A COMPARATIVE CLINICAL STUDY OF ENFLURANE AND HALOTHANE

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for the Degree of Master of Medicine
(ANAESTHESIA) in 1982.

D E C L A R A T I O N

This work is original and has not to my knowledge been submitted for a degree in any other University.

DR. KALPANA SHETH

This Dissertation has been submitted for examination with my approval and supervision.

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A C K N O W L E D G E M E N T

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A perspective study was carried out on a total of forty healthy adult patients (ASA Grade I - II) who were randomly allocated to one of two groups. The groups were identical in age and sex distribution; as well as the type of surgical procedure. One group received halothane (1-2%) in nitrous oxide - oxygen mixture (4 and 2 L/min respectively) and the other group received enflurane (0.8-2%) in nitrous oxide - oxygen mixture (4 and 2 L/min respectively). All the patients were allowed to breathe spontaneously. A statistical analysis was carried out on the following observations : blood pressure, heart rate, respiratory rate, hepatic functions, tidal and minute volumes and recovery time.

As compared to the initial (control) values, the halothane group showed a statistically significant increase in the heart and respiratory rates, arterial carbon dioxide tension and hepatic enzymatic levels. There was also a significant fall in the pH, systolic and diastolic blood pressures. There was a slight decrease in the tidal volume - not statistically significant. The minute volume remained fairly stable.

The enflurane group showed a statistically significant fall in the pH and the systolic blood pressure. The hepatic enzymatic levels were also elevated significantly. The diastolic blood pressure, respiratory rate, tidal and minute volumes and the arterial carbon dioxide tension remained fairly stable.

As compared to enflurane, patients in the halothane group had a statistically significant rise in the heart and respiratory

rates and arterial carbondioxide tension. The recovery time was prolonged in this group of patients. Patients in the enflurane group also showed stability of most of the cardio-respiratory parameters monitored and they seemed to have a rapid, pleasant recovery. Both agents were free of hepatotoxicity.

The overall impression was that enflurane seemed to be a better agent than halothane.

The development of halothane came as a result of intensive research in the field of halogenated hydrocarbons which started in 1930's. The popularity of electrosparking devices for major surgery necessitated the development of non-flammable anaesthetic techniques. During 1940's, the techniques which were based on the concept of balanced anaesthesia, were widely popularised.

By 1950's, anaesthesiologists were eagerly seeking a non-flammable agent. A new anaesthetic agent must have several properties characteristic of the ideal agent (Nicholas M. Greene, 1968):

1. The anaesthetic potency must be such that there is an adequate oxygen concentration in the breathing mixture.

2. The anaesthetic agent must be inert so that it does not undergo biotransformation. This permits the major portion of the agent to be exhaled by the lungs.

3. The agent should have limited solubility in water so as to have a reasonable induction time for modern operating room.

4. The agent should be relatively insoluble in fat so that the recovery time is not prolonged.

5. The compound should not react with the alkali used for carbondioxide absorption in closed circuits.

6. The anaesthetic agent in usual doses must not be toxic to

the parenchymatous organs nor have a detrimental effect on the cardiac dynamics.

7. Finally, the central nervous system decompression caused by the agent must produce a smooth induction and recovery.

In 1956, J. Raventos published a paper on the action of Fluothane. This study resulted in the synthesis of fluorinated hydrocarbons by Dr. C.W. Suckling. Michael Johnstone (1956) and Bryce Smith (1956) reported on the clinical use of halothane and gave the initial impetus for further clinical investigation. Various studies on action of halothane and its clinical applications have been studied by Deutch et al (1962), McGregor M. et al (1968) and Wenthe, F.H. et al (1962). The use of halothane spread to the United States in 1956 and this agent now enjoys world wide use. It gave anaethesiologists for the first time a controllable, potent, non-flammable, non-explosive anaesthetic agent which could be used with oxygen and nitrous oxide. The popularity achieved by this agent is due to its unique characteristics (table 1) Halothane, however popular, has a few undersirable side effects; hypotension (Burn, J.H. et al, 1957; Burns, T.H.S. et al 1957; Johnstone, M. 1956; Krantz, J.C. et al 1958, McGregor M. et al 1958; Payne, J.P. et al 1959, Price, H.L. et al 1963; Stephen, C.R. et al, 1958 and Virtue; R.W. et al 1962); dysrhythmias (Hudson, F. et al 1957; Johnstone M. 1956, Millar, R.A. et al 1958, Purchase, I.F.H. 1966; Raventos, J. 1956, Stephen, C.R. et al 1957, Stephen, C.R. et al 1958 and Sykes, M.K. 1965) increased sensitivity of the heart to catecholamines and hepatotoxicity.

