FLUOTHANE ANAESTHESIA IN INFANTS AND CHILDREN

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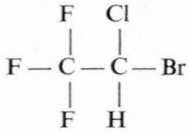
Fluothane is the trade name of the new volatile anaesthetic agent trifluorochlorobromethane (halothene).



From its structural formula, it will be seen that it is a derivative of ethane with 3 hydrogen atoms substituted by fluorine, 1 by bromine and 1 by chlorine. It is non-explosive and non-flammable both as a liquid and vapour mixed with oxygen, air or nitrous oxide. Fluothane is a clear, colourless liquid with S.G. of 1·86 at 20°C and boiling point of 51°C. The odour is sweetish, not unpleasant and completely non-irritating.

Some pharmacological actions of Fluothane have been described by Raventos[1] and more recently by Burn *et al.*[2] in a report to the British Medical Research Council. Several reports[3-12] on its use in clinical anaesthesia have appeared since December 1956. From these reports, mainly of its use in adults, it appeared that Fluothane might offer certain advantages in the field of paediatric anaesthesia, particularly in respect of the non-irritating properties of its vapour, ease of induction and speed of recovery and the reported absence of nausea and vomiting on recovery, although this latter finding was not consistent.

In the present trial, Fluothane was administered to 200 children, either as the principal anaesthetic agent (150 cases) or as an agent for induction before maintenance of anaesthesia with di-ethyl ether (50 cases). The age of the patients (Table I) varied from 2 days to 11 years. Patients were entirely unselected as far as pre-operative condition was concerned and included 1 case of bilateral acute lobar pneumonia, 4 cases of tracheotomy for severe respiratory distress, 2 cases of very severe toxaemia due to acute osteitis, and several asthmatics. Repeated anaesthetics with Fluothane were received by 12 patients, 2 of these on 9 occasions at weekly intervals. The type of surgery carried out is indicated in Table II.

TABLE I. AGE DISTRIBUTION OF CASES RECEIVING FLUOTHANE AND FLUOTHANE-ETHER SEQUENCE

Age	*Fluothane*	*Fluothane-ether*
0–2 weeks	6	2
2 weeks–1 year	20	8
1–5 years	66	21
5–11 years	58	19
Total	150	50

TABLE II. DISTRIBUTION OF CASES ACCORDING TO TYPE OF SURGERY

Type of Surgery	*Fluothane*	*Fluothane-ether*
Intra-abdominal	20	8
E.N.T...	25	14
Plastic	21	3
Eye	5	0
Hernia..	42	13
Urological	6	1
Other	31	11
Total	150	50

Premedication in all cases consisted either of pethidine and atropine or atropine alone given by intramuscular injection 1 hour before anaesthetic. The dose of pethidine was strictly according to body weight (0·5 mg. per lb.).

The dose of atropine was 1/300 gr. for children under 2 months of age, 1/200 gr. from 2 months to 1 year, 1/150 gr. from 1 year to 5 years and thereafter 1/100 gr. It was decided in view of the stress laid on the use of atropine with Fluothane by Michael Johnstone, to depart from our usual practice in omitting it from premedication in very small infants.[13]

ADMINISTRATION

Previous experience by one of us (A.B.B.) in the administration of Fluothane to dogs during its preclinical investigations, and the reports of clinical trials by others, have given a clear indication of the extreme anaesthetic potency of Fluothane vapour. This makes it important to ensure accurate measurement of vapour concentration in inhaled mixtures. At present, two types of apparatus are available for accurate administrations of known concentrations of Fluothane vapour within a wide range of temperatures and rates of flow. These are the Fluotec vaporizer[10] and the E.M.O.[14] Fluothane inhaler. Both are compensated for changes in ambient temperature and for change in temperature of liquid within the vaporizer caused by evaporation, and will deliver accurate vapour concentrations over a sufficiently wide range of flow rates for all clinical purposes. A third type of vaporizer is also available in the form of a modified Trilene bottle of the standard type found on the Boyle apparatus. This, however, is not temperature compensated and, in practice, wide variations in Fluothane concentrations are likely to be encountered in the use of this apparatus. In this series of cases the Boyle-type bottle was used on some 15 cases and then abandoned owing to marked temperature changes in the Fluothane caused by evaporation, leading to gross inaccuracy of delivered vapour concentration. In the remainder, Fluothane was administered from the Fluotec vaporizer or the E.M.O. in a vehicle of N_2O and O_2, O_2 alone, or air. It must be noted that internal resistance in the Fluotec inhaler is too high to permit its use as a 'draw over' inhaler and that when used with air, a means of delivering air through the vaporizer must be employed. The E.M.O. is so constructed that internal resistance is negligible at all concentrations and can be used as 'draw over'.

