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SOME CLINICAL IMPRESSIONS OF HALOTHANE

JOHN TAIT RUSSELL, M.B., B.CH. (RAND), D.A. (ENG.), D.A. (IRE.), *Senior Honorary Anaesthetist, Livingstone Hospital, Port Elizabeth*

Halothane (Fluothane), 2—bromo—2—chloro—1, 1, 1—trifluoro-ethane (CF_3-CHClBr) is about 2 years old, but has already proved itself to be an important addition to the anaesthetist's repertory. It is a new member of the halogen group of anaesthetics introduced by Imperial Chemicals Industries after exhaustive experiments on animals.

Physical Properties

Halothane is a liquid (producing a non-inflammable and non-explosive vapour) with a boiling point of 50·2°C, a specific gravity of 1·86 at 20°C, and a vapour pressure of 439 mm. Hg at 20°C. Its vapour is non-irritant and has a pleasant odour. Decomposition may occur when it is exposed to light, but this is prevented by the addition of 0·01% thymol and packing in dark-coloured bottles.

Pharmacology

Raventos[1] found the therapeutic ratio in animals to be 3·5, twice that of ether and chloroform. Surgical anaesthesia was produced with concentrations of 2-4%, induction taking up to 5 minutes without the usual 'stage of excitement'. Anaesthesia could be maintained with concentrations of 0·8-1·0%, a potency twice that of chloroform and 4 times that of ether. Hypotension, and respiratory arrest which is easily reversible by artificial respiration after stopping the halothane, were produced if the induction concentrations were maintained. Cardiac sensitivity to intravenous adrenaline was increased and bleeding was decreased. Recovery was rapid, even after long anaesthetics. Cardiac output was unchanged and electrocardiograms normal. A report by the Medical Research Council[2] showed, however, that cardiac output was reduced.

The mechanism of the hypotensive action of halothane is complex, possibly consisting of a central depressant effect, weakening of the myocardium and, to some degree, a peripheral ganglion block. As regards this latter action on the autonomic ganglia it is pointed out that the important practical aspect of this action is the potentiation of ganglion-blocking drugs such as d-tubocurarine or hexamethonium.

Johnstone[3] reports alarming drops in blood pressure and circulatory collapse after intravenous injections of 15 mg. of d-tubocurarine during halothane anaesthesia, and the accentuation of this collapse by positive- pressure inflation of the lungs.

The accentuation of parasympathetic action is a most important action of halothane, which results in a bradycardia and requires atropine to reverse the action. Riker and Wescoe (1951) showed that gallamine triethiodide (Flaxedil) has a specific action in paralysing the ability of the vagus to slow the heart, which should prove to give gallamine a special place in halothane anaesthesia. This was confirmed in this series of cases.

Types of Operation

Many different types of surgical procedures were undertaken in 300 cases. The youngest patient was 6 months-old and the oldest 87 years. The following is an analysis of the types of operation undertaken:

(1) *Gynaecological:* Abdominal 16 and vaginal 34; total 50.

(2) *Obstetrical:* Caesarian section 3.

(3) *Abdominal:* Upper 8 and lower 12; total 20.

(4) *Thoracic:* Lobectomy 20, pneumonectomy 5, thoracoplasty 7, hiatus hernia 5, thoracotomy 8, decortication 7, oesophagectomy 3, total gastrectomy 2 and bronchoscopy 2; total 59.

(5) *Ear, nose and throat:* Tonsillectomy 26, nasal 14 and laryngo-fissure 1; total 41.

(6) *Other:* Plastic 8, orthopaedic 24, thyroidectomy 26, head and neck 10, craniotomy 2, urological 6, angiogram 2, eyes 8, breast 23, varicose veins 4 and haemorrhoids and anal 17; total 130.

Total number of cases: 303.

There were 4 deaths in this series, none as a direct result of the anaesthetic. Three of the thoracic cases died later from other causes (2, carcinoma of oesophagus with secondary spread, and 1 gastric carcinoma with secondary spread who died of congestive cardiac failure and pulmonary oedema 10 days after the operation). The fourth death was caused by a malignant tumour of the temporal region with haemorrhage into the tumour. This patient died 12 hours after the operation having been unconscious before being taken to the operating theatre. The degree of unconsciousness,

however, was such that the patient still reacted violently to stimuli.

Premedication was relatively light: Promethazine 25-50 mg. 2 hours before operation, usually orally, and sometimes omitted; and pethidine 50-100 mg. and atropine 1/100 gr., 1 hour before the operation. Children, depending on age, were given pacatal, 1½ mg. per 1 lb. of body weight 2 hours before the operation and atropine ½ hour before the operation. On occasion pethidine or promethazine were used instead of pacatal. Atropine was always given to counteract the stimulation of the vagal action on the heart. Frequently a further 1/100 gr. atropine was given intravenously, if the operation was to be a long one. Morphine and its derivatives were not used because of their respiratory depressant effects.