TABLE 1

Properties of Halothane and Enflurane

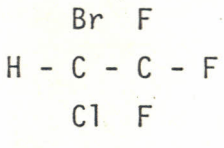
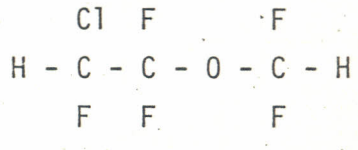
Properties	Halothane	Enflurane
		
Molecular Weight	197.4	184.5
Boiling Point (at 760 torr)	50.2°C	56.5°C
Specific Gravity	1.86 (22°C)	1.25 (25°C)
Vapour Pressure (Torr)	*243 (20°C)* 480 (37°C)	*175 (20°C)* 356 (37°C)
Odour	Pleasant Sweet	Pleasant Ethereal
Preservative	Necessary	Not Necessary
Solubility Metal	May react	Non-reactive
Alkali	Slight Decomposition	Stable
UV Light	Decomposes	Stable
Explosiveness	None	None
Partition Coefficients at 37°C		
Blood/Gas	2.3	1.9
Brain/Gas	4.1	2.6

TABLE 1 - Cont'd.....

Properties	Halothane	Enflurane
Fat/Gas	185	105
Liver/Gas	7.2	3.8
Muscle/Gas	6.0	3.0
Oil/Gas	224	98.5
Water/Gas	0.7	0.8
Rubber/Gas at 23^{o}C	120	74
Minimum Alveolar Concentration (MAC) for man as a % one atmosphere in Oxygen	0.75	1.7
in 70% N_2O	0.29	0.57
Biotransformation	20%	2.5%

These drawbacks necessitated the search for better and safer halogenated inhalational anaesthetic to continue.

Enflurane was first tested in animals by J. Krantz in 1963 and synthesisted by R. Terrell of Ohio Medical Products. It was found to possess safe anaesthetic properties in animals and Virtue et al (1966) confirmed these data in man. They found enflurane to be similar to halothane although there were certain differences (Virtue et al 1966). The safety and efficacy of enflurane as an inhalational anaesthetic in man was confirmed by a number of reports (Botty et al, 1968, Dobkin et al 1969, Lebowitz et al 1970 and Linde at al 1970). The characteristics of enflurane are summarised in Table 1. It provides rapid, smooth induction of and emergence from anaesthesia. It depresses

ventilation and circulation in a dose related manner. Mild transient alterations in metabolic measurements or blood chemistry have been observed, indicating absence of adverse effects on hepatic and renal functions (Clarke, R.S. et al 1976, Coleman, A.J. et al 1973 and Corall, I.M. et al 1977). The relatively low level of biotransformation (2.5%) of enflurane reduces the potential for possible nephrotoxic or hepatotoxic effects as compared to some fluorinated agents (Chase et al 1971) and Lowry et al 1977).

The aim of this study was to compare enflurane's cardiovascular, ventilatory and any pathological effects, particularly those pertaining to the liver, with those of halothane following the usual recommended anaesthetic concentration of each, on local individuals.

MATERIAL AND METHODS

The clinical material comprised of forty patients, which were divided into two equal groups; namely a halothane group and an enflurane group. The halothane group consisted of nineteen males and one female aged between 14-40 years (yrs) (mean 29.7 yrs) and weighing between 32-70 kilograms (kg) (mean 62.9 kg). The enflurane group consisted of nineteen males and one female aged between 12-60 years (mean 32.2 yrs) and weighing between 30-70 kgs (mean 63.7 Kg). The inclusion of one female in each group was by chance. The physical status of these patients was ASA classification I-II. All the patients were anaesthetised by the author, who also conducted the pre-operative patient evaluation and post operative patient follow-up. The latter extended to a minimal period of three weeks postoperatively. Two patients were studied each day, allocation being made to alternate groups, randomly. One particular Boyle's machine was used for the entire study and Magill type - A anaesthetic circuits were reserved for each agent for the entire study. All the patients were free from infection of any sort and were on no hepatotoxic drugs or drugs affecting the general body metabolism. The operations were not of major abdominal or thoracic nature and did not necessitate blood tranfusion. Initially it was thought that patients presenting for minor urological procedures, plastic repairs or orthopaedic operations would be particularly suitable. In practice, however, these groups were not readily available to the study. The study was therefore, centred on patients presenting for either minor ophthalmic procedures such as cataract extraction, penetrated

eye injury repair, removal of foreign bodies from the eye and E.N.T. procedures like tympanoplasty.

Organization of the study required a close co-operation with the surgical teams, laboratory staff and other collegues. Hospital lists had to be scrutinized for suitable patients.

