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A Comparison of the Maintenance and Recovery Characteristic of Sevoflurane-Nitrous Oxide Against Isoflurane-Nitrous Oxide Anaesthesia

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ABSTRACT

Background: To compare the maintenance and recovery characteristics of sevoflurane and isoflurane anaesthesia in Malaysian patients.

Method: This is a prospective, open labelled, randomized, controlled study. Sixty unpremedicated ASA I or II patients (aged 18-50 years), scheduled for elective breast lump excision were randomly allocated to receive either isoflurane or sevoflurane for the maintenance of anaesthesia following fentanyl and propofol intravenous induction. The systolic, diastolic, mean arterial blood pressure and heart rate were measured. The speed of recovery was measured by time to eye opening, time to following simple command, and time to correctly giving own names and address. The incidence of postoperative complication was also recorded.

Results: The trend of systolic blood pressure was significantly higher in the isoflurane group as compared to the sevoflurane group for the duration of anaesthesia ($p<0.001$, by ANOVA for repeated measurement) but the trend of heart rate was similar for both groups. The recovery time was faster in the isoflurane group. [mean time of eye opening (SD)=6.8 (2.2) vs 10.7 (4.4) min, $p<0.001$; mean time of sticking tongue out (SD)=7.9 (2.9) vs 11.5 (4.7) min, $p<0.01$; mean time of giving own name (SD)=7.8 (2.7) vs 11.8 (4.8) min, $p<0.001$, mean time of giving own address (SD)=8.4 (2.9) vs 12.0 (4.7) min, $p<0.01$]. No major adverse effects were encountered postoperatively and the incidences of minor adverse effects were low in both groups.

Conclusion: We concluded that sevoflurane is a safe alternative to isoflurane but in these short procedures, awakening time was surprisingly slower than after isoflurane.

Keywords: Anaesthesia general; anaesthesia inhalational; isoflurane; maintenance; recovery; sevoflurane

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INTRODUCTION

Sevoflurane is a fluorinated ether inhaled anaesthetic agent recently introduced in Malaysia. It has a low blood gas solubility of 0.69[1]. This agent has been investigated in animals[2,3] and a number of studies[4-7] has also been undertaken in man. These investigations suggest that sevoflurane maintains anaesthesia safely without disturbances of the cardiovascular system and its low solubility may provide more rapid emergence from anaesthesia than is possible with the existing volatile anaestheties. Of those in current use, isoflurane has the lowest blood gas solubility of 1.46[8]. Gupta et al[9] showed that recovery after propofol induction and isoflurane maintenance of anaesthesia in unpremedicated, spontaneously breathing patients undergoing arthroseopic surgery was rapid. Many studies[4-7,10,11] conducted to compare the emergence of sevoflurane anaesthesia with isoflurane anaesthesia have showed that emergence and early recovery from sevoflurane anaesthesia was significantly faster than isoflurane anaesthesia. However the duration of anaesthesia from these studies was of intermediate to long duration lasting close to or more than one hour. There are to our knowledge no studies evaluating emergence after sevoflurane anaesthesia as compared to isoflurane anaesthesia in short surgical procedures. The objective of this randomized, open label trial was to evaluate and compare the maintenance and recovery profiles after sevoflurane-nitrous oxide and isoflurane-nitrous oxide anaesthesia in Malaysian patients undergoing breast lump excision lasting approximately 30 minutes.

MATERIALS AND METHODS

The study protocol was approved by the University of Malaya Medical Centre Ethical Committee. Sixty women, ASA physical status I or II, aged 18-50 yrs, scheduled for elective breast lump excision were studied. After obtaining written informed consent, patients were assigned by block randomization to the sevoflurane or the isoflurane group using an open (nonblinded) study design. Patients with a history of hypersensitivity to halogenated anaesthetics, or taking medications known

Table I. Characteristics of the patients and procedure (mean ± SD).

	Isoflurane n = 30	Sevoflurane n = 30
Age, yr	31.4 (9.1)	30.5 (10.6)
Weight, kg	53.5 (8.0)	50.6 (9.3)
ASA I:II	30:0	29:1
Duration of anaesthesia, min	21.8 (8.8)	18.9 (7.6)
Propofol dose, mg/kg	2.6 (0.6)	2.4 (0.7)
Fentanyl dose, mcg/kg	1.1 (0.3)	1.2 (0.3)

No significant difference between the two groups.

Table II. Recovery profiles (mean ± SD).

	Isoflurane n = 30	Sevoflurane n = 30
Time to eye opening, min	6.8 (2.2)***	10.7 (4.4)
Time to follow command to stick tongue out, min	7.9 (2.9)**	11.5 (4.7)
Time to giving name, min	7.8 (2.7)***	11.8 (4.8)
Time to giving date of birth, min	8.4 (2.9)**	12.0 (4.7)

** $p<0.01$, *** $p<0.001$ between the two groups.

Table III. Incidence of postoperative complications [number of patients (percentage of patients)].

