WAS IT HALOTHANE? A CASE REPORT

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WITHIN the past few years the numerous provocative reports which have appeared in the literature with regard to halothane have either acclaimed the product as a valuable addition to the anaesthesiologist's armamentarium or accused it as a causative factor in postoperative liver necrosis. However, the data so far presented have been unconvincing in establishing a causal relationship between any one anaesthetic agent and liver necrosis, as pointed out by Gingrich and Virtue.¹ These observers reported the occurrence of liver necrosis after cyclopropane and epidural anaesthesia. Only time will tell whether or not halothane is "guilty as charged." Meanwhile, the following report is presented in the interest of adducing further evidence.

CASE REPORT

A 20-year-old Mexican female was admitted to the hospital on January 31, 1965, with a diagnosis of cholecystitis probably secondary to cholelithiasis. She weighed 160 pounds and was 62 inches in height. In her history she denied jaundice, haematemesis, melena, cardiac or respiratory disease, prior surgery, or allergies. She did not smoke or drink. Physical examination was negative except for symptoms referable to the present problem. Blood pressure was 135/80, pulse 80/min., and respiration 16/min. Haemoglobin was 13.6 gm. and haematocrit 40. W.B.C. was 10,700 and B.U.N. 9. Cholecystograms taken on February 3 and repeated on February 4 reported "non-visualization of the gall bladder."

She was scheduled for an elective cholecystectomy and cholangiogram on February 5. At 6:15 A.M. on the morning of surgery, she received as premedication meperidine 75 mg., pentobarbital 100 mg., and atropine 0.6 mg. The pre-induction vital signs were blood pressure 110/80, pulse 96, and respirations 18. Haemoglobin was 14.0 gm. and haematocrit 43. Induction of anaesthesia was started at 7:50 A.M. with 200 mg. of thiopental and 60 mg. of succinylcholine for intubation with a #38 cuffed tube. This was easily done under direct vision. A nasogastric tube was inserted for drainage and aspiration of gastric contents. A cardioscope monitor was used throughout surgery.

The induction was smooth, and the operation was started at 8:15 A.M. At 8:35 A.M. a Bird respirator was connected into the anaesthesia circuit and was continued until 10:40 A.M., at which time respirator was removed from the circuit. The operation was completed at 11:35 A.M., and anaesthesia ended at 11:50 A.M. At this time the patient was extubated and was breathing adequately.

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She was awake, alert, and responsive. Blood gases were drawn strictly for didactic purposes. The pH was 7.45, P_{CO_2} 36, P_{O_2} 156, base excess -1.8, and standard bicarbonate 22.5. The estimated blood loss was 390 c.c., and 600 c.c. of 5 per cent dextrose and water were given. Blood pressure and vital signs remained stable throughout surgery.

Surgical exploration of the abdomen was negative except for the gall bladder, which was found to be small, contracted, and filled with stones. It was difficult to isolate the cystic duct because of reactive scar tissue around the cystic duct and at the junction with the common duct. The cystic duct was estimated to be 1 to 2 mm. in diameter when it was finally isolated by a transverse incision just distal to the gall bladder and blunt dissection. A small wire probe was introduced via the cystic lumen into the common duct. Attempts at introducing a polyethylene catheter for the operative cholangiogram were unsuccessful. The cholecystectomy was otherwise uneventful.

In the recovery room the blood pressure and pulse were stable ranging from 110/80 to 130/80, with the pulse between 90 and 80 over a 2½-hour observation period. Demerol 75 mg. i.m. was given at 12:45 P.M. for pain. The patient was co-operative and practised deep breathing and coughing.

On the ward (February 6) the patient's temperature showed elevation to 100° F. Her blood pressure was stable. Demerol 75 mg. was given i.m. for pain. Fluid intake and urinary output were as follows:

February 5: Intake 600 c.c., output 400 c.c.
February 6: Intake 3100 c.c., output 950 c.c.
February 7: Intake 940 c.c., output 800 c.c.
February 8: Intake 1020 c.c., bathroom privileges
February 9: Intake 200 c.c., bathroom privileges

The patient was discharged February 10 following 5 days of uneventful post-operative observation. Acetaminophen 300 mg. was prescribed for pain. On February 12 the sutures were removed in the out-patient clinic, and the patient was doing well.