PRE-OPERATIVELY

All the patients were visited pre-operatively and detailed notes were made regarding facts such as previous anaesthetic, idiosyncrasies, alcohol, tobacco intake and concurrent drug therapy. The essential pre-operative investigations included an electrocardiogram, chest X-Ray and Liver function tests. The latter included the stimations of :

a. Alkaline phosphatase (ALP)
b. Lactate Dehydrogenase (LDH)
c. Serum glutamic oxaloacetic transaminase (SGOT)
d. Serum glutamic pyruvic transaminase (SGPT)
e. Prothrombin time Index (PTI)

The pre-operative physical status was graded using the criteria suggested by the American Society of Anaesthesiologists (ASA). The pre-operative working protocol used is shown in Fig. 1.

PRE-MEDICATION

Patients presenting for surgery were pre-medicated with pethidine 1.5mg/Kg and atropine 0.3 - 0.6 mg intramuscularly, half an hour before induction of anaesthesia.

FIGURE 1

PRE-OPERATIVE PATIENT CARD

STUDY CARD NO	DATE	PATIENT'S NAME	SEX M/F	AGE	TRIBE	WARD	A.S.A	WT.

HOSPITAL NO.	PHYSICAL STATUS	BLOOD GROUP	BODY BUILD	DIAGNOSIS	OPERATION
I.P.					
D.P.					

PRE-OP SYSTEMIC COMPLICATIONS 1 = NONE 2 = MODERATE 3 = SEVERE

CVS	RS	CNS	GU	ENDO	HEP	GI	OTHER (SPECIFY)
☐	☐	☐	☐	☐	☐	☐	_____

PAST HISTORY 1 = YES 2 = NO 5 = NOT KNOWN

JAUNDICE	BLOOD TRANSFUSION	RADIOTHERAPY	BILIARY TACT	ALLERGY OTHER (SPECIFY)
☐	☐	☐	☐	_____

PRE-OP TREATMENT AND SOCIAL HABBITS 1 = YES 2 = NO 3 = LIGHT 4 = HEAVY 5 = NOT KNOWN

PHENOTHIAZINES	STEROIDS	HORMONE REPLACEMENT THERAPY	TRICYCLIC ANTIDEPRESSANTS
☐	☐	☐	☐

NITROFURANTION	ALCOHOL	TOBACCO	MAOI-S	PILL	OTHER (SPECIFY)
☐	☐	☐	☐	☐	_____

ESSENTIAL PRE-OP INVESTIGATIONS 1 = YES 2 = NO

LFTS	EKG	BP	PULSE	C X R	BGA	BV
☐	☐	☐	☐	☐	☐	☐

PRE-MEDICATION	TIME	DOSE
PETHIDINE		
ATROPINE		

IMMEDIATE PRE-ANAESTHETIC PREPARATION

On arrival of the patient in the anaesthetic room, the heart rate, arterial blood pressures, respiratory rate, tidal and minute volumes were measured. Following Allen's test, the left radial artery was catheterised in all patients using teflon abbocath - T - cannula size 20 F.G. The first arterial sample was withdrawn in a heparinized syringe for blood chemistry at this stage.

INDUCTION OF ANAESTHESIA

Anaesthesia was induced with thiopentone sodium, 4-5 mg/kg. This was followed by succinylcholine, 1 mg/kg. to facilitate orotracheal intubation, after 2-3 minutes of mask ventilation with 100% oxygen. The larynx was sprayed with 4% lignocaine prior to intubation.

MAINTENANCE OF ANAESTHESIA

Anaesthesia was continued with either halothane or enflurane in a nitrous oxide-oxygen mixture (N_2O 4 L/min and O_2 2L/min). The patients were allowed to breathe spontaneously via a semi-closed Magill's system - Mapleson type A.

Halothane was added in an initial concentration of 1-2% from a calibrated Fluotec Mark 3 Vaporiser but the maintenance was usually 1.5%. Enflurane was initally added in a concentration of 0.8-3% from a cyprane enfluotec vaporiser, the maintenance was usually at 2%

MONITORING

The patient, when stable, was maintained at approximately 1 MAC value of each agent (halothane 0.75% and enflurane 1.7%) for at least fifteen minutes. The following variables were measured during this period :

(a) Heart rate (HR) by manual counting of the radial artery pulsations.

(b) Systolic and diastolic blood pressures by auscultation over the brachial artery using a cuff and an aneroid syphgmomanometer which had been previously calibrated against a mercury column.

Electrocardiographic recording was not carried out at this stage due to technical shortages.