TECHNIQUE AND RESULTS

The 'Fluotec' percentage fluothane vaporizer was used either with the standard Boyle's machine or the Oxford inflating bellows. Where possible a 4-litre gas flow per minute (50% nitrous oxide with oxygen), employing a Waters absorber unit, was used with the percentage vaporizer for the sake of economy, as advocated by Brennan *et al.*[4] In this series the circle absorber was not used on account of the possible dangerous high percentage concentration that, as Hudon, Chang and others have shown, might result.[5-8]

The 'fluotec' vaporizer has been shown to be accurate to within 0·05% at rates of gas flow between 4 and 10 litres per minute at all normal operating-theatre temperatures.[9] Possessing a thermostat the vaporizer was found to work exceedingly well.

The use of the 'fluotec' vaporizer with the Oxford bellows was found to be a most satisfactory technique, but it increased the amount of halothane required.

Induction was usually a sleep-dose of thiopenthone, as most patients find an injection preferable to 'the mask'. With nitrous oxide, oxygen and halothane, or halothane and air (using the Oxford bellows), induction was rapid, particularly in children, and the switch-over to ether gratifyingly easy when required, as pointed out by Bull *et al.*[10] There was no stage of excitement in any of these cases. Initially a 2% concentration was adequate for a reasonably rapid and pleasant induction with no coughing or breath-holding; a great asset for patients with difficult veins.

Relaxation was fair, but not comparable to that achieved with the relaxant drugs. Succinylcholine chloride was generally used for endotracheal intubation as a time-saving measure, for 15 minutes was usually required to facilitate intubation with halothane. Adequate relaxation for upper abdominal operations was not obtained with halothane alone as the hypotension was the limiting factor. Relaxant drugs had to be added for this type of operation. Of these the most satisfactory is gallamine triethiodide (Flaxedil), only half or less of the usual doses being required. Because of its atropine-like action gallamine decreased the tendency to a bradycardia and, as a rule produced, if anything, a slight tachycardia. As our experience with halothane increased, the tendency was to use a lower percentage of halothane with slightly larger doses of gallamine, which resulted in rapid recovery from a smooth and flexible anaesthetic—most satisfactory to both surgeon and anaesthetist. Only once was neostigmine considered necessary, and this drug, given intravenously after a dose of 1/50 gr. atropine, produced no muscarine-like action in a dose of 2·5 mg.

d-Tubocurarine was not used, for a number of workers have confirmed Johnstone's finding[3] of alarming drops in blood-pressure after 15 mg. doses followed by positive-pressure ventilation. There is a real risk of circulatory collapse. In fact, positive-pressure ventilation increases the hypotensive effects of halothane and smaller percentages should be used.[11]

Respiration was quiet initially, but increased in rate and decreased in depth as anaesthesia deepened, resulting in inadequate ventilation. If spontaneous respiration was wanted at this stage, the halothane concentration had to be decreased. Otherwise respiration had to be assisted.

This tachypnoea is a distinct disadvantage and small doses of pethidine were not found to relieve this to the extent that occurs with the trichlorethylene tachypnoea. Surgical stimulation occasionally produced a deeper respiration temporarily or produced a peculiar respiratory pattern consisting of a deep inspiration and expiration followed by a long pause.

Occasionally, if an endotracheal tube had not been passed, a crowing type of respiration resulted from surgical stimuli. But this seldom lasted, particularly if the depth of anaesthesia was increased.

Control of respiration was easily obtained without the addition of relaxant drugs. The assistance of the respiration was necessary, to some extent, in the majority of cases.

The pulse slowed an anaesthesia deepened, rates of 40 per minute being not unusual if the intravenous atropine had been omitted. Atropine usually remedied this.

The blood pressure fell 20-30 mm. of Hg within a short time. If, however, when this occurred, the halothane percentage was reduced, the blood pressure usually rose or, at least, did not continue to fall. Constant vigilance is necessary throughout and the pulse and blood pressure should be recorded at least every 4-5 minutes and even more frequently until anaesthesia has been stabilized.

The pulse rate did not always decrease in proportion to the drop in blood pressure, and not infrequently hypotension was present with some degree of tachycardia.

Blood replacement must be meticulous because the resulting vasodilatation prevents the normal vasoconstrictive response to blood loss and the blood pressure sometimes falls rapidly. This phenomenon occurs to a greater or lesser extent with most anaesthetics in present-day use, accurate blood replacement being an essential part of modern theatre technique.

In patients exhibiting signs of shock following haemorrhage or accidents, halothane was useful because a high oxygen percentage could be used; induction was quick and the blood-pressure fall minimal with adequate care. Induction was usually achieved with a 1·5% concentration and for maintenance of anaesthesia as little as 0·5% was sufficient for most patients. A warm, pink patient was the usual finding. In fact, the patient resisted surgical assaults with an unusual equanimity.

