PRELIMINARY EXPERIENCE WITH ENFLURANE

C.S. Chan

Department of Anaesthetics
Queen Mary Hospital
Hong Kong

C.S. Chan, MBBS, DA, FFARCS
Consultant Anaesthetist

SYNOPSIS

Clinical experience with the use of enflurane on one hundred fifty patients was presented. The drug was found to be a very satisfactory inhalational anaesthetic. The advantages and disadvantages of enflurane are briefly discussed. Although enflurane is not free from undesirable features, in some instances it may be a better alternative to halothane for inhalational anaesthesia.

INTRODUCTION

The hepatotoxicity associated with halothane (1) and the nephrotoxicity associated with methoxyflurane (2) have been a source of concern to anaesthetists. Enflurane is a volatile anaesthetic recently introduced into this region. Reports in the literature indicate that enflurane is, among other things, safer with regards to the liver and kidneys when compared with halothane and methoxyflurane respectively. A preliminary study was carried out on 150 cases to evaluate the clinical usefulness of enflurane in our anaesthetic practice.

The chemical structure and physical properties of enflurane are shown in Table I, together with those of halothane and methoxyflurane for comparison. Enflurane is a halogenated methyl ether like methoxyflurane, but its physical properties resemble those of halothane which is a halogenated hydrocarbon. Its blood/gas partition coefficient is less than that of halothane; therefore, induction and recovery are rapid. However, the minimum alveolar concentration (MAC) for enflurane is twice that of halothane, meaning that it is only half as potent.

Table I

Structure and physical properties of enflurane, halothane and methoxyflurane

Approved Name	Enflurane	Halothane	Methoxyflurane
Structure	Cl F F H-C-C-O-C-H F F F	Br F H-C-C-F Cl F	Cl F H H-C-C-O-C-H Cl F H
Boiling point (at 760 torr)	56.5°C	50.2°C	104.7°C
Molecular weight	184.5	197.4	165.0
Vapour pressure (torr) (20°C)	175	243	25
Blood/gas partition coefficient (37°C)	1.9	2.3	13
Oil/gas partition coefficient	98.5	224.0	930.0
MAC in O_2 (in young adults)	1.68	0.75	0.16

MATERIALS AND METHODS

150 patients were anaesthetized with enflurane at the Queen Mary Hospital between July 1980 and May 1981. The age and sex of the patients were shown in Table II. The operations done covered many specialties, including general surgery, gynaecology, orthopaedics, ENT, radiodiagnosis, eye and dentistry.

Table II

Age and sex of patients

		Number of patients
Age (year):	0 to 1	2
	1 to 12	37
	13 to 40	61
	41 to 60	32
	61 to 80	14
	more than 80	4
Sex:	male	85
	female	65

The vaporizer used for enflurane was the Enfluratec (Cyprane). This temperature- and flow-compensated vaporizer is calibrated in increments of 0.2% from 0 to 1% and in increments of 0.5% from 1 to 5%. For children, the anaesthetic circuit used was the Ayre's T-piece with Jackson-Rees modification; for adults, either the Magill attachment or closed circuit was used.

In most cases atropine and pethidine were given for pre-medication in standard doses. This was omitted in some cases, especially in small children.

Enflurane was employed for inhalational induction in small children. In older children and adults, induction was carried out with intravenous thiopentone. Enflurane was introduced for inhalation together with nitrous oxide and oxygen (2:1 ratio). The concentration of enflurane vapour was increased in 0.5% increments every four breaths until a concentration of 4% was reached. Adequate level of surgical anaesthesia usually was achieved in 5 minutes.

For maintenance of anaesthesia a concentration of enflurane vapour of 1.0 to 2.5% was required. As with other drugs, there is an individual variation in response to enflurane. In general a higher concentration was needed for small children. The mode of breathing was in most cases spontaneous. Patients receiving neuromuscular blocking agents for relaxation were not included in this study; in these cases the concentration of enflurane vapour need only be small, thus making it pointless to determine the time of recovery at the end of the anaesthetic.

RESULTS

Adequate level of surgical anaesthesia was usually achieved in 5 minutes.

Some drop in blood pressure occurred during induction; for example, from 120 mm Hg systolic to 90 mm Hg systolic. The degree of hypotension was in proportion to the depth of anaesthesia and an excessive drop could mean that a relative overdose had been administered. With surgical stimulation the blood pressure tended to rise somewhat towards the pre-induction level. Pulse rate remained steady throughout the operation.

Respiration was slightly depressed, mainly affecting tidal volume rather than frequency. In one adult patient undergoing a simple gynaecological operation, respiration was so depressed that assisted breathing had to be carried out. In another adult patient with myasthenia gravis undergoing subtotal thyroidectomy for thyrotoxicosis, controlled ventilation was employed, without the use of neuromuscular blocking drugs.

Muscle relaxation under enflurane anaesthesia was found to be adequate, for example, for orchidopexy when the testis was situated at the internal inguinal ring.

