

# HEPATOCELLULAR DAMAGE DUE TO HALOTHANE ANAESTHESIA

Pages with reference to book, From 262 To 263

Barkat A. Charania, Nusrat U. Khan, Parveen Charania ( Charania Hospital, MA. Jinnah Road, Karachi. )

## Abstract

To determine the hepatotoxic effect of halothane anaesthesia, liver function tests were done a day prior to surgery in 41 cases undergoing various elective operations. The tests were repeated on 7th post operative day to see the derangement.

Statistically significant rise in serum bilirubin, ALT and alkaline phosphatase was found post-operatively. As certain groups of patients are more prone to develop halothane induced hepatotoxicity, damage in these cases could be prevented by careful pre-operative assessment (JPMA 38: 262 , 1988).

## INTRODUCTION

Halothane (Fluothane) a non-explosive halogenated hydrocarbon, which is structurally similar to chloroform is one of the most widely used general anaesthetic agents. It is also known to cause hepatic injury and post operative jaundice.<sup>1-7</sup> Most studies suggest that a particular group of patients like obese elderly females, patients with unexplained spiking pre-operative fever, those exposed to halothane in the preceding 6 weeks, and those known to develop jaundice and liver damage after exposure to halothane are prone to develop such a damage<sup>8-11</sup>..

The present study was done to see the extent of liver damage following long halothane anaesthesia during a major surgery. There was no added risk to the patient because only liver function tests were added to the list of pre and post operative tests.

## PATIENTS AND METHODS

Fortyone patients undergoing various elective surgical procedures under halothane anaesthesia were selected for the study. None of the patients were jaundiced or had history of jaundice in the past. Pre-operative liver function tests (serum bilirubin, ALT and alkaline phosphatase) a day prior to surgery were within normal limits in all the cases. Liver function tests were repeated on the 7th post operative day to see the changes indicating hepatocellular damage.

Statistical analysis was done using critical freedom ratio (F-ratio) or 99% probability level, and students' T test.<sup>12</sup>

## RESULTS

Of 41 cases, there were 21 males and 20 females. Except for 3 children under 12 years of age, all were adults.

Significantly higher post operative values were obtained for serum bilirubin, ALT and alkaline phosphatase, suggesting hepatic damage by halothane (Table I).

**TABLE I Pre and Post Operative Results.**

		Mean	SD	F. ratio	99% probability Level or Critical 'F' ratio
Mg%					
Serum	Pre-op	0.56	0.13	29.0	2.11
Bilirubin	Post-op	0.91	0.54		
SGPT	Pre-op	21.93	6.97	2.64	2.11
U/L	Post-op	37.27	11.37		
Serum Alk.	Pre-op	28.22	12.44	6.85	2.11
Phos- phatase	post-op	54.34	32.57		
U/L					

SD = Standard Deviation

'F' Ratio = Freedom Ratio

**TABLE II. Frequency of abnormal Tests.**

Parameters of LFTs and their normal values	Number of tests done	Number of tests in which post-op. values were found abnormal
Bilirubin 0–1.2mg%	41	7
SGPT 5–40 units/lit.	41	14
Alk. Phosphatase 15–69 units/lit.	41	8
Total	123	29
%		23.58

Table II shows the percentage frequency of abnormal liver function tests seen post operatively. Of 123 liver function tests done post operatively in 41 cases, 29 (23.58%) tests were found to be abnormal in 22 patients.

## DISCUSSION

The role of halothane in the production of post-operative hepatic damage and jaundice is controversial because hepatic damage following general anaesthesia was seen even before halothane was used as an anaesthetic<sup>8</sup>. Later it was thought that hypoxia caused by excessive use of nitrous oxide along with halothane is the cause of hepatic damage, rather than halothane alone<sup>2</sup>.

Hepatotoxicity following the use of halothane usually mild to moderate with slight derangement has been reported in one or more components of liver function tests in about 20% cases<sup>9,10</sup>. Similar findings were seen in the present study (23.58%). Fulminating hepatotoxicity, though rare, is mostly seen in adults<sup>11</sup>.

Children are often less vulnerable to hepatic damage than adults.<sup>5,11</sup> Severe hepatic necrosis occurs in

individuals who have previously been exposed to halothane. However, failure to produce similar damage in animals, the rarity of hepatic damage in humans and the delayed appearance of hepatic damage, suggests that halothane is not a direct hepatotoxin but is probably a sensitizing agent.<sup>12</sup> It also seems likely that the reduction of halothane through a minor metabolic pathway results in a toxic metabolite that destroys the hepatocytes.<sup>12</sup>

To reduce the frequency and severity of hepatotoxicity following the use of halothane, a minimum gap of 3 months has been suggested between 2 halothane anaesthesias.

## REFERENCES

1. Stock, J.G.L. and Strunin, L. Unexplained hepatitis following halothane. *Anaesthesiology*, 1985; 63:424.
2. Burns, T.H. Unexplained hepatitis following halothane (letter), *Anaesthesia*, 1987; 42 : 76.
3. Adams, A.P. Halothane and the liver. *Br. Med. J. (Clin. Res.)*, 1986; 293 :1023.
4. Walton, B., Simpson, B.R., Strunin, L., Doniach, D., Perrin, J. and Appleyard, A.J. Unexplained hepatitis following halothane. *Br. Med. J.*, 1976; 1: 1171.
5. Inman, W.H.W. and Mushin, W.W. Jaundice after repeated exposure to halothane; a further analysis of reports to the Committee on Safety of Medicine. *Br. Med. J.*, 1978; 2 : 1455.
6. Neuberger, J. and Williams. R. Halothane anaesthesia and liver damage. *Br. Med. J.*, 1984; 289:1136.
7. Sherlock, S. Halothane hepatitis. *Lancet*, 1978;2:364.
8. Brunson, J.G., Eckman, P.L. and Campbell, J.B. Increasing prevalence of unexplained liver necrosis. *N. Engl. J. Med.*, 1957;257: 52.
9. Wright, R. Controlled prospective study of the effect on liver function of multiple exposure to halothane. *Lancet*, 1975; 1: 817.
10. Trowell, J. Controlled trial of repeated halothane anaesthetics in patients with carcinoma of uterine cervix treated with radium. *Lancet*, 1975;1 :821.
11. Wark, H. Prospective study of liver function in children following multiple halothane anaesthetics at short intervals. *Br. J. Anaesth.*, 1986; 58: 1224.
12. Committee on Safety of Medicine. Halothane hepatotoxicity. *Current problems* 18, 1986; Sept: 1-2.