Alcohol and Indian porphyrics

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Summary: The role of alcohol as the precipitating factor in the induction of acute attacks of acute intermittent porphyria was studied in an Indian population. Thirty-four teetotal patients with acute intermittent porphyria, in remission, were given 60 ml of 30% ethanol. Except for two patients, all had negative Watson-Schwartz tests prior to the alcohol. Within 24 hours, the Watson-Schwartz test became positive in 16 of these 32 patients (50%). In 8 out of the 34 patients (23.5%) a clinical attack was precipitated, including both patients who had a positive Watson-Schwartz test prior to the alcohol.

It was concluded that alcohol does precipitate an acute attack in a significant percentage of patients of Indian origin with acute intermittent porphyria. Patients already excreting porphobilinogen are at a greater risk of developing an acute attack on alcohol ingestion. This study is the first from India and probably first of its kind to be reported from any country.

Introduction

Acute intermittent porphyria (AIP) is an inborn error of metabolism transmitted as an autosomal dominant trait with variable expressivity and leading to an hepatic over production of porphyrin precursors.¹ The role of alcohol as a precipitating factor for production of attacks of AIP has been studied in Danish, German and British patients in the past with variable results.^{2–4} The contentious results obtained by these earlier workers prompted us to determine the role of alcohol in expression of the clinical symptoms in patients of Indian origin with AIP. In India, more than half of the cases of AIP have been reported from this part of the country – the Bikaner district of Rajasthan.^{5,6} The habit of alcohol ingestion being uncommon in this community, alcohol was given as a test dose to these patients.

Patients and methods

The present work was conducted in 34 teetotal volunteers suffering from AIP, but in remission at the time of study. Patients were diagnosed on the basis of clinical history, family history and urine examination for porphobilinogen. All the patients had at least two documented acute attacks, proved

by Watson-Schwartz tests for urinary porphobilinogen. Informed consent was obtained from all the patients and they were admitted to a well-equipped respiratory care unit. Respirators, intravenous glucose, propranolol and other supportive drugs were kept ready to combat any complication arising out of precipitation of an acute attack. Watson-Schwartz tests were performed in all the patients prior to the administration of the alcohol.

An oral test dose of 60 ml of 30% ethanol was given to each patient. [100% ethanol (supplied by the hospital laboratory) was diluted with distilled water.] Clinical examination and the Watson-Schwartz test were done at 12 hourly intervals for 72 hours. All the patients were re-examined at 6 weeks.

Results

Sixteen out of 32 patients (50%), having a negative Watson-Schwartz test prior to the alcohol, developed a positive Watson-Schwartz test in their urine within 24 hours. Eight out of a total number of 34 patients (23.5%) studied, developed an overt clinical attack of AIP. Two of these patients were already excreting porphobilinogen, as evidenced by a positive Watson-Schwartz test prior to the alcohol.

Generalized abdominal pain, mild tenderness and red coloured urine were seen in all the patients

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Accepted: 12 February 1991

in whom a clinical attack was induced. Three patients complained of nausea/vomiting, and pain in the extremities. Palpitations, hypertension, paraesthesiae and psychosis were each seen in 2 patients. A single patient developed distal myopathy of lower limbs with vocal cord paresis and breathlessness in addition to abdominal pain, passage of red urine, vomiting and palpitations. No mortality or long term morbidity was seen at 6 weeks follow-up in any of the subjects studied.

Discussion

Increased hepatic activity of δ -aminolaevulinic acid (δ -ALA) synthetase has been suggested by many workers⁸⁻¹⁰ in AIP. Zail and Joubert¹¹ conclusively demonstrated it by using a microassay procedure. Stanley *et al.*¹² concluded that when symptomatic porphyric patients were challenged with alcohol, hepatic δ -ALA synthetase activity was raised and it led to increased urinary porphyrin excretion which reversed with abstinence. The role of alcohol as a precipitating factor of an acute attack of AIP has been a subject of controversy. While Goldberg *et al.*³ and Doss *et al.*⁴ implicated alcohol as a definite precipitating factor, With² failed to do so and was of the opinion that alcohol restriction is unwarranted.

In the present study 8 (23.5%) of the 34 patients

challenged with alcohol developed an acute attack. Increase in urinary porphobilinogen excretion was documented by the development of a positive Watson-Schwartz test in 16 (50%) of the 32 patients with a previously negative test. The two patients with a prior positive Watson-Schwartz test developed an acute attack.

Abdominal pain and passage of red coloured urine were the commonest clinical features in the induced attack. The number of previous attacks of AIP or the time lapsing between the last attack and the administration of alcohol did not have any significant bearing on the effect of alcohol in these patients. No mortality or long term morbidity (at 6 weeks) occurred in any of the subjects studied.

We conclude that alcohol does precipitate clinical attacks in a significant percentage of patients of Indian origin with AIP and that the risk of induction of attacks is especially great if the patient is already excreting porphobilinogen.

Since no specific measures to treat an acute attack are available to date²⁻⁴ prevention of acute attacks in porphyrics is of the utmost importance and for this porphyrics should avoid taking well recognized porphyrinogenic agents. It is, therefore, recommended that advice should be given to the patients and carriers of acute intermittent porphyria, that even in the remission phase, they should avoid alcohol.

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