A COMPARATIVE STUDY BETWEEN DESFLURANE AND SEVOFLURANE IN RECOVERY TIME AND RECOVERY CHARACTERISTICS ON PATIENTS FOR ELECTIVE ORTHOPAEDIC PROCEDURE

by

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ABBREVIATIONS

ASA	American Society of Anaesthesiologists.
BIS	Bispectral Index Scale.
CSF	Cerebral Spinal Fluid.
DBP	Diastolic Blood Pressure
DSST	Digit Symbol Substitution Test
EEG	Electroencephalogram
GABA	Gamma Amino Butyric Acid
LMA	Laryngeal Mask Airway
MAC	Minimum Alveolar Concentration
MMS	Mini Mental State test
PACU	Post Anaesthetic Care Unit
PONV	Post Operative Nausea and Vomiting
SBP	Systolic Blood Pressure
SD	Standard Deviation
TIVA	Total Intra-Venous Anaesthesia

ABSTRAK

Keselamatan semasa pembiusan berkait rapat dengan kestabilan tekanan darah, pernafasan dan kebolehan mempertahankan reflek salur pernafasan. Selain risiko komplikasi pembedahan, pembiusan juga mempunyai risiko dan ini menyebabkan pesakit perlu diawasi dengan rapi oleh staf yang berpengalaman di bilik pemulihan selepas pembiusan.

Dengan adanya ubat pembiusan yang baru seperti desflurane, yang mempunyai tahap kelarutan yang rendah didalam darah iaitu 0.42, sepatutnya memberikan kadar kesedaran dari pembiusan dengan cepat. Pesakit yang pulih kadar kesedarannya dengan cepat selepas pembiusan mungkin tidak perlu diawasi atau memerlukan masa yang singkat berada di bilik pemulihan tanpa memberikan risiko kepada pesakit. Konsep ini dikenali sebagai ' fast-track'.

Satu kajian rawak (single blinded) telah dijalankan di Hospital Universiti Sains Malaysia bermula bulan Jun 2004 sehingga Jun 2005. Ia melibatkan pesakit seramai 60 orang yang menjalani pembedahan ortopedik dalam jangka masa 2 jam. Mereka dibahagikan kepada 2 kumpulan yang sama rata.

Objektif kajian ini adalah untuk menguji kebaikan desflurane sebagai ubat pembiusan, serta ia membolehkan pesakit sedar dengan cepat dan mengalami kurang kesan samping. Kesemua pesakit dibius dengan menggunakan ubat fentanyl, propofol dan atracurium. Semasa pembedahan, pesakit diberi sama ada desflurane 6% atau sevoflurane 2% (yang mempunyai nilai 1 MAC untuk kedua-dua ubat dalam 100% oxsigen) berserta 30% oxsigen dan 70% nitrous oxida. Untuk pelumpuhan pesakit, infusi atracurium diberikan dan fentanyl sebagai ubat penahan sakit. Tekanan darah dan denyutan nadi dicatat sebelum pembiusan, sebelum intubasi, selepas intubasi dan setiap 10 minit sehingga pembedahan selesai. Bispectral index scale (BIS) di pasang untuk menilai tahap pembiusan.

Tahap stimulasi dalam menyedarkan pesakit terhad kepada sokongan secara lisan serta dengan menepuk bahu secara perlahan setiap 10 saat. Masa dan perubahan nilai BIS dicatat bermula dari penutupan ubat bius sehingga pesakit membuka mata dan patuh kapada arahan yang ringkas. Semasa proses menyedarkan pesakit, sebarang komplikasi diperhatikan dan dicatat. Komplikasi juga diperhatikan semasa dibilik pemulihan.

Kajian ini mendapati terdapatnya perbezaan masa untuk mencapai tahap kesedaran selepas pembiusan diantara desflurane dan sevoflurane (7.21±1.82 minit, untuk desflurane; 12.55±2.70 minit, untuk sevoflurane: $p<0.001$) dan masa untuk mematuhi arahan ringkas (8.33±1.77 minit, untuk desflurane; 13.52±2.65 minit, untuk sevoflurane: $p<0.001$) untuk pembedahan yang memakan masa lebih kurang 2 jam. Perubahan pada nilai BIS dengan

masa menunjukkan adanya perbezaan di mana ianya lebih cepat dengan desflurane berbanding dengan sevoflurane. Tetapi tiada perbezaan untuk tekanan darah dan denyutan nadi semasa pembiusan dijalankan diantara dua kumpulan. Terdapat 5 (16.7%) kejadian komplikasi untuk kumpulan sevoflurane. Tetapi tiada perbezaan dari segi statistik.

Ringkasan dari kajian ini menunjukkan desflurane mempunyai tahap kestabilan yang sama dengan sevoflurane dari segi tekanan darah dan denyutan nadi serta kesan samping tetapi desflurane mempunyai tahap kesedaran pembiusan yang cepat.

ABSTRACT

The safety of anaesthetic recovery is closely related to the speed of which the patient reaches a state of stable circulation, respiration and well maintained reflexes. Apart from the risk of surgical complications, the risk of residual anaesthetic effects, are the reason for keeping patients in a highly staffed, and high surveillance recovery unit.

With the new rapidly eliminated inhalational anaesthetic agent, such as desflurane, having low blood gas solubility coefficient (0.42), it is supposed to offer a rapid recovery. The so-called fast-track concept means that the patient is so well recovered when he leaves the operating theatre that the recovery unit may be by-passed without any risk for the patient.