	Isoflurane n = 30	Sevoflurane n = 30
Nausea and vomiting	3 (10%)	3 (10%)
Dizziness	1 (3%)	2 (7%)
Coughing	2 (7%)	0 (0%)

No significant difference between the two groups, by Chi square test.

to influence anaesthetic or analgesic requirements were excluded. Patients who were pregnant or breast-feeding as well as those with clinically significant cardiovascular, pulmonary, renal or hepatic disease were also excluded.

All patients were fasted overnight and no premedication was administered prior to the induction of anaesthesia. After placement of an intravenous cannula, anaesthesia was induced intravenously with fentanyl l mcg/kg, followed by propofol 2-3 mg/kg over 15 s until the loss of eyelash reflex. Induction of anaesthesia was standardized and conducted by the same investigator (YKC).

After loss of the eyelash reflex, the study drugs were introduced to maintain the anaesthesia. In group I, isoflurane and nitrous oxide 66% in oxygen was used and in group S, sevoflurane and nitrous oxide 66% in oxygen was used. Initially 3% of isoflurane or 6% of sevoflurane was used (MAC values: sevoflurane 2.20%, isoflurane 1.15%). Shortly after the skin incision these was reduced to 1% of isoflurane and 2% of sevoflurane until the end of the surgery. Additional doses of fentanyl (0.5mcg/kg) were administered if necessary to control acute haemodynamic responses. During the maintenance period, patients breathed spontaneously through an oral airway and facemask. Anaesthesia was maintained with a total fresh gas flow of approximately 4.5 L/min, using Mapleson A breathing system. Noninvasive blood pressure measurements, heart rate, peripheral oxygen saturation were recorded before induction (baseline), at induction and every two minutes thereafter until emergence from anaesthesia. At the end of the procedure, the wound was infiltrated with bupivacaine 0.5% with adrenaline by the surgeon and the administration of the volatile anaesthetic and nitrous oxide was discontinued simultaneously. The time of discontinuation of the anaesthetic agent was recorded. The total dosage of fentanyl and propofol used was also recorded.

A second investigator (CLC), who was blinded to the agent used, assessed all recovery parameters. The time at which the patients opened their eyes to commands were recorded. These emergence times were assessed at 15 s intervals after the cessation of anaesthetic agents. The times at which the patients were able to respond to verbal command to stick their tongue out were recorded. The time at which they could correctly state their name and date of birth were also recorded. Incidences of any adverse experiences during recovery such as nausea, vomiting, coughing, dizziness etc were recorded.

Statistical analysis

Results are expressed as mean (SD). Student's t test was used to analyse age, weight, duration of anaesthesia, propofol dose and fentanyl dose. Mean time to eyelash reflex mean time to follow command, to give name and to give date of birth were analysed using a non parametric test. Haemodynamic data were analyzed using analysis of variance (ANOVA) for repeated measurements and t test where appropriate. The incidence of postoperative complications between the two groups was analysed using Chi-square test. A two tailed probability of less than 0.05 was the criterion for statistical significance.

RESULTS

A total of sixty patients were studied. Thirty patients were randomized to the isoflurane group and thirty patients to the sevoflurane group. The two patient groups did not differ in age, weight, ASA status, duration of anaesthesia, dose of propofol and fentanyl (Table I). Changes in systolic blood pressure (SBP) and heart rate (HR) are shown in Fig. 1 and Fig. 2 respectively. There were no differences between the groups with regard to

Fig. 1 Changes in systolic blood pressure during anaesthesia and at emergence. *(Data shown as mean. ***p<0.001 between the two groups, by ANOVA for repeated measurements.)*