(c) Respiratory rate (RR) counted visually over a period of one minute.

(d) Minute volume (MV) using Wright's respirometer.

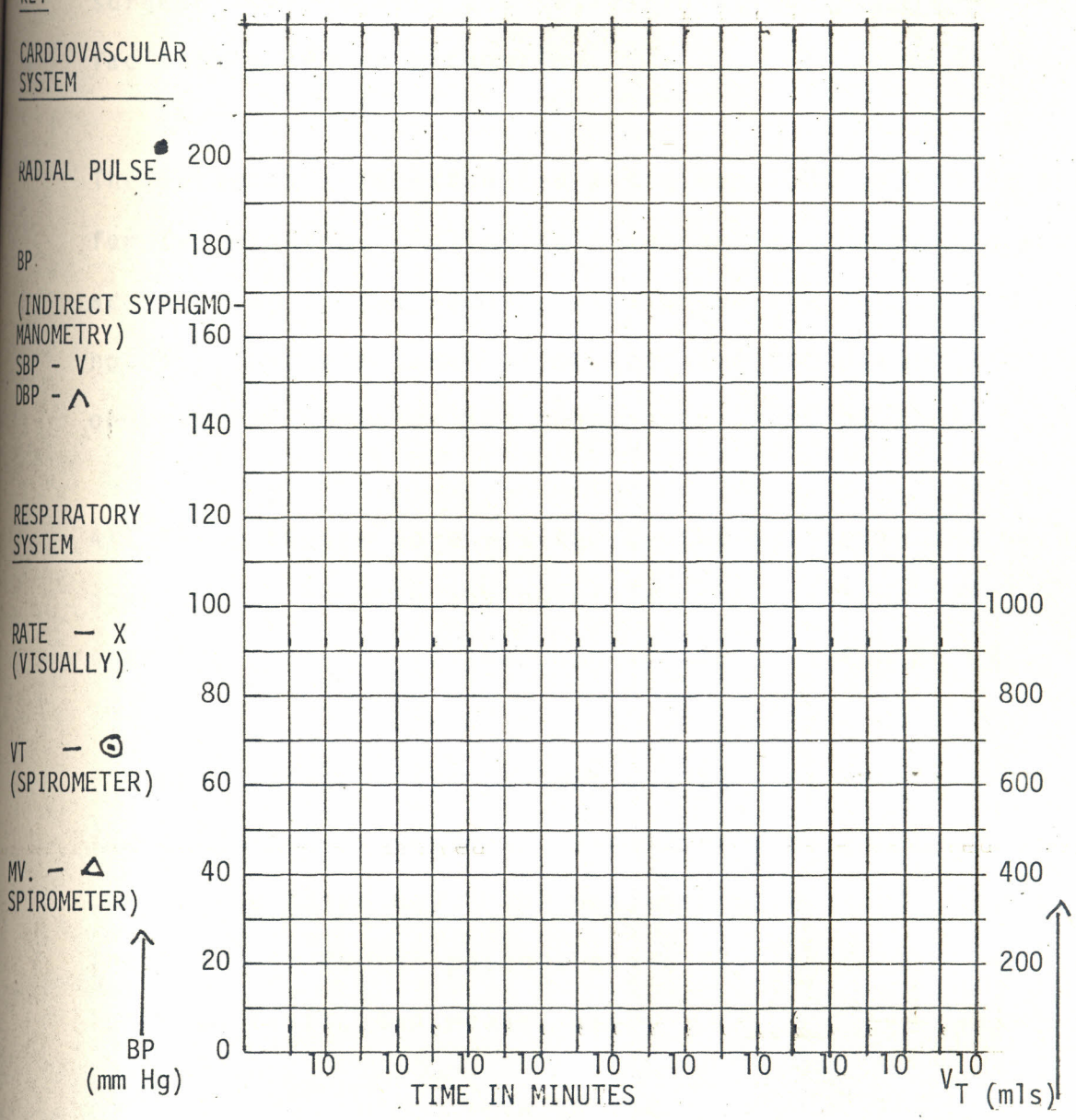
(e) Tidal Volume (VT) taken as a mean of several readings using the respirometer.

(f) Blood gas analysis using Instrumentation Laboratory blood gas analyser - Model 213. 1cc. of arterial blood was anaerobically at each time, withdrawn in a heparinized syringe for the determination of the arterial blood gases immediately before induction of anaesthesia, 30 minutes after induction and then 30 minutes after termination of anaesthesia. The patient monitoring record used is shown in figure 2.