A randomized single blinded prospective study was conducted in Hospital Universiti Sains Malaysia from June 2004 to June 2005 involving a total of 60 ASA I patients planned for elective orthopedic procedures with duration of surgery less then 2 hours. The patients were allocated into 2 equally numbered groups, desflurane (n=30) and sevoflurane (n=30).

The objectives of the study were to compare the effect of desflurane versus sevoflurane as inhalational agent for maintenance, on recovery time and side effects.

All patients were induced with intravenous fentanyl, propofol and atracurium. Intraoperatively, either desflurane 6% or sevoflurane 2% (which are equivalent to 1MAC of both agents in 100% oxygen) was used together with 30% oxygen and 70% nitrous oxide. Atracurium infusion was used as a muscle relaxant and fentanyl was given for analgesia. Hemodynamic parameters (blood pressure and heart rate) were recorded on arrival, pre-intubation, post-intubation and every 10 minutes until the end of the surgery. Bispectral index scale (BIS) was used to monitor anaesthetic depth.

During emergence, stimulation of patients was limited to verbal encouragement to open eyes with a tap on the shoulder at 10 seconds interval. Time was recorded from discontinuation of anaesthetic until patients opened their eyes and obeyed simple commands. The changes in BIS values with time were recorded as the inhalational agent was discontinued. At the same time, patients were observed for any complications during emergence and at the recovery room.

From this study, there was significant difference between desflurane and sevoflurane in terms of recovery time, which included time to open eyes (7.21±1.82 minutes, for desflurane versus 12.55±2.70 minutes, for sevoflurane with $p < 0.001$) and time to obey command (8.33±1.77 minutes, for desflurane versus 13.52±2.65 for sevoflurane with $p < 0.001$), with the duration of operation within 2 hours. The changes in BIS values with time showed significance difference between the groups, which was faster with desflurane

groups. However, there was no significant difference in term of hemodynamic parameters between the groups. There were 5 (16.7%) incidence of complications during emergence/recovery in patients who received sevoflurane. However it was not statistically significant.

In summary, this study showed that desflurane has a faster recovery time with similar hemodynamic and side effects as compared to sevoflurane.

1. INTRODUCTION

The history of ambulatory anaesthesia is as old as the history of anaesthesia itself. Expansion of outpatient anaesthesia proceeded slowly until the late 1970s and early 1980s. Webb and Graves, describing their experience from 1949 to 1959, estimated that an average of 1200 patients a year had outpatient surgery. This was 5 % of the total anaesthetics provided at their hospital.

Further expansion of ambulatory anaesthesia was minimal until the mid-1980s. At that time, freestanding ambulatory surgery centres began to proliferate, as did hospital-based programs. By 1987, hospital-affiliated ambulatory surgery accounted for 9.8 million operations or about 45 % of the total surgery volume in the United States (Henderson *et al.*, 1991).

The advantages of lower cost, lower rate of infection, less patient anxiety and greater convenience were well established (Poole *et al.*, 1999). Factor involved is the development of new anaesthetics agents that allow patients to recover more rapidly. Furthermore, the development of technology gives us more advantages, for examples, to monitor patient's depthness during anaesthesia by using Bispectral Index Scale (BIS) which is invented in year 1996.

BIS is a dimensionless number scaled from 0 – 100, with 100 represent as awake EEG and zero representing complete electrical silence (cortical suppression). Bispectral Index Scale

(BIS) level between 45 and 55 was targeted in the BIS monitored patients where depth of anaesthesia was assessed by clinical criteria in the control group. Results showed Bispectral Index Scale monitoring reduced propofol usage and hastened recovery after propofol anaesthesia, whereas in desflurane anaesthesia it was associated with improved patient satisfaction (Luginbuhl *et al.*, 2003). Another study showed that the consumption of both propofol and sevoflurane decreased significantly (29% and 40%) with the use of Bispectral Index Scale (Yli *et al.*, 1999).

The inhalational agents continue to have a prominent role in the provision of general anaesthesia. Among them, isoflurane is the commonest agent used in this country and also throughout the world. Many studies have been done on the use of isoflurane as an inhalational agent.

Now, with this new era of inhalational anaesthesia, these anaesthetic agents currently used, started being replaced by newer agents, which have the characteristic features almost close to ideal anaesthetic properties. These include sevoflurane and desflurane (N.J.O Keeffe and T.E.J. Healy., 1999). Both provide a greater degree of control of anaesthetic depth and a more rapid immediate recovery from anaesthesia than is currently available with other inhaled agents because of their decreased solubility.

Desflurane is currently used widely in the United States of America and parts of Europe. Compared with sevoflurane, desflurane has the additional advantage of being extremely resistant to degradation and biotransformation.

Sevoflurane is currently in widespread clinical use in Japan and parts of South America. Compared with desflurane, sevoflurane has the additional advantage of being non-irritating to the airway. Inhalational induction of anaesthesia with sevoflurane is achieved rapidly and easily. Meanwhile, desflurane is extremely irritating to the airway when used as a inhalational induction agent (Young and Apfelbaum 1995).

However, a study done by Mahmoud *et al.*, (2001) and Eshima *et al.*, (2003) found that there was no significant difference in respiratory responses between desflurane and sevoflurane given through the laryngeal mask airway (LMA). The instability of sevoflurane with carbon dioxide absorbents and its in vivo biotransformation, produce potentially toxic by-products particularly if used with low flow anaesthesia. However, a study done by Bito *et al.*,(1997) on human found that no significant difference in compound A production was observed during sevoflurane anaesthesia at a gas flow rate of 2L/min versus 0.5 L/min.