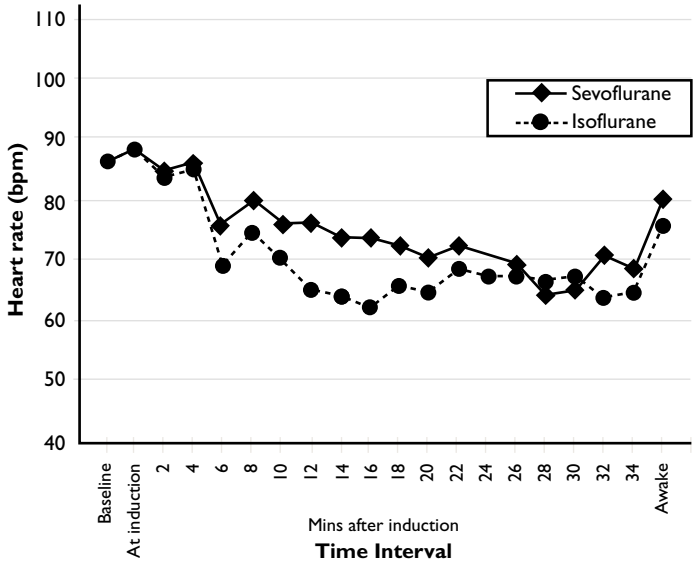
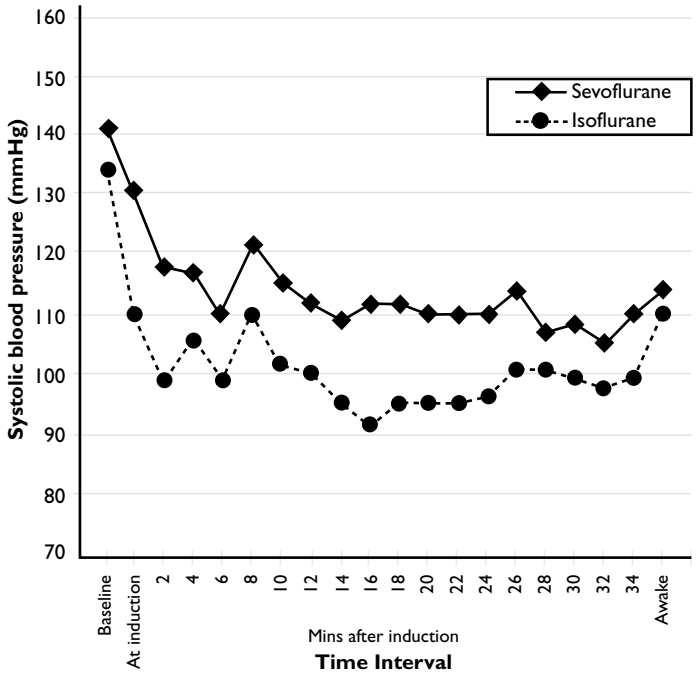


Fig. 2 Changes in heart rate during anaesthesia and at emergence. *(Data shown as mean.There is no significant difference between the two groups, by ANOVA for repeated measurements.)*



baseline measurements of systolic blood pressures (Fig. 1). After induction systolic blood pressure decreased in both groups and continued to be below baseline during the anaesthesia and at emergence. This decrease in systolic blood pressure was significantly greater ($p<0.001$) in the sevoflurane group. There were no differences between the groups with regard to baseline measurements of heart rates (Fig. 2). Six minutes after induction, heart rate had decreased below baseline in both groups and continued to be lower than baseline thereafter. At emergence, heart rate gradually increased approaching baseline value in both groups. There is no significant difference in heart rate changes for the duration of the study between patients receiving isoflurane and sevoflurane ($p=0.244$). Emergence and recovery data are summarised in Table II. Compared to the sevoflurane group, the emergence times from the end of administration of the volatile agents to eye opening to command, response to simple command by sticking the tongue out, and ability to correctly state their name and date of birth were all significantly shorter in the isoflurane groups.

The incidence of adverse experiences in the recovery room is given in Table III. Nausea was noted in 3 patients each in both the isoflurane and sevoflurane groups (10%), all were mild and none required treatment with any antiemetic drugs. Vomiting was not observed in any patients. Coughing was observed in two patients in the isoflurane group (3%) and was self limiting. Dizziness was observed in one patient in the isoflurane group (3%) and two in the sevoflurane group (7%).

DISCUSSION

We have shown that, for the most part, clinically comparable haemodynamic effects occur during isoflurane-nitrous oxide and sevoflurane-nitrous oxide anaesthesia. In our study the systolic blood pressure measured in the sevoflurane patients averaged 12 mmHg lower than those of the isoflurane patients during the maintenance. This is in agreement with Campbell C et a1[6] who showed a difference of 10 mmHg. However this small difference is unlikely to have any clinical implication in these young ASAI-II patients undergoing elective breast lump excision. We also showed that heart rate did not differ between the two groups, again this is in agreement with the study by Campbell C et al[6].

The surprising finding in our study was that the recovery time from sevoflurane anaesthesia was longer than with isoflurane. This is in contrast to previous studies[4-7,10,11] comparing isoflurane anaesthesia with sevoflurane anaesthesia, all of which showed a faster recovery with sevoflurane anaesthesia. However the methodology of our study is different from previous studies[4-7,10,11] comparing isoflurane with sevoflurane anaesthesia. The duration of anaesthesia in our study is about 20 minutes in both groups, whilst the duration in these studies[4-7,10,11] varied from 1-5 hours. This may explain the difference in our result.