FIGURE 2

OPERATIVE PATIENT MONITORING CARD

PATIENT MONITORING



BGA	PRE-OP	30 MINS OF ANAESTHETIC	30 MINS POST-OP
PH.			
PCO_2			
PO_2			
SO_2			
HCO_3			
BE			

The volatile anaesthetic was gradually reduced when the skin closure was started and totally discontinued when the surgeon started with the last skin stitch. This was to facilitate smooth extubation.

The patients were extubated and given 100% oxygen by mask for two minutes. Following anaesthesia, the patients were accompanied to the recoveryward where the recovery time was noted. This was taken to be the time the patients could obey verbal commands and mention the name of their home town.

All the patients were visited by the author in the wards post operatively to note any possible complications arising, with specific interest in the complications listed in Fig. 3.

Further postoperative patient visits were made over three days for clinical assessment. The liver function tests were carried out on the third day. The patients were usually discharged on the third or fourth postoperative day and called for liver function tests, two weeks later.

EVALUATION

Statistical comparisons of measured variables were made using student's paired t test for each group separately. Individuals from the two groups treated at comparable alveolar concentrations were compared by the t test for unpaired samples. The results were considered significant when P was <0.05. The clinical observations and complications were also taken into account in the overall assessment of the two agents.

FIGURE 3

POSTOPERATIVE COMPLICATIONS NOTED OVER THREE DAYS

NO. OF SYMPTOMS REPORTED		OTHERS (SPECIFY)
USUAL SLEEP		
USUAL APPETITE		
NO SLEEP		
FEEL AWFUL		
FEEL WELL		
NAUSEA		
VOMITING		
DIARRHOEA		
CONSTIPATION		
ALERT		
CONFUSED/DISORIENTED		
PAIN		
ANAEMIA		
OLIGURIA		
INFECTION		
COUGH		
SPIT		
PYREXIA		
JAUNDICE		
SMELL OF ANESTHESIA		
NUMBNESS-TINGLING		
HAEMORRHAGE		
HYPOTENSION		
BREATHLESSNESS		
LARYNGOSPASM		
I/V DRIP		
N/G TUBE		
E/T TUBE		
AMBULENT		
DRY MOUTH		
WEAKNESS		
MUSCLE SORENESS		
HEAVY ARMS & LEGS		
POOR-COORDINATION		
SWEATING		
TREMBLING		
HOT & COLD SPELLS		

RESULTS

The control pre-anaesthetic ventilatory, cardiovascular and hepatic enzymatic values of each patient were within normal limits Table 2 summarises the results of various parameters measured or calculated when the two drugs were compared.

TABLE 2

Control (pre-anaesthetic) values (means ± S.D) There were no significant differences between the halothane and enflurane groups

Parameter	Units	Halothane	Enflurane
Heart rate (HR)	beats/min	83.9 ± 19.2	95.6 ± 17.
Systolic blood pressure (SBP)	mmHg	126.0 ± 20.1	131 ± 23.1
Diastolic blood pressure (DBP)	mmHg	73.0 ± 22.5	72.6 ± 20.
Respiratory rate (RR)	Resp/min	24.4 ± 6.2	22.2 ± 5.8
Tidal Volume (V_T)	mls	283.5 ± 131.1	240 ± 76
Minute Volume (M_V)	L/min	6.7 ± 2.8	5.9 ± 2.5
pH		7.45 ± 1.6	7.4 ± 0.04
Arterial carbondioxide Pressure ($PaCo_2$)	mmHg	32.4 ± 12.1	31.5 ± 9.0
Arterial Oxygen Pressure (PaO_2)	mmHg	80.2 ± 40.1	79.3 ± 24.4
Arterial Oxygen Saturation (SaO_2)	%	94.9 ± 4.2	89.6 ± 19.8
Plasma bicarbonates (HCO_3)	mEq/L	21.1 ± 4.3	18.8 ± 5.3
Base excess (BE)	mEq/L	- 1.7 ± 2.3	- 3.2 ± 3.4
Alkaline phosphatase (ALP)	iu/L	76.6 ± 14.3	84.1 ± 15.7
Lectatedehydrogenase (LDH)	iu/L	138.3 ± 17.4	125.4 ± 25.1
Aspertate aminotransferase (SGOT)	iu/L	26 ± 11.7	25.3 ± 8.7
Alanine Amino transferase (SGPT)	iu/L	24.1 ± 8.2	24.8 ± 6.5
Prothrombin time Index (PTI)	Secs	1.04 ± 0.1	1.03 ± 0.16

HALOTHANE ANAESTHESIA

The heart rate showed a tendency to rise; the systolic arterial blood pressure showed a fall ($P < 0.0005$) and so did the diastolic ($P < 0.0087$). The respiratory rate showed a rise ($P < 0.0003$) whereas the V_T had a tendency to fall. The M_V remained fairly stable.