INDUCTION

It was found that patients became unconscious after 2-3 minutes' inhalation of 1·5-2% Fluothane vapour. A very characteristic pattern of events occurred during this induction period, the salient points of which were as follows: (1) There was no objection to inhaling the mixture that could be attributed to unpleasant odour or irritation. (2) A tranquil state was reached very rapidly—usually in the first minute—in which all signs of apparent nervousness, when present, disappeared, yet consciousness and, in older children, ability to converse intelligently, remained unimpaired. (3) Following this tranquil state, there appeared a very brief stage, lasting only a few seconds, which could be construed as 'second stage' anaesthesia. (4) This was followed by very rapid loss of consciousness and the appearance of profound relaxation during the 2nd or 3rd minute of inhalation.

This stage of loss of consciousness was accompanied by a definite fall in blood pressure which averaged 25 mm. Hg, and an obvious decrease in amplitude of respiration and slight increase in rate. In 4 cases in which respiratory minute volume was recorded, this drop amounted to as much as 50% of normal. This state of profound relaxation and shallow breathing was found to be most misleading and any pain stimulus applied, immediately produced brisk movement on the part of the patient, a rise in blood pressure to near pre-anaesthetic level, and an increase in amplitude of respiration.

Most striking, however, was that at this stage, after some 3 minutes of inhalation of 1·5-2% vapour, laryngoscopy could be performed with ease. The jaw was very relaxed and the vocal cords wide open. Stimulation of the pharynx by the laryngoscope, however, or an attempt to pass an endotracheal tube, resulted in closure of the cords and a cough or series of coughs which seemed to be fully coordinated and not at all in the nature of a 'spasm'. Withdrawal of the stimulus was rapidly followed by the return of rhythmical respiration, and in only one case did we experience anything that could be termed 'laryngeal spasm' during induction, in spite of repeated deliberate attempts to produce one. Continued stimulation of the larynx did sometimes provoke breath holding.

To provide conditions satisfactory for endotracheal intubation without provoking coughing, we found it necessary either to apply topical anaesthesia to the larynx at an early stage, say after about 3 minutes, or to continue giving 2% vapour for a full 10 minutes. This period of 10 minutes was also found to be the average time necessary before surgical stimulus could be applied without causing the patient to move; it provided satisfactory operating conditions for all extra-abdominal procedures. Relaxation, however, was frequently not sufficient to permit all intra-abdominal procedures.

MAINTENANCE OF ANAESTHESIA

Fluothane was used as the agent to maintain anaesthesia in 150 cases. After induction as outlined above, it was found that the application of the stimulus of surgery caused a rise in blood pressure from the earlier fall to within 10 mm. Hg. of the level before anaesthesia. This frequently continued for the duration of the operation, especially if adequate anaesthesia could be maintained with concentrations of Fluothane not exceeding the region of 1%. This concentration was found satisfactory for most extra-abdominal procedures, although it was sometimes necessary to maintain concentrations of up to 2%.

For abdominal operations requiring much relaxation 2% Fluothane was not always adequate. Increase in Fluothane concentration did improve relaxation but the increased depth of anaesthesia was invariably accompanied by marked decrease in respiration and fall in blood pressure to levels as low as 80 mm. Hg. We feel that where relaxation with 2% vapour alone is inadequate, it is preferable either to resort to the use of muscle relaxants to provide the desired degree of relaxation or to change over to ether for maintenance. In this series 20 cases received muscle relaxants, succinyl choline being used 15 times and gallamine 5 times. When a relaxant was used, Fluothane concentration was decreased to 1%, and under these circumstances we noticed no major alteration in blood pressure provided that meticulous attention was paid to maintaining blood volume. In the cases which received gallamine, neostigmine preceded by atropine was used at the end of operation. This too was followed by no untoward circulatory changes. We do feel,

however, in the light of reports on the 'vagotonic' action of Fluothane that neostigmine should be used with caution and that elimination of Fluothane should be allowed to take place as far as possible before neostigmine is given.