Pupils remained small throughout the general anaesthetic.

At the termination of the anaesthetic conscious-

ness returned rapidly, usually in 5-10 minutes. This was the case even when the operation lasted up to 4 hours. In one orthopaedic case for reimplantation of the ring finger the duration of the anaesthetic was 5¼ hours, yet the patient took 6 minutes to recover consciousness; in this patient the intraoperative end tidal PCO_2 varied between 32 and 37 mm Hg.

The incidence of post-operative nausea, vomiting and shivering were shown in Table III.

DISCUSSION

Advantages of enflurane

No preservation is required for enflurane. This is in contrast to halothane, in which the thymol used as a stabilizer tends to cause problem with the vaporizer (particularly the Fluotec Mk II).

Enflurane is non-flammable and non-explosive in oxygen. It is pleasant to inhale, at the same time inducing minimal production of saliva and secretions. Enflurane has a low blood and tissue solubility. This means that induction and recovery are rapid (3). Indeed the level of anaesthesia may be controlled easily.

The biotransformation rate of enflurane is 2.4% (4). This is much less than that of halothane (20%) (5, 6), and methoxyflurane (50%)(7). Furthermore there is no evidence that patients receiving barbiturates or other drugs have raised serum fluoride concentrations after enflurane anaesthesia (8); neither does enflurane appears to produce enzyme induction for its own metabolism at a subsequent exposure (9). Being metabolically stable may be beneficial to operating room personnel, that is, if one believes chronic exposure to trace anaesthetic gas/vapour constitutes a health hazard.

So far reports of hepatic damage after enflurane anaesthesia are rare. The effect of enflurane on the liver is less than halothane, especially with respect to repeated exposures (10, 11). Indeed it has been suggested, based on the data currently available, that enflurane may be a suitable alternative to halothane when repeated inhalation anaesthesia are required (12).

Some degree of muscle relaxation is achieved with enflurane. If a non-depolarizing neuromuscular blocking drug is used with enflurane, a reduction of the dose of the former is required (13). Enflurane is a useful agent for supplementing "balanced" anaesthesia, because it potentiates the non-depolarizing neuromuscular blocking agent and also allows a rapid return of consciousness at the termination of anaesthesia. The fine calibration of the Enfluratec vaporizer at the lower range (in increments of 0.2% up to 1%) is a bonus in this respect, especially suitable for Chinese patients whose tolerance for anaesthetic drug is much less than people of the Caucasian race.

Under enflurane anaesthesia arrhythmia is less likely to occur than with halothane when adrenaline is injected (14) for haemostasis. Intraocular pressure decreases with enflurane anaesthesia. The degree of lowering is irrespective of the depth of anaesthesia (15). Enflurane anaesthesia is associated with minimal nausea and vomiting.

Disadvantages of enflurane

Enflurane impairs cardiac performance (16). A close watch has to be kept on the blood pressure particularly at the induction phase before surgical stimulation begins. Severe hypotension at this stage usually means relative overdosage, provided hypovolaemia is not present.

Enflurane is also a potent ventilatory depressant (17). The tidal volume of the patient has to be closely monitored, again particularly at induction. Any excessive depression should be overcome immediately with assisted ventilation.

Breakdown of enflurane yields fluoride metabolites. The mean peak serum inorganic fluoride concentration following enflurane anaesthesia is in the region of 20 umol litre^{-1} (18). This is much less than the serum concentration of 50 umol litre^{-1} necessary to cause fluoride nephrotoxicity. Nevertheless it would be prudent to avoid enflurane in patients with pre-existing renal dysfunction (12).

Convulsive EEG patterns occur under deep enflurane anaesthesia especially when associated with hypocapnia (19). Tonic-clonic twitchings of muscle may develop. These are signs of enflurane overdosage and should be reversed by allowing anaesthesia to lighten and $PaCO_2$ to rise. It would be advisable to avoid using enflurane in patients with epilepsy (12).

Shivering is not uncommon after enflurane anaesthesia. However, the cool temperature of the operating room (20°C) must have contributed to the greatly increased incidence of shivering in those patients in whom the operation lasted more than one hour.

Volume for volume, enflurane is about twice as expensive as halothane. Considering that enflurane is only half as potent as halothane, it means that an anaesthetic employing enflurane is going to cost four times as much as one using halothane.

Table III

Incidence of nausea, vomiting and shivering
(Per cent in brackets)

Duration of operation	Number of Cases	Incidence of		
		Nausea	Vomiting	Shivering
up to 1 hr	89	2 (2.2%)	0 (0%)	9 (10.1%)
1 to 5¼ hr	61	8 (13.1%)	5 (8.2%)	18 (29.5%)
(Total)	150	10 (6.7%)	5 (3.3%)	27 (18%)

CONCLUSION

Enflurane is a very satisfactory inhalational agent for clinical anaesthesia. Although it has undesirable features, in some instances it may be a better alternative to halothane for inhalational anaesthesia.

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