The blood chemistry showed a highly significant decrease in pH ($P < 0.000002$). This reduction was due, primarily, to an increase in $PaCo_2$ ($P < 0.008$) and secondarily to a decrease in base excess ($P < 0.00004$). The expected rise in PaO_2 was only slight ($P < 0.03$) with the arterial haemoglobin saturation also showing a slight tendency to rise. All the hepatic enzyme levels were markedly elevated in the immediate postoperative period (i.e. two days later)

ALD $P < 0.000008$

LDH $P < 0.011$

SGOT $P < 0.009$

SGPT $P < 0.00003$

PTI $P < 0.0000009$

All the above enzyme levels were found to be within normal limits by 13-15 postoperative day. The recovery time from anaesthesia was found to be 17.6 min $\pm$ 4.4.

ENFLURANE ANAESTHESIA

The heart rate had a tendency to rise; the systolic blood pressure was reduced after enflurane administration ($P < 0.0009$). The diastolic blood pressure remained fairly stable. The respiratory parameters, RR, V_T and M_V remained fairly stable. The same was

true for $PaCo_2$, PaO_2 and SaO_2. pH estimations showed a fall ($P<0.0013$) with a significant decrease in the plasma bicarbonates ($P<0.04$).

The majority of the hapatic enzymes showed increased levels but none of these were clinically significant.

ALP - $P<0.007$

SGOT - $P<0.0087$

SGPT - $P<0.014$

PTI - $P<0.005$

The enzymes were found to have reached preoperative levels by 13-15t postoperative days. The patients recovered from anaesthesia after 11.5 min $\pm$ 7.2.

COMPARISON OF THE TWO DRUGS

The parameters which showed statistically significant differences during anaesthesia at comparable alveolar concentration levels were the heart rate, respiratory rate, pH and arterial carbon-dioxide tension.

The heart rate increased by 6% with halothane and by 4.5% with enflurane ($P<0.04$). The respiratory rate increased by 21% with halothane and by 3.5% with enflurane ($P<0.00013$). The pH dropped by 3.1% with halothane and by 1.2% with enflurane ($P<0.014$). The $PaCo_2$ increased by 47.5% with halothane and by 13% with enflurane ($P<0.0042$).

The base deficiet was greater in the halothane group as compared to the enflurance group. None of the above agents showed significant changes in the hepatic function tests studied.

TABLE 3

Comparison of the parameters measured during halothane and enflurane anaesthesia with their means and S.D. Statistical comparisons were made at 1 MAC concentration by student's t test for independent series $P^* < 0.05$

Parameters	Units	During Halothane anaesthesia	During Enflurane anaesthesia	P Values
H.R	beats/min	89.29 ± 16.95	99.98 ± 16.66	0.04*
SBP	mmHg	103.81 ± 17.13	108.42 ± 12.35	0.32
DBP	mmHg	68.93 ± 11.88	72.09 ± 11.97	0.14
RR	Resp/min	29.53 ± 8.6	22.97 ± 2.41	0.0013*
V_T	mls	241.5 ± 27.1	221.28 ± 32.5	0.188
M_V	L/min	5.53 ± 2.4	5.99 ± 1.7	0.091
pH		7.22 ± 0.1	7.31 ± 0.10	0.014*
$PaCo_2$	mmHg	47.9 ± 9.2	35.7 ± 7.2	0.0042*
PaO_2	mmHg	112.1 ± 25.2	100.5 ± 33.7	0.23
SaO_2	%	98.25 ± 2.3	95.05 ± 5.0	0.35
HCO_3	mEq/L	18.95 ± 6.3	17.8 ± 4.5	0.50
BE	mEq/L	- 8.7 ± 5.6	- 7.85 ± 6.8	0.002*
ALP	iu/L	92.8 ± 13.9	102 ± 18.4	0.09
LDH	iu/L	150.7 ± 23.6	134 ± 25.9	0.05
SGOT	iu/L	37 ± 4.5	33.9 ± 8	0.06
SGPT	iu/L	34.7 ± 7.2	29.8 ± 4	0.6
PTI	secs	1.2 ± 0.1	1.17 ± 0.16	0.3

D I S C U S S I O N

Like previous studies in this field performed by other workers (Calverley and Smith, N.T. et al., 1978; Deutsch, et al 1962), the present study included normal healthy patients undergoing surgery for small surgical procedures. Some of these patients were of advanced age but had neither cardiac nor respiratory disease. Three patients in each group were found to be moderate alcoholics. These three patients, according to our preoperative investigations, showed no signs or symptoms of hepatic function disturbance which would have made them unsuitable for the study.