Morio M[12] in a multi-hospital clinical study in Japan, comparing sevoflurane anaesthesia with enflurane anaesthesia, showed that emergence from sevoflurane anaesthesia is not faster than enflurane anaesthesia. Saito S et al[13] in his study in Japanese patients also showed that emergence from sevoflurane anaesthesia

is not faster than enflurane anaesthesia. They suggested that although the rapidity of recovery is partly due to low blood gas partition coefficient, solubility of volatile anaesthetics in the tissue especially the brain may also has a strong influence. The lower tissue solubility mediates a more rapid recovery by two mechanisms[14]. First, the brain time constant will be shorter. Second, the elimination from the body will be more rapid. The tissue/blood partition coefficient of sevoflurane (1.7)[14] has been shown to be similar to enflurane (1.7)[13] but higher than isoflurane (1.57)[14], this may explain the delayed emergence of patients receiving sevoflurane anaesthesia as compared to isoflurane anaesthesia. We postulate that the tissue/blood solubility is a more important factor than blood gas solubility in predicting speed of recovery when the duration of anaesthesia is short. However further studies would need to be conducted to evaluate this hypothesis.

This study can be criticised in that the investigator who recorded maintenance characteristics was not blinded as to the anaesthetics used. Although objective measures were used (e.g. automated recording of hemodynamic values), the possibility of observer bias cannot be completely excluded. However the subjective measurements, such as emergence times, were measured by a second investigator who was blinded to the anaesthetics used.

We conclude that when compared with isoflurane-nitrous oxide, maintenance with sevoflurane-nitrous oxide is associated with clinically comparable haemodynamic stability. However in this short procedure, awakening time was slower than after isoflurane anaesthesia.

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REFERENCES

1. Strum DP, Eger EI II. Partition coefficients for sevoflurane in human blood, saline and olive oil. Anesth Analg 1987; 66:654-6.
2. Cook TL, Beppu WJ, Hitt BA, Kosek JC, Mazze RI. Renal effects and metabolism of sevoflurane in Fischer 344 rats: An in vivo and in vitro comparison with methoxyflurane. Anesthesiology 1975a; 43:70-7.
3. Strum DP, Eger EI, Johnson BH, et al. Toxicity of sevoflurane in rats. Anesthesia and Analgesia 1987; 66:769-73.
4. Smith I, Ding Y, White PF. Comparison of induction, maintenance and recovery characteristics of sevoflurane-N20 and propofol-sevoflurane-N20 and propofol isoflurane-N2O anaesthesia. Anesth and Analg 1992; 74:253-9.
5. Frink EJ Jr, Malan TP, Atlas M, Dominguez LM, DiNardo JA, Brown BR Jr. Clinical comparison of sevoflurane and isoflurane in healthy patients. Anesth and Analg 1992; 74:241-5.
6. Campbell C, Nahrwold ML, Miller DD. Clinical comparison of sevoflurane and isoflurane when administered with nitrous oxide for surgical procedures of intermediate duration. Can J Anaesth 1995; 42:884-90.
7. Quinn AC, Newman PJ, Hall GM, Grounds RM. Sevoflurane anaesthesia for major intra-abdominal surgery. Anaesthesia 1994; 49:567-71.
8. Eger RR, Eger EI II. Effect of temperature and age on the solubility of enflurane, halothane, isoflurane and methoxyflurane in human blood. Anesth Analg 1985; 64:640-2.
9. Gupta A, Larsen LE, Sjoberg F, Lindh ML, Lennmarken C. Thiopentone or propofol for induction of isoflurane based anaesthesia for ambulatory surgery? Acta Anaesthesiol Scand 1992; 36:670-4.
10. Elbert TJ, Robinson BJ, Uhrich TD, Mackenthun A, Pichotta PJ. Recovery from sevoflurane anaesthesia: a comparison to isoflurane and propofol anaesthesia. Anesthesiology 1998; 89(6):1524-31.
11. Eriksson H, Haasio J, Korttila K. Recovery from sevoflurane and isoflurane anaesthesia after outpatient gynaecological laparoscopy. Acta Anaesthesiol Scand 1995; 39:377-80.
12. Morio M. Comparative clinical study on sevoflurane and enflurane. Jpn J Anesthesiol 1987; 36:S50.
13. Saito S, Goto F, Kadoi Y, Takahashi T, Fujita T and Mogi K. Comparative clinical study of induction and emergence time in sevoflurane and enflurane anaesthesia. Acta Anaesthesiol Scand 1989; 33:389-90.
14. Yasuda N, Targ AG, Eger EI II. Solubility of I-653, sevoflurane, isoflurane and halothane in human tissues. Anesth Analg 1989; 69:370-3.