RECOVERY

The return of consciousness in all cases was rapid. After short periods of anaesthesia, lasting up to 20 minutes, consciousness returned within 5-7 minutes. After longer periods return of consciousness was delayed up to 10 minutes and occasionally to 15. This recovery time was seldom exceeded even after operations lasting up to 3 hours, except where there had been very extensive surgery or doubt about adequacy of blood replacement. The nature of the recovery was striking in that protective reflexes returned early and mental alertness was regained very rapidly. It was not uncommon to find patients after operations which produced minimal post-operative pain sitting up, fully alert, within 10 minutes of leaving the operating table. The most notable feature in recovery was the almost complete absence of nausea and vomiting. Only one case in the series receiving Fluothane as the sole or principal anaesthetic vomited during recovery. This patient, who had an appendicectomy, was also the only patient in the series to receive a dose of pethidine in excess of 0·5 mg. per lb. as premedication. He, in fact, received 1 mg. per lb. As important as the absence of actual vomiting is the absence of nausea. No indication of post-recovery nausea was encountered.

Generalized shivering was noticed frequently during the early stages of recovery. No accurate record of the incidence of this was kept but some degree of generalized shivering lasting for $\frac{1}{2}$ -1 minute was noticed in the majority of cases. In 2 cases shivering was violent and lasted for 3-4 minutes.

FLUOTHANE-ETHER SEQUENCE

In 50 cases anaesthesia was induced with Fluothane at 1·5-2% concentration as described above, anaesthesia being maintained thereafter with N_2O, O_2 and ether. In these cases the initial fall in blood pressure and decrease in respiratory amplitude was noticed but there was a return to normal levels within 2 minutes of change-over from Fluothane to ether. Thereafter the picture remained as usually seen with ether anaesthesia. The following observations were made:

1. Change-over to ether after 3-4 minutes of 1·5-2% Fluothane was not associated with laryngeal spasm or coughing, even when ether was introduced abruptly. For example, it was possible to move the ether control on the standard Boyle's bottle from closed to full-open in a matter of 10 seconds.
2. Recovery in this series was not accompanied by the shivering seen with Fluothane alone.
3. Vomiting during recovery was seen in 10 cases.
4. Return of mental alertness was as is usually seen after ether anaesthesia.

COMMENT

Fluothane is an extremely potent anaesthetic agent, inhaled concentrations of 1-2·5% being sufficient to provide anaesthesia for almost all surgical procedures in children. Succinyl choline and gallamine can be safely employed to procure added relaxation with low concentration of Fluothane, should this be necessary.

The non-irritant properties and not unpleasant smell, the speed and smoothness of action, offer distinct advantages over other inhalation agents as a method of induction in paediatric anaesthesia.

Rapid recovery and quick return of mental alertness and in particular the striking absence of nausea and vomiting are of inestimable value both from the point of view of general comfort and especially for the safety of the patient. We have found this particularly so in those plastic and orthopaedic cases where fixation posture makes vomiting during recovery hazardous in the extreme. This rapid recovery, however, carries the disadvantage of rapid awareness of post-operative pain and it is notable that Fluothane appears to provide little or no residual analgesia. Care must therefore be taken in the judicious and fairly early use of post-operative analgesics to avoid restlessness and distress due to pain. To attempt to cover pain during the recovery period by the use of heavier premedication may be dangerous because it is likely to increase the respiratory depression during anaesthesia.

Fluothane is non-flammable and non-explosive and so has the advantage of being usable with impunity in the presence of diathermy.

The method of administration is simple and Fluothane can be administered in air or with N_2O-O_2 mixtures. Its extreme potency, however, demands accurate control of vapour concentration and, whilst its use on an open mask[4] and in closed circuit apparatus[7] has been described, we feel very strongly that there is a very real danger of delivering unknown concentrations which may become dangerously high. Changes in concentration of as little as 0·5% V/V cause marked changes in depth of anaesthesia.

