It is widely acknowledged that isoflurane is less hepatotoxic than its predecessors, halothane and enflurane. We present a 68-year-old man who developed fulminant and fatal hepatic necrosis two days after open cholecystectomy done under isoflurane anesthesia. Laboratory findings included grossly elevated transaminases and bilirubin, and prolonged prothrombin time. Serological studies were negative for viral hepatitis. Postmortem examination demonstrated centrilobular necrosis of liver. [Indian J Gastroenterol 2006;25:41-42]

Prolonged prothrombin time. Serological tests were negative for viral hepatitis. Postmortem examination demonstrated centrilobular necrosis of liver. [Indian J Gastroenterol 2006;25:41-42]

Fatal isoflurane hepatotoxicity without re-exposure

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Isoflurane is less hepatotoxic than its predecessors, halothane and enflurane. We present a 68-year-old man who developed fulminant and fatal hepatic necrosis two days after open cholecystectomy done under isoflurane anesthesia. Laboratory findings included grossly elevated transaminases and bilirubin, and prolonged prothrombin time. Serological studies were negative for viral hepatitis. Postmortem examination demonstrated centrilobular necrosis of liver. [Indian J Gastroenterol 2006;25:41-42]

Postoperative hepatic injury has been reported after anesthesia with halothane, enflurane, desflurane and isoflurane. The latter three resist biodegradation more than halothane.1 Hepatotoxicity results from an immune response directed against hepatic proteins altered by trifluoroacetyl or trifluoroacetyl-like metabolites of the anesthetics. Only a few cases of hepatotoxicity causally related with isoflurane have been reported, a finding consistent with its lower metabolism and lower levels of formed trifluoroacetyl proteins.2

A 68-year-old man with history of chronic obstructive lung disease and previous truncal vagotomy and gastrojejunostomy was admitted with symptoms of acute cholecystitis since three days. He had no history of hypertension and no alcohol abuse. Clinical findings included right upper quadrant tenderness, positive Murphy’s sign and mild fever. Ultrasonography showed gallstones and gall bladder wall thickening. Serum white blood cells were 11,000/mm³, and serum bilirubin, alkaline phosphatase, AST and ALT were normal. After fluid resuscitation, antibiotics and analgesics, open cholecystectomy was performed. Anesthesia was induced with intravenous thiopentone 5 mg/Kg and vecuronium 0.1 mg/Kg. He was intubated and maintained with isoflurane up to 1.5% in a 1:1 mixture of nitrous oxide-oxygen. His blood pressure under anesthesia was within normal limits, and no peroperative respiratory complications were recorded.

On the first postoperative day he developed tachypnea, tachycardia, and hypotension (70/40 mmHg) for 5 min. Lung scintigrapy showed small areas of irregular perfusion due to emboli. Treatment consisted of intravenous fluids, inotropic agents and heparin infusion. Two days postoperatively he developed right upper quadrant pain with fever, vomiting, and a rise in liver enzymes to twice the normal limit. Serum white blood cells was 18,100/mm³, serum bilirubin 3.8 mg/dL, alkaline phosphate 823 IU/L, AST 6200 IU/L, ALT 1900 IU/L, LDH 12,600 IU/L and INR peaked at 3.

Three days postoperatively he developed abdominal distension, decreased mental status and agitation. Serum white blood cells peaked at 24,000/mm³, AST 20,200 IU/L, ALT 7200 IU/L, LDH 20,730 IU/L, bilirubin 4.4 mg/dL and INR 3.7. Serological tests for hepatitis A, B and C were negative. Ultrasonography revealed normal portal, mesenteric and hepatic vascular systems and intrahepatic ducts.

The next day the liver enzymes levels decreased to AST 7610 IU/L and ALT 431 IU/L, with anuria and bilateral pulmonary infiltrate. He developed multi-system organ failure and died on the sixth day postoperatively.

On post-mortem liver wedge biopsy, there was confluent necrosis (Fig) and sinusoidal congestion involving predominantly zones 3 and 2. There were zones of confluent bridging necrosis linking adjacent central veins as well. In some areas, necrosis extended to the entire hepatic lobule.

Halothane, isoflurane, enflurane and desflurane undergo oxidative metabolism catalyzed by hepatic
cytochrome P450 2E1. Drugs that are minimally metabolized may be safer anesthetic choices. Reductive metabolites produced under hypoxic conditions produced centrilobular necrosis in the liver of rats. However in most human cases of halothane hepatitis, hypoxemia has not been a recognized association.

Isoflurane is less hepatotoxic than its predecessors, halothane and enflurane. Sinha et al provided direct evidence that the drug can induce liver injury and should therefore be considered as a potential cause of serum transaminase elevation in any patient who is exposed to this anesthetic. Weitz et al reported fulminant, fatal hepatic necrosis after uneventful isoflurane anesthesia in a patient without previous liver disease. No anti-trifluoroacetyl antibodies could be detected in the patient’s serum. Turner et al described fulminant hepatic necrosis six days after an uneventful operation under isoflurane anaesthesia. Postmortem examination demonstrated centrilobular necrosis of the liver, with clinical findings similar to our case report.

In summary, we report fatal hepatic necrosis after isoflurane anesthesia in a patient who had not been sensitized by previous exposure to isoflurane.

References

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