Recovery was rapid. Recovery-time is not in direct proportion to the length of the operation, but it increased with the duration of the anaesthetic. If, however, the percentage concentration was reduced towards the end of the operation, this greatly facilitated a more rapid recovery; the administration of halothane could be stopped 10-15 minutes earlier and in most cases ,recovery of reflexes ensured

in the theatre. In this series the recovery times have improved with increasing experience, the average time now being 10-15 minutes. A striking feature is the rapid return of mental alertness, a valuable asset for out-patients. Violent shivering was not uncommon. This, however, appeared to have no deleterious effect, probably because it arises as a compensatory reaction to the loss of heat during operation.

Complications and Advantages

Extubation was sometimes attended by some degree of laryngospasm, which was never troublesome and could be quickly controlled by the insertion of a pharyngeal airway and the administration of oxygen.

Analgesia was poor. Many patients, particularly those who had thoracotomies performed, required intravenous administration of analgesics before leaving the theatre. This was not felt to be a disadvantage because timely administration of analgesics prevented restlessness.

Salivary and Bronchial Secretions were diminished and pharyngeal suction was usually not necessary at the conclusion of the operation.

Post-operative Vomiting was minimal. Only 2 patients in this series vomited for 1 day. In both cases the vomiting ceased when the post-operative analgesic was changed. Most patients felt no nausea and, if analgesics were administered in time, were comfortable.

With adrenaline ventricular tachycardia and extrasystoles were produced in 2 patients—in 1 after a submucous resection of the septum and in the other after a bilateral intranasal antrostomy. In both cases cocaine with adrenaline was injected submucosally. Immediate reduction of the halothane concentration resulted in a return to normal rhythm within a few minutes. But the experience was alarming because the possibility of ventricular fibrillation has to be considered.

Johnstone[3] reported ventricular extrasystoles in 12 cases; in each case there was some degree of underventilation.

Ventricular tachycardia was reported by Millar[12] after subcutaneous injection of adrenaline. Burns[13] found that ventricular extrasystoles were not of the multifocal variety usually considered the precursor of ventricular fibrillation. This statement, in the light of our present knowledge of halothane, should be accepted with caution. If the marked depression of respiration with its associated risk of sub-oxygenation and carbon-dioxide retention is taken into account, the possibility of the precipitation of ventricular fibrillation cannot be discounted.

In thoracic surgery the minimal bleeding from the necessarily large incision, the ease with which the respiration can be controlled (especially with the addition of small doses of gallamine) the smoothness and flexibility of the anaesthesia, the rapid return of consciousness and the satisfactory immediate post-operative breathing associated with this anaesthetic are of great assistance in this type of work.

The gravid uterus is considerably relaxed by halothane. For this reason its use in obstetrics is contra-indicated. Mackay[14] appears to be the first worker to record this and several others[15-17] have since observed this property. In 3 Caesarian sections in which I administered the anaesthetic (nitrous oxide, oxygen and halothane), blood loss *per vaginam* was considerable and the uterus failed to contract in spite of 2 intravenous injections of 0·5 mg. of ergometrine. Not until the halothane was stopped and a few minutes had elapsed to allow some recovery from its effects, did the uterus contract.

Porphyria. There was no opportunity to use halothane in the cases of porphyria which are prevalent in this area.

DISCUSSION

There seems no doubt that there is a place for halothane in modern anaesthetic practice. Its merits and demerits are as follows:

Advantages

(*a*) Ease of administration due to its potency and flexibility.

(*b*) Pleasant and rapid induction and recovery for the patient.

(*c*) Reduction of bleeding without the fussiness and possible dangers of other hypotensive techniques.

(*d*) Use in shocked patients possible because of high oxygen percentage and, with proper care, minimal disturbance of blood pressure.

(*e*) Prevention of the shock syndrome if blood replacement is adequate.

(*f*) Relative safety if used with care by an experienced administrator. An accurate percentage vaporizer is necessary.

(*g*) Non-explosive and non-inflammable.

Disadvantages

(*a*) Production of bradycardia and hypotension, requiring constant vigilance.

(*b*) Marked depression of respiration leading to hypoxia and carbon dioxide retention unless anaesthesia is maintained in a 'light' plane or respiration is assisted.

(*c*) Sensitization of the cardiac muscle to the action of adrenaline with the possibility of ventricular fibrillation.

(*d*) Relaxing effect on the uterine muscle of the pregnant uterus, which virtually excludes its use in obstetrical anaesthesia.

These properties bear a resemblance to those of chloroform and, to some extent, of trichlorethylene (also halogen compounds) but, up to the present, from all acounts, halothane appears safer particularly when compared with the former.

(*e*) *Expense.* The present price is over £13-0-0 per bottle of 250 cc.—sufficient for 15-20 cases.

SUMMARY

The clinical effects of halothane, as observed in 300 administrations, are discussed. The need for an accurate vaporizer, and the necessity for care in administration are stressed. Advantages and disadvantages are summarized.

I should like to thank Imperial Chemical Industries for the supply of fluothane with which I carried out this work. Also I should like to express my appreciation for the help and invaluable advice given me by my partner Dr. R. A. Moore Dyke.

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