Having low blood gas solubility coefficient of 0.42, desflurane is supposed to offer rapid induction and recovery from its anaesthetic effects. Use of desflurane leads to a more rapid emergence and shorter time to extubation compared to sevoflurane (Nathanson *et al.*, 1995).

2. DEFINITIONS

2.1 Sevoflurane;

Fluorinated methyl isopropyl ether, use as anaesthetic inhalational agent.

2.2 Desflurane;

Fluorinated methyl ethyl ether, use as anaesthetic inhalational agent.

2.3 Recovery Time;

Time from discontinuation of inhalational agents to opening eyes (eyes open) in response to call and to obey command (obey command) after completion of operation (recovery).

2.4 Recovery Characteristic;

Absence or presence of any complications during emergence from anaesthesia, and recovery period, such as breath holding, vomiting and laryngospasm.

3. OBJECTIVES

3.1 General Objective:

To assess the advantages of desflurane as a new inhalational agent.

3.2 Specific Objectives:

1. To determine whether desflurane has faster recovery time than sevoflurane.
2. To determine that desflurane has less undesirable effect (vomiting, laryngospasm, and breath holding) during recovery time than sevoflurane.
3. To determine that desflurane is more haemodynamically stable than sevoflurane

4. LITERATURE REVIEWS

4.1 Inhalational Anaesthetics history

Inhalation anaesthetics are substances that are brought into the body via the lungs and are distributed via the blood into the different tissues. The main target of inhalation anaesthetics is the brain.

Inhaled anaesthetic agents include nitrous oxide (the oldest of all inhalational anaesthetics) and various halogenated agents: desflurane (halogenated solely with fluorine-halogenation increases potency and is essential to ensure non-flammability), halothane (halogenated with fluorine, chlorine, and bromine), isoflurane (halogenated with fluorine and chlorine), and sevoflurane (halogenated solely with fluorine).

Halothane was the first fluorinated inhalational anaesthetic that was wildly successful, rapidly displacing all other older potent inhaled anaesthetics. Efforts to develop other halogenated anaesthetics with more of the characteristics of the ideal inhaled anaesthetic agent than halothane led to the introduction of isoflurane, desflurane, and sevoflurane.

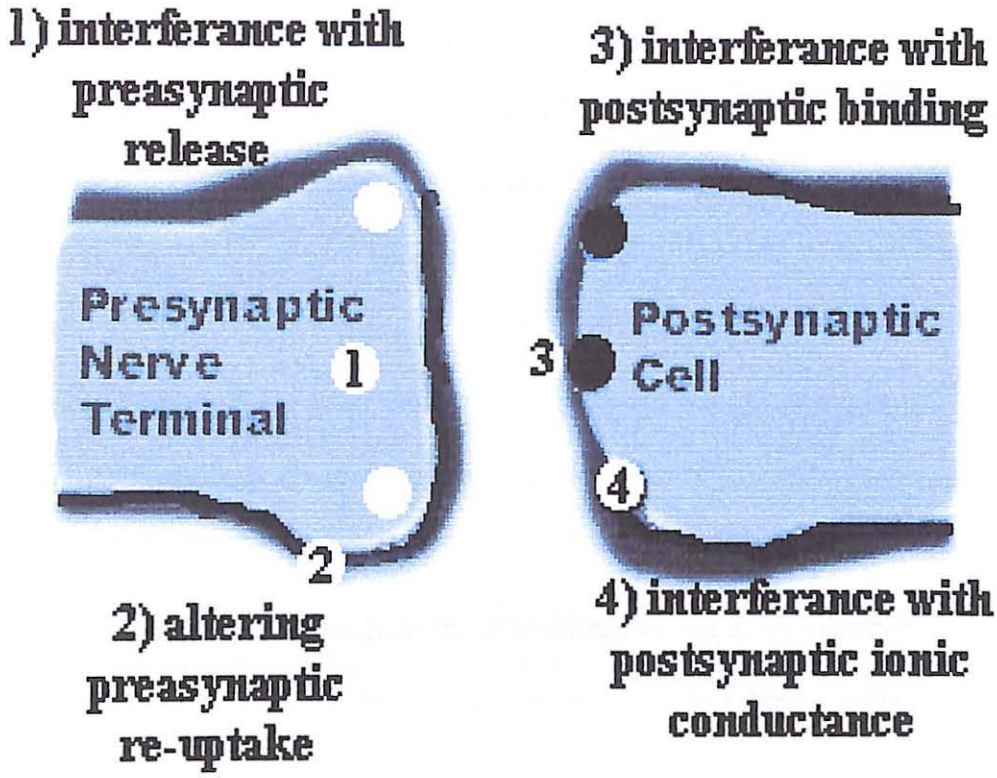

Figure 4.1 Possible mechanisms of action of inhalational anesthetics

Inhaled anaesthetics act in different ways at the level of the central nervous system (Figure 4.1). They may disrupt normal synaptic transmission by interfering with the release of neurotransmitters from presynaptic nerve terminal (enhance or depress excitatory or inhibitory transmission), by altering the re-uptake of neurotransmitters, by changing the binding of neurotransmitters to the post-synaptic receptor sites, or by influencing the ionic conductance change that follows activation of the post-synaptic receptor by neurotransmitters. Both, pre- and postsynaptic effects have been found.

