Halothane-Induced Fulminant Hepatic Failure

A S Puri, S S Sikora, Rakesh Aggarwal, S R Nair

Departments of Medical Gastroenterology and Surgical Gastroenterology,
Sanjay Gandhi Postgraduate Institute of Medical Sciences, Post Box 375, Lucknow 226 014

Abstract

Fulminant hepatic failure developed in the early postoperative period in a patient after third exposure to halothane. Exclusion of other causes of postoperative jaundice and temporal relationship of jaundice to anesthesia suggested halothane as the etiologic agent for the submassive necrosis, which was documented at postmortem liver biopsy. (Indian J Gastroenterol 1993; 12: 100-1).

Key words: Drug hepatotoxicity, halothane hepatitis.

Since its introduction into clinical use in 1956, halothane has been widely used because of its advantages of high potency, lack of inflammability and general smoothness of administration. However, halothane toxicity has been reported from several western countries and in USA, this drug has been largely replaced for anesthesia in adults by other compounds. Surprisingly, despite its widespread use, there are no reports of halothane toxicity from our country.

We report a patient with fatal fulminant hepatic failure (FHF) due to halothane; this, to the best of our knowledge, is the first report of halothane toxicity from India. The aim of this report is to highlight the preventable aspect of this uncommon but potentially lethal complication.

A 50 year old man presented to us in April 1992 with a four-week history of bloody diarrhea and abdominal pain. He was assessed to have severe idiosyncratic ulcerative colitis on the basis of clinical, endoscopic and laboratory criteria. He did not respond to intensive medical treatment and an emergency local colectomy, Brooke's ileostomy and closure of rectal stump were done under general anesthesia (GA) using halothane. Resected colon showed pancolitis with transmural ulcera tions in the transverse colon. Needle biopsy of the liver showed pericholangitis. Postoperative course was complicated by occurrence of intra-abdominal abscess, wound dehiscence and frontal lobe cerebral infarction.

In August 1992, he presented with persistent purulent discharge from the abdominal wound and retraction of ileostomy. He underwent and dilation under GA for evacuation of pus from the rectal stump; followed in September 1992 by revision and relocation of ileostomy. Halothane was used on both these occasions also. No hypertension was recorded during either of the operations. He developed moderate grade fever on the first post-operative day after the third surgery followed by rapidly deepening jaundice. Liver span by percussion was 6 cm. He lapsed into coma on the sixth post-operative day.

Total leucocyte count was 15800/L (65% polymorphs, 30% lymphocytes and 12% monocytes). Serum liver function test values are shown in the Table 1. Ultrasonography did not show any evidence of biliary obstruction. Serum HBSAg, IgM anti-HBe and anti-HCV (anti-C-100-5) were negative. He died on the twelfth postoperative day of massive intrabdominal bleed due to the coagulopathy. Postmortem liver histology showed massive hepatic necrosis with focal macrovesicular fatty change.

Halothane hepatitis as an entity had been seriously questioned due to absence of definite diagnostic criteria and the similarity of its clinical features to those of viral hepatitis. Availability of serological markers for detection of recent infection with both hepatotropic viruses has resolved this issue to a large extent and has led to better acceptance of hepatic toxicity of halothane. Prospective studies have shown that liver enzyme abnormalities occurred more frequently after repeated exposure to halothane than after the use of other anesthetics. Two types of biochemical liver dysfunction associated with halothane have been described. A mild rise in serum transaminases may occur in as many as 25% of patients exposed to halothane. Fulminant hepatic failure fortunately is encountered in only very small proportion of patients who have been exposed to halothane on more than one occasion.

In our patient, halothane was considered to be the cause of liver injury in view of the rapid appearance of jaundice after third exposure to halothane, and marked elevation and the rapid rate of decline in the serum transaminases. Underlying chronic liver disease was excluded by liver biopsy performed during the first surgery. Applying the 'Causality Assessment Criteria' as suggested by the Council for International Organization of Medical Sciences (CIOMS) a score of 6 is obtained which is highly suggestive of drug induced liver disease. The demonstration of submassive necrosis on postmortem

<table>
<thead>
<tr>
<th>Table 1: Serum liver function tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
</tr>
<tr>
<td>--------------------------------</td>
</tr>
<tr>
<td>Pre-operative</td>
</tr>
<tr>
<td>3rd day post-operative</td>
</tr>
<tr>
<td>7th day post-operative</td>
</tr>
</tbody>
</table>

*SAP, Serum alkaline phosphatase*
Table 2: Guidelines of Committee on Safety of Medicines for halothane use (1986)

1. A careful anesthetic history should be taken to determine previous exposure and previous reactions to halothane.
2. Repeated exposure to halothane within a period of 3 months should be avoided unless there are overriding clinical circumstances.
3. A history of unexplained jaundice or pyrexia in a patient following exposure to halothane is an absolute contraindication to its future use in the patient.

Liver biopsy further strengthens the case as this lesion has been consistently seen in previously reported cases of fatal hepatitis due to halothane.

Factors associated with increased risk of halothane-induced liver damage include middle age, female gender, obesity, multiple exposures and genetic susceptibility. On the basis of these risk factors practical guidelines have been suggested by the Committee on Safety of Medicines (Table 2) to reduce the risk of halothane-induced liver injury.

We feel that this fatal complication could have been avoided in our case if these guidelines had been followed. As the guidelines are very simple and practical, the onus for the prevention of halothane hepatitis lies to a large extent with the treating surgeons and anesthesiologists.

References