Despite the differences in the concentration of the anaesthetics, these concentrations represented comparable MAC concentration used in the two groups. There were also no significant differences in the baseline parameters measured and the groups were therefore considered comparable.

CARDIOVASCULAR EFFECTS

The present study confirms the results of some previous studies on halothane (Eger et al 1979) and on enflurane (calverley et al 1979). When administration of halothane or enflurane was uncomplicated by anaesthetic adjuvants or change in $PaCo_2$, the effects seen in man are those of cardiovascular depression. This cardiac depression is found at light levels of anaesthesia and proceeds to profound depression at deep levels (Eger, E.I., 1979).

In our study there was an increase in the heart rate with both the agents, with respect to baseline values but statistically significant only in case of halothane. One patient in the halothane group was noted to have bradycardia (pulse rate of 58/min). This can be

attributed to the loss of homeostatic baroreflex control of the heart rate with the use of halothane (Morton, M.M. et al 1980). The increase in the heart rate suggest increased sympathetic activity, increased sensitivity to such activity, decreased parasympathetic activity or decreased sensitivity to parasympathetic impulses. In fact during light anaesthesia, the pre-eminent response to surgical stimulation is the sympathetic one (Prys Roberts et al 1971., Devault M. et al 1969), while during deep anaesthesia, a parasympathetic response seems to prevail.

The stability of heart rate is a noteworthy feature of enflurane anaesthesia (Dobkin et al 1969). Although a variety of dysrhythmias may appear during enflurane anaesthesia, their occurance is infrequent (Dobkin et al 1969., Linde et al 1970., Lebowitz et al 1970 and Hanguet et al 1974). The ECG, hence the rhythm feature, was not monitored in this study due to technical problems at the time of the study. But other workers have found the heart rate and rhythm to remain exceptionally stable under clinical conditions when the inhaled enflurane concentration is maintained below 3% (Dobkin et al 1968., 1969). Earlier animal studies suggested that enflurane sensitized the heart to epinephrine (Byles et al 1971, McDowell et al 1968., Virtue et al 1966) but this seems to be substantially less with enflurane than with halothane.

BLOOD PRESSURE

Early animal data showed that decrease in blood pressure was a dose related phenomenon with both agents (Edmond, I, Eger 1979., Byles P.H. et al 1971). The reduction in systolic blood pressure

of 10-15 mm Hg caused by halothane is mainly due to decreased myocardial contractility.

Hypotension is characteristic of enflurane induction. In fit subjects, the systolic pressure significantly falls by 10-20 mm Hg., normally returning to control levels when surgical stimulation begins and remains stable during maintenance (Potent Inhalational Anaesthetic - Ethrane; Abbot Laboratories). The greater reduction in the systolic blood pressure with enflurane is due to marked reduction of pre-load, after load and some myocardial depression.

There was also a reduction in diastolic blood pressure with halothane whereas, the diastolic pressure with enflurane remained fairly stable.

VENTILATORY EFFECTS

Studies in both, dog and man have shown that alveolar ventilation decreases with increasing depth of halothane anaesthesia. Merkel and Eger (1963) demonstrated a linear rise in $PaCo_2$ in dogs above an alveolar concentration of halothane of 0.7%. Studies in man at known alveolar concentrations of halothane show similar findings. (Munson et al 1966). Similar findings were noted in this study. There was an increase in the respiratory rate and a decrease in the tidal volume with the use of halothane. The combination of these responses produces a decrease in alveolar ventilation with a proportional increase in arterial partial pressure of carbondioxide ($PaCo_2$).

Induction of anaesthesia with enflurane has been consistently reported as smooth and rapid. Rapidity is attributable to its potency and low blood/gas partition co-efficient (Egilmez et al 1972, Virtue et al 1966). The pleasant odour and non-irritating effects of enflurane make it to be well tolerated by the patient. The concentration of inspired enflurane can be increased fairly rapidly during induction usually without causing breath holding, cough, bronchospasm, laryngospasm or swallowing (Dobkin et al 1969). However, like other halogenated inhalation anaesthetics, enflurane is respiratory depressant. During early period of anaesthesia, enflurane causes dose related ventilatory depression. This is evidenced by an increase in $PaCo_2$ and a decrease in tidal volume. In this study, the respiratory rates were noted to remain unchanged or were slightly altered during enflurane anaesthesia. Similar observations were made by Helrich et al (1969) and Linde et al (1970). There was a decrease in the tidal volume with enflurane, but the minute volume remained fairly stable. Respiratory depression is usually indicated by a decrease in tidal volume. Tidal volumes can vary considerably in the same plane of anaesthesia in the same patient, but have been reported as lying between 250-400 mls. during maintenance with approximately 2% enflurane in adults (Botty, C. Brown, et al 1968).