Direct interaction with the neuronal plasma membrane is very likely, but indirect action via production of a second messenger also remains possible. The high correlation between lipid solubility and anaesthetic potency suggests that inhalation anaesthetics have a hydrophobic site of action. Inhalation agents may bind to both membrane lipids and proteins. It is at this time not clear which of the different theories are most likely to be the main mechanism of action of inhalation anaesthetics.

The Meyer-Overton theory describes the correlation between lipid solubility of inhaled anaesthetics and MAC. It suggests that anaesthesia occurs when a sufficient number of inhalation anaesthetic molecules dissolve in the lipid cell membrane. The Meyer-Overton rule postulates that the number of molecules dissolved in the lipid cell membrane and not the type of inhalation agent that causes anaesthesia. Combinations of different inhaled anaesthetics may have additive effects at the level of the cell membrane.

However, the Meyer-Overton theory does not describe why anaesthesia occurs. Critical Volume Hypothesis further expanded the Meyer-Overton rule. Critical Volume Hypothesis stated that the absorption of anaesthetic molecules could expand the volume of a hydrophobic region within the cell membrane and subsequently distort channels necessary for sodium ion flux and development of action potentials necessary for synaptic transmission. The fact that anaesthesia occurs with significant increase in volume of hydrophobic solvents and is reversible by compressing the volume of the expanded hydrophobic region of the cell membrane supports Critical Volume Hypothesis.

The protein receptor hypothesis postulates that protein receptors in the central nervous system are responsible for the mechanism of action of inhaled anesthetics. This theory is supported by the steep dose response curve for inhaled anesthetics. However, it remains unclear if inhaled agents disrupt ion flow through membrane channels by an indirect action on the lipid membrane, via a second messenger, or by direct and specific binding to channel proteins.

Another theory describes the activation of Gamma-Aminobutyric acid (GABA) receptors by the inhalation anesthetics. Volatile agents may activate GABA channels and hyperpolarize cell membranes. In addition, they may inhibit certain calcium channels and therefore prevent release of neurotransmitters and inhibit glutamate channels. Volatile anesthetics share common cellular actions with other sedative, hypnotic or analgesic drugs.

Each of the above mentioned theories described a unitary theory of narcosis. They all concentrate more or less on unique site of action for inhaled anesthetics. The true mechanism of action of volatile anesthetics may be a combination of two or more such theories described as multisite action hypothesis. Currently used inhalation anaesthetics include isoflurane, sevoflurane, desflurane and nitrous oxide.

Ideally, inhalation agents should provide a quick induction and emergence from anaesthesia, good analgesia, muscle relaxation, easy maintenance of anaesthesia, rapid and predictable metabolism or elimination independent of renal and hepatic function, no

undesirable drug interactions, no side effects or toxicity. The intention is always to improve safety and to increase the control of the anaesthetic by the anaesthesiologist.

History of inhalation anaesthetic started over 150 years ago (Figure 4.2). It began with the discovery of the anaesthetic properties of nitrous oxide, diethyl ether, and chloroform in the 1840s was followed by a hiatus of about 80 years before other inhaled anaesthetics were introduced. Then these were followed by ethylene, cyclopropane, trichloroethylene, isopropenyl vinyl in the 1930's and 1940's. In 1950, all inhaled anaesthetics, with the exception of nitrous oxide, were flammable or potentially toxic to the liver.

Halothane, a halogenated hydrocarbon was synthesized in 1951 and subsequently introduced into clinical practice in 1956. Shortly thereafter methoxyflurane appeared in the early 60's followed by enflurane and isoflurane in the 70's. Methoxyflurane was pulled from the market because of its nephrotoxic potential. Two other inhalation anaesthetics were synthesized in the 70's but were only introduced early 90's. The first of the two, sevoflurane was introduced in 1990 in Japan although it was first invented in United States. Desflurane was introduced into clinical practice in 1992.

Currently, both sevoflurane and desflurane have gained approval and acceptance for use in Great Britain, United States and most of other countries. However, desflurane is still new in Malaysia, and it is still not widely used.