Hazards

Against these advantages which Fluothane offers in clinical use, must be set the various hazards which may be encountered in the present state of our knowledge of this drug. In this respect, respiratory depression and hypotension stand foremost.

Respiratory depression carries with it the risk of hypoxia and carbon-dioxide retention. The former, it is true, may be largely compensated for by administering Fluothane in an oxygen-rich mixture, and when this is done clinical manifestations of hypoxia are absent. Administered in air, however, signs of anoxia advancing to definite cyanosis are sometimes seen. Carbon-dioxide excess can of course occur during administration both in oxygen-rich atmosphere and in air, and both this and anoxia sometimes have adverse effects on the cardio-vascular system. During Fluothane anaesthesia, however, respiration can be assisted or even fully controlled with great ease provided normal airway precautions are observed, and in this way the disadvantage of respiratory depression may be overcome. The detection of what constitutes an undesirable degree of respiratory depression, on the other hand, is more difficult to assess accurately unless one has facilities for continuous measurement of respiratory exchange. In the absence of such facilities, one must rely on clinical acumen and experience. We feel that respiratory depression during Fluothane anaesthesia must be looked for most carefully at all times and that it is wiser to err on the side of over-ventilation by assisting respiration when in any doubt than to risk insidious hypoxia and hypercarbia by permitting spontaneous respiration of

questionable adequacy to persist. In this connection too, it is important to choose premedication so that it will not aggravate respiratory depression.

Hypotension. The mode of production of the fall in blood pressure during the administration of Fluothane is by no means clear. Animal experiments[2] suggest that depression of the central vasomotor mechanisms plays a part and that there is some reduction in cardiac output. The extent to which these factors operate in the intact human subject has not yet been determined. Clinical reports have shown that the hypotension is easily reversible by pressor drugs, but whether it is necessary to employ them by routine is questionable and the degree of hypotension must be taken into consideration. The clinical picture of hypotension under Fluothane anaesthesia is one of a warm, vasodilated patient with good peripheral blood flow. In the non-atropinized patient, there is also bradycardia and the blood pressure falls to lower levels than in the atropinized subject. The picture in fact resembles what has been described as neurogenic hypotension. It is most important, however, to note that in this state, blood loss will not be compensated for by normal physiological mechanisms and blood lost during surgery under Fluothane anaesthesia must be replaced with the same care as during spinal anaesthesia. This is doubly important in infants and children, where initial blood volume is small and small amounts of blood lost comprise a relatively large proportion of circulatory blood volume. The degree of hypotension becomes increasingly severe with administration of increasing concentrations of Fluothane but in this series we have not encountered pressures below 90 mm. Hg if concentration of 2% is not exceeded. We hesitate to say that the hypotension can be ignored unless severe, but in this series it has not given cause for alarm and, provided blood volume was replaced to keep pace with blood loss, return of blood pressure to pre-operative levels occurred promptly when Fluothane administration was stopped. The mechanism of production of the hypotension, however, requires further investigation and, in view of the suspicion that diminished cardiac output may play a part, it must be viewed with caution.

No studies of renal or hepatic function from which conclusions can be drawn were undertaken in this series. Creatinine clearance and inulin and P.A.H. clearance performed on two cases, however, suggests that the effect of Fluothane on glomerular filtration rate and renal plasma flow is similar to that seen with other general anaesthetic agents.

CONCLUSION AND SUMMARY

The use of Fluothane as the anaesthetic in 200 operations on children is described and discussed. We feel that Fluothane offers distinct advantages as an induction agent in paediatric anaesthesia and that the striking absence of vomiting during recovery found in this series can be of great value. The rapidity and mode of recovery too make it an admirable agent for out-patient use. The respiratory depression and cardiovascular effects seen, however, are of such a nature that further investigation is most desirable. Great care in administration is necessary at this early stage in knowledge of the pharmacological action of Fluothane and we feel it is important to use an accurately calibrated vaporizer for administration.

We wish to thank Dr. J. F. W. Mostert for permission to publish the results of this series of cases. Messrs. I. C. I. Pharmaceuticals have made generous supplies of Fluothane available. We also wish to thank our surgical colleagues for their patience and cooperation while we were using this anaesthetic.

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