The next hospital visit was on February 16, 1965, when the patient was seen for chills, fever, and emesis of 2 days' duration. Trimethobenzamide (Tigan®) 200 mg. i.m. was given. Tincture belladonna-elixer phenobarbital drams 1 after meals, acetaminophen, and paregoric were also given for symptoms of gastroenteritis. A blood count at this time showed haemoglobin 13.2, haematocrit 40, and W.B.C. 8300.

The patient returned on February 17 with persistent abdominal pain and nausea and periodic emesis, although she was retaining water satisfactorily. She was readmitted to hospital on February 18 in the early morning, with complaints of nausea, vomiting, and singultus. W.B.C. was 14,600 with 67 bands, haemoglobin 12, and haematocrit 39. S.G.O.T. was 7000, alkaline phosphate 17, and bilirubin 5.5. The serum was icteric. The abdomen presented generalized tenderness with voluntary guarding, especially over the right upper area. Sounds were hypoactive. Scleral icterus was noted. There was also complaint of generalized itching. The patient was quite somnolent and not in acute distress, and occasionally scratched herself. Vital signs were temperature 98.6, pulse 72, respiration 18,

and blood pressure 130/70. The admitting diagnostic impression was (1) sub-hepatic abscess, and (2) R/O common duct stone.

Prior to this admission a private physician had given the patient chlorpromazine (Thorazine®) 40 mg. and meperidine (Demerol®) 75 mg. i.m. at 10:30 P.M. and had referred her to this hospital.

At 9:00 A.M. on the day of admission the patient was found comatose. Funduscopy showed no abnormalities. On lumbar spinal puncture, the cerebrospinal fluid was found colorless with 2 cells, 2 polymorphonuclears, protein 12 mg., and glucose 78 mg./100 c.c. Initial pressure was 310 mm. H₂O, and final pressure was 243 mm. Laboratory record showed B.U.N. 55, blood sugar 150 mg./100 c.c.

Arterial gas analysis showed pH 7.355, P_{CO_2} 35, P_{O_2} 80, standard bicarbonate 9.7, base excess 5.2. The W.B.C. was 14,400, differential 41 bands, 41 per cent polymorphonuclears, 10 per cent lymphocytes, 5 per cent monocytes, and 3 per cent eosinophils; haemoglobin was 10.5 and haematocrit 32.

Blood chemistry showed serum alkaline phosphatase 21 King-Armstrong units; bilirubin was 5.5, and S.G.O.T. was 320.

Electrolyte analysis showed sodium 123, chloride 78, potassium 3.7, and carbon dioxide 23.

Following a tonic convulsion at 3:45 P.M., a neurologic consultation was obtained, and the patient was examined at 4:00 P.M. and at 7:00 P.M. No localizing signs were observed on examination or by electroencephalogram. A left carotid arteriogram revealed no evidence of supertentorial mass lesion. A pneumoencephalogram was non-contributory. The neurologic diagnostic impression was to rule out cerebral oedema secondary to toxic compound, encephalitis, or a pseudo-tumor.

On February 19 at 3:00 A.M., when the patient was transferred to the intensive care unit, her C.V.P. was 5 mm. H₂O. She vomited 200 c.c. of dark material. Respiration ceased and the patient was intubated and placed on I.P.P. breathing. Blood pressure was 70/50 and increased 110/70 with neosynephrine drip. The pupils were fixed and dilated.

On February 20 the patient's status was unchanged. Minimal urine output was noted. At 9:00 P.M. vital signs were not obtained and the patient was pronounced dead.

The autopsy report revealed (1) terminal bronchopneumonia, and (2) massive liver necrosis.

The question now arises: Was the halothane to blame?

SUMMARY

Details of a case of postoperative death from massive liver necrosis following halothane anaesthesia are presented.

REFERENCE

1. GINGRICH, T. F. & VIRTUE, R. W. Postoperative Liver Damage: Is Anesthesia Involved? *Surgery*. 57: 241 (1965).