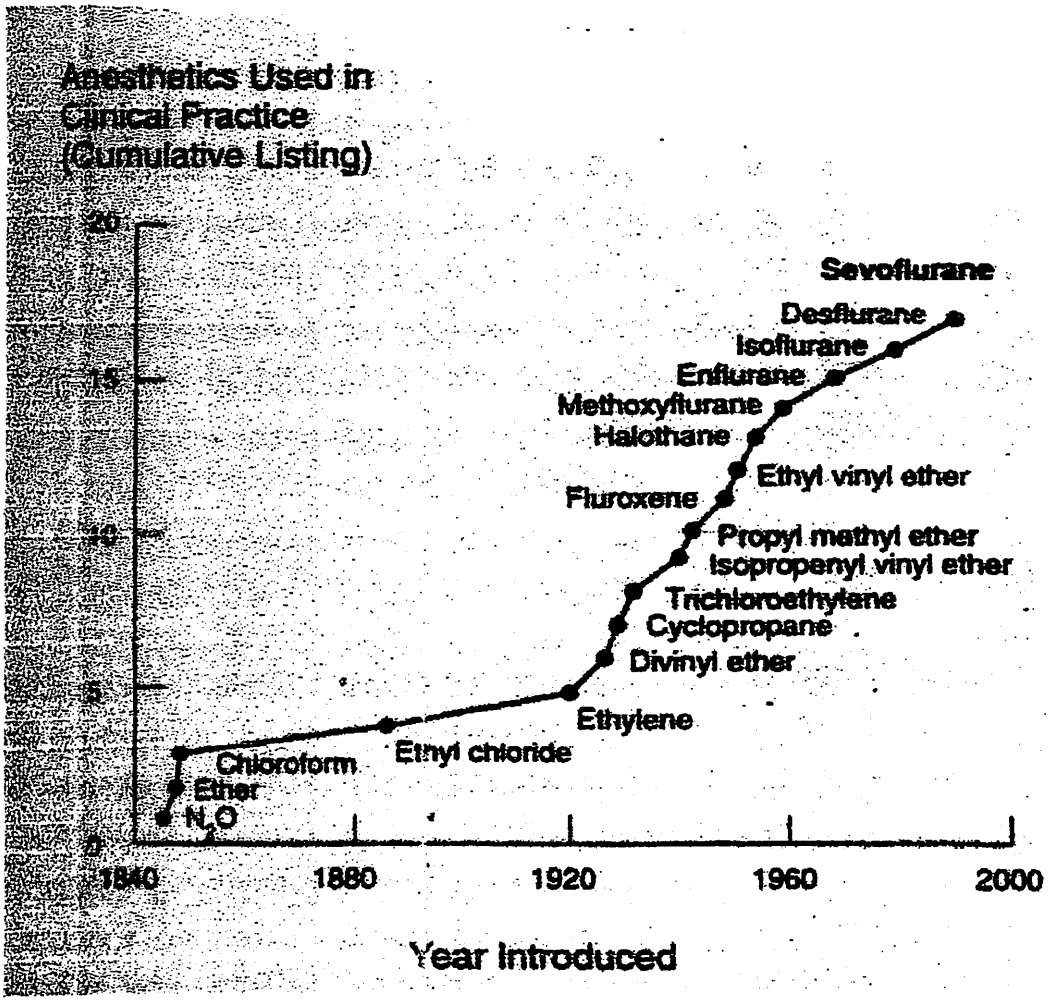

Figure 4.2 Inhaled anaesthetics introduced into clinical practice.

4.2 Physical Properties of Desflurane

Desflurane is a fluorinated methyl ethyl ether (Figure 4.3) differing from isoflurane only in the substitution of fluorine for chlorine on the alpha-ethyl carbon (Figure 4.4).

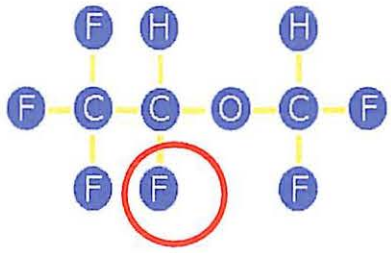

Figure 4.3 Chemical structures of desflurane.

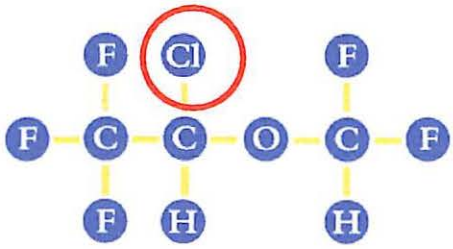

Figure 4.4 Chemical structures of isoflurane.

Desflurane has a pungent odor (figure 4.5). The boiling point of desflurane is 22.8C and it saturated vapor pressure is 664 mmHg at 20 C. So, desflurane would boil at normal operating room temperature. Therefore, it cannot be administered with a standard vaporizer. A new type of vaporizer technology addresses this property, producing a regulated concentration by converting desflurane to a gas (heated and pressurized vaporizer that requires electrical power), which is then blended with diluent fresh gas flow (Figure 4.6).