W. H. Wahba (1980) found that the curare-like action (not reversible with neostigmine) of enflurane paralyses the diaphragm in deeper planes of anaesthesia. This, together with, the central depressant action of enflurane, both contribute to hypoventilation seen in deeper planes of anaesthesia. Respiratory depressant effects of

enflurane are atleast partly antagonised by surgical stimulation (Black et al 1977).

GAS EXCHANGE

Arterial carbondioxide tension tends to rise in patients breathing enflurane spontaneously. There is a mild fall in the pH signifying a tendency towards respiratory acidosis (Ribiero et al 1979). In this study we noticed the fall in pH to be more marked with halothane than with enflurane. The patients maintained a fairly stable PaO_2, near normal levels; similar observations were made by Botty et al (1968) and Dobkin et al (1969). Similar findings were observed in this study with the use of halothane under similar conditions.

RECOVERY TIME

The duration of recovery was based on the time interval between the end of the volatile anaesthetic administration and return of full conciousness. In practice full conciousness was considered to have returned when the patient could respond to verbal commands and give his correct home town address. The shorter recovery time with enflurane (11.5 min.$\pm$7) as compared to that of halothane (17.6 min.$\pm$4) was earlier noted by Govaerts and Sanders (1975) and Korttila and collegues (1977). The latter authors also found faster recovery of driving skills after enflurane than with halothane. The faster recovery from enflurane, which is due to its low blood/gas partition co-efficient, is an advantage in a busy unit with a limited number of recovery nurses.

In general, patients emerging from enflurane anaesthesia quickly became lucid and soon regained their appetites and asked for oral sips. This is very desirable in small children.

BIOCHEMICAL CHANGES IN LIVER FUNCTIONS

Four enzymes were chosen specifically and prothrombine time index as indices of liver function

ALP - signifying liver cell damage and biliary obstruction

LDH - widely distributed in the heart, skeletal muscle, liver, kidney, brain, and red blood cells.

SGOT - signifying liver damage and skeletal and heart muscle derangement

SGPT - signifying liver cell damage

PTI - signifying liver cell damage

As the clinical signs of "halothane hepatitis" are reported to be evident within two weeks after anaesthesia (Johnston et al 1979), it was decided to draw blood samples pre-operatively; 3-4 days and 13-15 days post-operatively. These samples of blood were drawn at the same time of the day on each occasion in order to eliminate changes attributable to diurnal variations. Three patients in each group, who were moderate alcohol drinkers, showed a significant rise in the levels of ALP, LDH and PTI in the immediate post-operative period. This was not taken into any significant account as the number of patients in this study was small. In general, noneof the forty patients studied, showed any clinical features suggestive of hepatotoxicity.

In all the patients, the level of enzymes returnedto approximate

pre-operative values in two weeks time.

Two patients in the enflurane group had slight oozing, post-operative from the wound. Two patients in the same group had wound sepsis which responded effectively to antibiotics. No major complications were identified.

Six patients in the halothane group complained of dry mouth, four of smell of anaesthetic, four of vomiting, three of nausea and five of weakness and reduced energy. These complications could probably be attributed to central depression, which is true for both agents, though more marked with halothane. The difference in the incidence between the two agents might have resulted from the lower solubility of enflurane relative to halothane and hence, a slower elimination of the latter. Alternatively, the matabolism of halothane to bromide may have produced levels significant to cause central nervous system effects. Either of these or some unknown mechanism may account for the greater number of adverse symptoms after halothane than enflurane. Comparative study by Storms, H. L. et al (1980) had shown similar post-operative findings.

C O N C L U S I O N

In this study, the cardiorespiratory and hepatic effects of halothane and enflurane anaesthesia in the black African population of forty patients are similar to those reported on white Americans and Europeans. It was found in our study that enflurane seemed to offer some advantages over halothane. This includes : fairly stable cardiorespiratory functions, absence of hepatotoxicity and a rapid pleasant recovery. Although the heart rhythm was not monitored, it was found to be stable. Apart from its high cost, enflurane is a good alternative to halothane when considering the intra-and postoperative sequlae. The risk of so called "halothane hepatitis", although contraversial, must be borne in mind when subjecting a patient to repeated halothane anaesthesia in periods less than six weeks. With the possible cessation of trichloroethylene supplies, the anaesthetists may in future, consider enflurane as the first alternative inhalation agent to halothane in many clinical situations.

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