about the nature of treatment being given. The patients included in the study were selected from the arsenic clinic on the basis of history of drinking arsenic-contaminated water (50 μg/L; ≥ 0.05 mg/L) for 2 years or more and clinical symptoms and signs of chronic arsenicosis. The symptoms and signs of patients were evaluated by an objective scoring system before and after treatment. The scoring system followed is summarized in Table 1. Any possible therapy-related side effect was monitored in every patient. All the patients were kept hospitalized during the study period.

Patients who stopped drinking arsenic-contaminated water for more than 5 months before inclusion into the trial, those who smoked, drank alcohol, took hepatotoxic drugs, and were found positive for hepatitis B virus surface antigen were excluded from the study. Ages below 18 years and pregnancy were also exclusionary. Informed consent was obtained from every patient before inclusion into the study. The study was cleared by the ethical committee of the institute.

Before inclusion into the study, all the patients underwent evaluation of their hemogram, liver function, prothrombin time, blood sugar, urea, and creatinine, and routine examination of urine and stool. Abdominal ultrasonography and upper gastrointestinal endoscopy were done to look for portal hypertension. A needle liver biopsy was obtained on all patients willing to provide informed consent.

Skin was biopsied from unexposed areas by punch biopsy technique for histologic evaluation before and after treatment. Hyperkeratosis, acanthosis, papillo-