Figure 4.5 Inhalational agent, desflurane

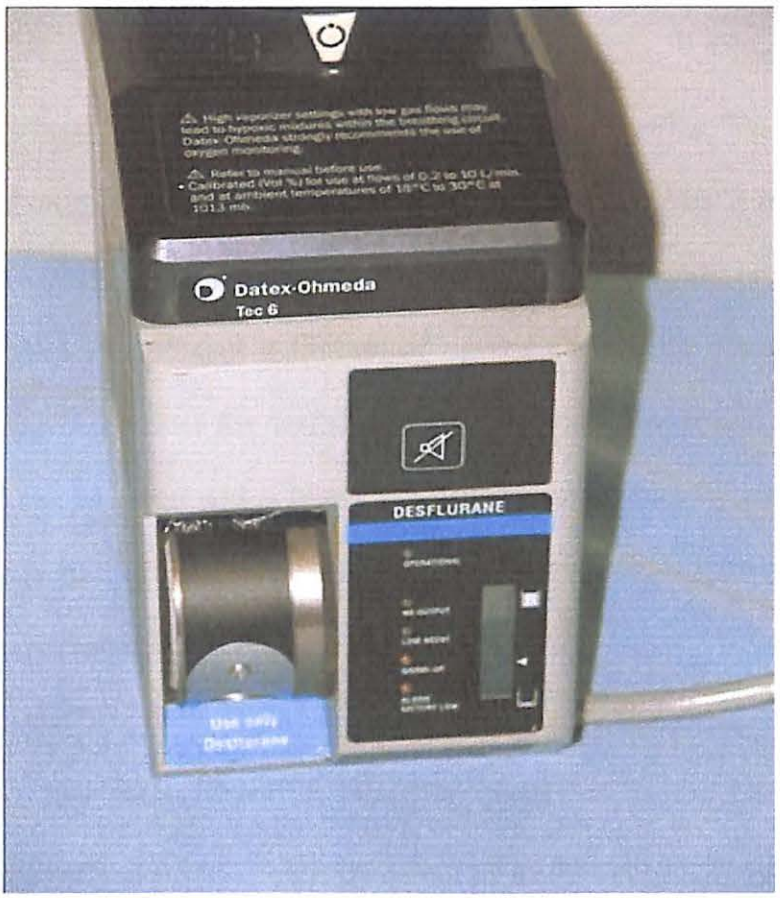

Figure 4.6 TEC 6 vaporizer

The ideal anaesthetic agent produces anaesthesia while allowing the use of a high concentration of oxygen. The minimum alveolar concentration (MAC) of an anaesthetic agent at one atmosphere that abolishes movement in response to a noxious stimulus in 50% of subjects provides the standard definition of inhaled anaesthetic potency. In 30 to 60 year-old patients, MAC values for desflurane is 6.0% at one atmosphere, which indicates the potency and can be given with a high concentration of oxygen. By contrast, the MAC for nitrous oxide is 104% at one atmosphere, and it must be given in a pressurized chamber due to safety considerations.

Solubility of an anaesthetic agent in blood is quantified as the blood:gas partition coefficient, which is the ratio of the concentration of an anaesthetic in the blood phase to the concentration of the anaesthetic in the gas phase, when the anaesthetic is in equilibrium between the two phases.

A low blood:gas partition coefficient reflects a low affinity of blood for the anaesthetic, a desirable property because it predicts a more precise control over the anaesthetic state and a more rapid recovery from anaesthesia. The blood:gas partition coefficients for inhaled anaesthetics vary from a low of about 0.45 for nitrous oxide and desflurane and 0.65 for sevoflurane to 1.4 for isoflurane and 2.4 for halothane.

Desflurane has a blood:gas partition coefficient of 0.42 (Eger, 1987), the lowest of all of the available volatile agents which means equilibration and recovery are likely to occur quickly.

4.3 Clinical Properties of Desflurane

4.3.1 Induction of anaesthesia

Desflurane has a blood:gas partition coefficient of 0.42 (Eger, 1987), the lowest of all of the available volatile agents which means equilibration are likely to occur quickly and leads to rapid induction and rapid recovery. However, the ability to deliver an inspired concentration sufficiently high to induce anaesthesia is limited by the effects of the anaesthetic vapor on the patient's airway.

As we know that desflurane has a pungent odor. This made desflurane extremely irritating to the airway and, therefore, is not really suitable for induction of anaesthesia. The irritability grading was desflurane > isoflurane > sevoflurane (TerRiet *et al.*, 2000). They compared the pungency and tolerability of the inhaled anaesthetics in eighty-one unpremedicated patients (n=27, each group) inhaled 2 MAC of isoflurane (2.3%), desflurane (12%) or sevoflurane (4%) for 60 seconds from an anaesthetic breathing circuit via a mask. They found that one sevoflurane patient coughed, but completed the study period, whereas 11 isoflurane patients and 20 desflurane patients coughed, objected verbally or removed the mask forcefully.

Both desflurane and isoflurane are pungent, Wilhelm *et al.* (1998) studied desflurane in comparison with isoflurane on the effects of intubation (in term of heart rate and blood pressure) in paediatric ENT patients and they found that intubation conditions were better for desflurane (excellent or good 20 of 22) than for isoflurane (12 of 20).

Van Hemelrijck *et al.* (1991) studied desflurane in comparison with propofol-nitrous oxide in outpatients undergoing laparoscopic procedures. They found that inhalation inductions were associated with high incidence of apnoea (26%), breath holding (39%), and coughing (22%) in desflurane alone group. However the above incidence reduced with desflurane-nitrous oxide group.

Smooth induction of anaesthesia is best carried out using either an intravenous induction agents or sevoflurane and when the patient is anaesthetized then only desflurane gradually introduced for maintenance anaesthesia.

4.3.2 Maintenance of Anaesthesia.

The important of maintenance anaesthesia is to achieve an appropriate "depth" of anaesthesia. These are done by titrating the inhalational anaesthetic agents given to the patients. It is important to recognize that equilibration between the two phases means the same partial pressure exists in both phases. Equilibration does not mean equality of concentration in two bio-phases.

Factors determining partial pressure gradients for establishment of anaesthesia are (a) transfer of inhaled anaesthetic from anesthetic machine to alveoli (anaesthetic input) which in turn depends on inspired partial pressure, alveolar ventilation, characteristics of anaesthetic breathing system, and functional residual capacity of individual patient, (b) transfer of inhaled anaesthetic from alveoli to arterial blood (anaesthetic loss) which in turn depends on blood:gas partition coefficient, cardiac output, and alveolar to venous partial

pressure difference, and (c) transfer of inhaled anaesthetic from arterial blood to brain (anaesthetic loss) which in turn depends on brain:blood partition coefficient, cerebral blood flow, and arterial to venous partial pressure difference (Figure 4.7).

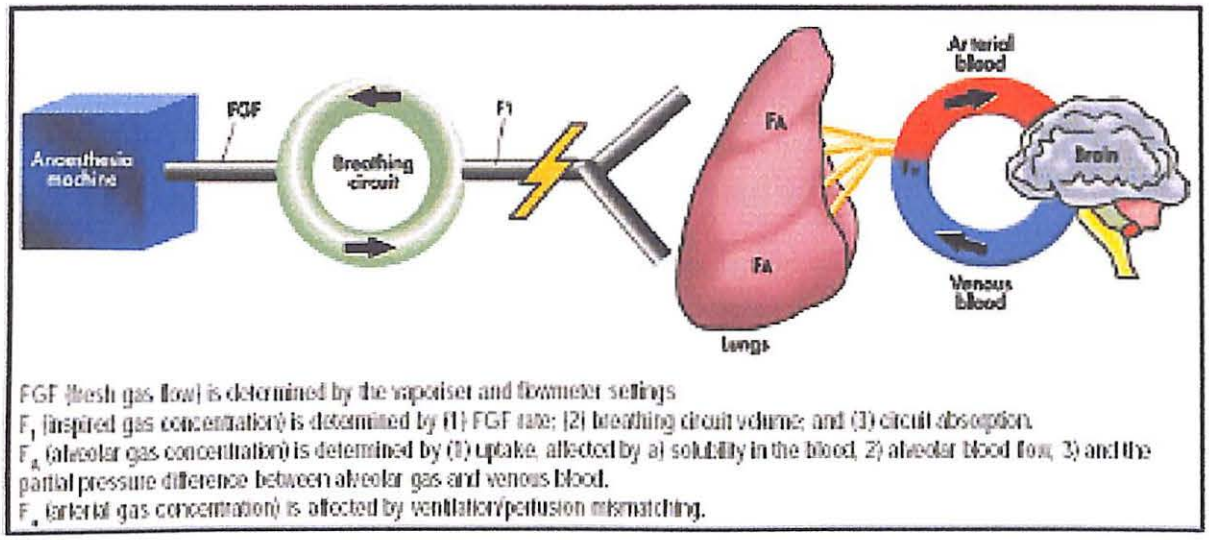

Figure 4.7 Anaesthetic circuits

Because desflurane has low blood and tissue solubility, it would be expected that equilibration between the inspired concentration and the blood concentration should occur more rapidly and to a greater degree than with other volatile agents. This gives more control over depth of anaesthesia, and should mean more rapid recovery.

There was faster equilibration between inhaled and exhaled concentrations of desflurane compared with isoflurane (Lee *et al.*, 1993). The alveolar concentration closely approximates the blood concentration. After 5 minutes, the ratio of alveolar and inhaled

concentration for desflurane was 0.9, whereas after 1 hour, the ratio of alveolar and inhaled concentration for isoflurane was still 0.75.

There have been several studies that examined the use of desflurane in patients undergoing cardiac surgery. Thomson *et al.* (1991) compared the use of desflurane with isoflurane in patients undergoing coronary artery surgery. They found no difference in the incidence of electrocardiographic changes, indicating myocardial ischaemia, or in outcome. Desflurane does not sensitize the myocardium to epinephrine (Moore *et al.*, 1993), although desflurane can slow atrioventricular conduction (Boban *et al.*, 1992) and can cause junctional bradycardia (Rampil *et al.*, 1989).

Parsons *et al.* (1994) compared anaesthesia with desflurane and low-dose fentanyl with high-dose fentanyl and midazolam in patients undergoing coronary artery bypass surgery. They found that desflurane group had lower heart rates and blood pressures throughout the procedures. Again there was no measurable difference in outcome between the two groups.

At concentration up to 1.0 MAC, neither sevoflurane nor desflurane increased heart rate, whereas isoflurane caused an initial increase in heart rate that was sustained with increasing MAC (Ebert TJ *et al.*, 1995). However, in the study, they also found that at above 1.0 MAC, both desflurane and sevoflurane were associated with an increase in heart rate, and the increase was more pronounced with desflurane. Rapid increases in inspired concentrations of either isoflurane or desflurane have been shown to initiate tachycardia

(Bedforth *et al.*, 2000). The use of nitrous oxide with desflurane may diminish this effect (Cahalan *et al.*, 1991).

Mean arterial blood pressure was measured in adult volunteers who were not premedicated. Sevoflurane, isoflurane, and desflurane produced dose-dependent decreases in mean arterial blood pressure, and the effects were comparable (Ebert TJ *et al.*, 1995). Desflurane cause the cardiac index to remain unchanged, while the systemic blood pressure falls in ventilated patients. In spontaneously breathing patients, the cardiac index increased (Weiskopf *et al.*, 1991).

Desflurane cause peripheral vasodilatation (Jones *et al.*, 1990), direct coronary vasodilation (Merin *et al.*, 1991) and produced an overall reduction in cardiac work (Boban *et al.*, 1992). A progressive decreased in forearm vascular resistance was observed with increasing concentrations of sevoflurane, isoflurane, and desflurane (Ebert *et al.*, 1995).

This decrease became statistically significantly lower with sevoflurane at 1.5 MAC than with desflurane or isoflurane. These makes potential improvement in coronary blood flow was offset by a fall in the perfusion pressure resulting from the peripheral vasodilatation and the tachycardia. It also rises the potential for coronary steal syndrome. However, Hartman *et al.*, (1991) failed to find any evidence for this, using a canine model of coronary artery disease.

Other pharmacodynamic effects of desflurane on various organ systems are similar with other inhalational anaesthetics. Desflurane produced a dose-dependent decrease in tidal volume with an increase in respiratory rate (Lockhart *et al.*, 1991). The net effect was a reduction in minute alveolar ventilation (Jones *et al.*, 1990). There was an increase in arterial carbon dioxide levels and a depression of the ventilatory response to carbon dioxide. There was also an increase in the intrapulmonary shunt fraction and an increase in the physiological dead space (Lockhart *et al.*, 1991).

At concentrations of 6% desflurane is extremely irritating to the airway. It caused coughing, breath holding, and laryngospasm, making it unsuitable for use for inhalation induction in both children and adult (Zwass *et al.*, 1992; Bunting *et al.*, 1995). The mechanism is unknown but it was believed that there are sites in the upper airway (larynx and above) that respond with sympathetic activation during rapid increases in desflurane concentration independent of systemic anaesthetic changes. These responses, while lesser than those seen with rapid increases to the lung may represent direct irritation of airway mucosa. Eshima *et al.*, (2002), showed that there was no significant difference in airway responses during desflurane and sevoflurane administration via a laryngeal mask airway for maintenance of anaesthesia.

Eger *et al.*, (1994), found that there was no evidence of bronchospasm during induction of anaesthesia in asthmatics with desflurane and in vitro studies. This suggests that desflurane produces concentration-dependent bronchodilation as with other inhalational agents (Mazzeo *et al.*, 1994; Park *et al.*, 1998).

Desflurane significantly depressed neuromuscular function, reducing the force of contraction of the adductor pollicis muscle and increasing the degree of titanic fade (Caldwell *et al.*, 1991). It also provided sufficient relaxation to allow tracheal intubation.

Desflurane potentiated the action of muscle relaxants similar to the other volatile agents (Caldwell *et al.*, 1991; Lee *et al.*, 1992; Ghouri & White., 1991). The above effects were more pronounce with desflurane than propofol (Zhou TJ *et al.*, 2000). Routine monitoring of neuromuscular activity is recommended even when a single bolus dose of muscle relaxant is administered during anaesthesia.

Rampil *et al.*, (1988) showed that desflurane had an effect on the EEG similar to isoflurane, producing burst suppression at lower doses. At an MAC greater than 1.66%, the EEG becomes isoelectric. In human volunteers, it produced burst suppression at concentration above 1.24 MAC (Rampil et al., 1991a), with no evidence of epileptiform activity, despite attempts to provoke excitatory activity experimentally. There have been no reports of epileptiform activity associated with desflurane to date.

Lutz *et al.*, (1990) demonstrated in dogs that desflurane produces dose-dependent cerebral vasodilation. It also produced a dose-dependent reduction in cerebral metabolism (Newberg *et al.*, 1983). Strebel *et al.*, (1995) showed that autoregulation was impaired under desflurane anaesthesia, when compared with propofol. Ornstein *et al.*, (1993) demonstrated that in humans with intracranial mass lesions, the effect of desflurane on the

cerebral circulation was similar to isoflurane and that the cerebrovascular response to carbon dioxide was maintained.

Talke *et al.*, (1996) compared the effect of desflurane and isoflurane on lumbar CSF pressure in normocapnic patients without an intracranial mass lesion anaesthetized with propofol infusion. They found that both desflurane and isoflurane at 0.5 and 1 MAC, respectively, were associated with an increase in CSF pressure under these conditions.

Despite advances in anaesthetic technique and technology, intraoperative awareness continues to occur with alarming regularity. The psychological effects on patients and the medicolegal consequences to providers have created the need for a reliable monitor of the hypnotic component of anaesthesia.

A new technology known as bispectral index scales (BIS) has the potential to put an end to the devastating occurrence of intraoperative awareness, as well as improve the overall effectiveness of anaesthetic delivery and surgical experience (Ouellette *et al.*, 1998).

Bispectral index scale measures the hypnotic effect of anaesthetic and sedative agents on the brain and records a single number that ranges from zero (absence of brain activity) to 100 (completely awake). The BIS monitor provides a continuous measurement of the hypnotic state or state of consciousness, awareness, and recall.

A BIS sensor is required for obtaining the brain activity signal from a patient. The sensor can either be a one-piece sensory strip, which has location markers to facilitate placement, or four individual leads placed on the patient at specific sites (Figure 4.8).

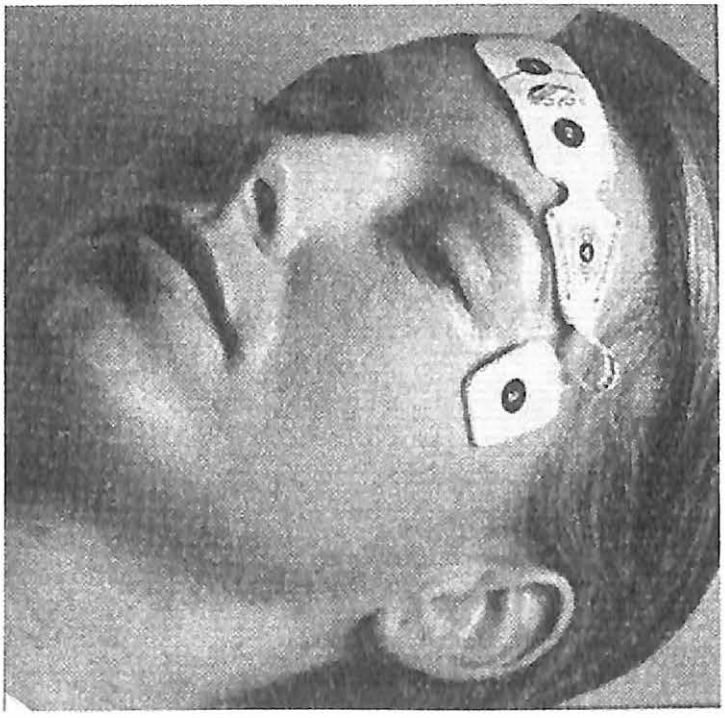

Figure 4.8 Bispectral Index Scale sensor placed on the patient.