CHAPTER I
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The practice of anaesthesia started with inhalational agents in 1840 which remained the standard technique for induction of anaesthesia for over one hundred years. Induction of anaesthesia with inhalational anaesthetic agents was abandoned because it was slow, smelly, caused excessive salivation and resulted in coughing and vomiting. An increasing interest in intravenous anaesthetic technique has resulted from the availability of more efficacious intravenous drugs and drawbacks of inhalational agents like toxicity, high cost and anaesthetic gas pollution in the operating and recovery room.

In 1920s, tribromethanol and barbiturates were used. During the 1930s and 1940s, hexobarbitone became very popular, despite its limitation like muscle movement. During the same period it was appreciated that thio derivatives of diallyl barbiturates were valuable hypnotics. Since late 1930s, thiopentone remained the most popular intravenous anaesthetic agent despite prolonged duration of action and delayed recovery.

In 1980s, propofol was introduced in clinical practice which has a definite advantage of having faster recovery along with its antiemetic effect. However its negative inotropic and respiratory depressant effect is more than that of thiopentone. In situations where rapid induction and rapid recovery is desirable,
propofol remains the drug of choice.\cite{7}

Inhalational induction may be preferable in paediatric patients, in adult patients with needle phobia, in patients where there is a difficulty in establishing intravenous line. However, the principle indication for inhalational induction in adults is anticipated difficulty in control of the airway. Inhalational agents are free from hangover effect and risk of anaphylaxis is also avoided.\cite{8}

Since the 1930s, the anaesthetic agents were developed in the light of some understanding of structure activity relationships. So, a number of agents, principally ethers, were introduced between 1930 and 1940.\cite{9} These were either potentially explosive or toxic. Halothane was the first halogenated hydrocarbon which was brought into clinical practice by Bryce-Smith and O'Brien in 1956.\cite{10} It is non combustible, apparently non-toxic, sweet smelling and allows a rapid, clear headed recovery as compared to older anaesthetics. It suffers from many drawbacks most important of which are myocardial depression and halothane hepatitis on repeated exposure.\cite{11}

Between 1959 and 1966, Terrell and his associates synthesised more than 700 compounds in a programme intended specifically to produce a better inhalational anaesthetic agent. The 347th and 469th compound in this series were halogenated methylethyl ethers, enflurane and isoflurane.\cite{9} Close on the heels of isoflurane and enflurane, another compound desflurane was invented. Enflurane has poor induction characteristics and potential to cause seizures.\cite{12}
Isoflurane has some definite advantages over halothane and enflurane like haemodynamic stability and being non-epileptogenic.\textsuperscript{13} It also has low blood:gas partition coefficient which provide rapid induction but its irritant effect on respiratory tract limits its use as an inhalational induction agent.\textsuperscript{14} Desflurane has still lower blood:gas solubility coefficient approaching that of nitrous oxide allowing for early induction and easy titrability but this agent is also irritant to the airways.\textsuperscript{15} In addition complex vaporization technique is required for desflurane.\textsuperscript{16}

To overcome these drawbacks, search for improved agent continued and sevoflurane was synthesised in 1968 by Regan at Travenol Laboratories, Illinois while he was investigating series of halomethyl polyflouroisopryl ethers. This compound was initially reported by his coworkers in 1971.\textsuperscript{17} It was released for clinical use in Japan in May 1990. Sevoflurane is related structurally to isoflurane and enflurane and shares many of the physical properties of these drugs.\textsuperscript{16} The blood:gas partition coefficient of sevoflurane is 0.69 which is comparable to the blood:gas solubility of both N\textsubscript{2}O and desflurane.\textsuperscript{16} The low blood:gas solubility of sevoflurane permits rapid induction of anaesthesia as it rapidly equilibrates with the inspired concentration. In addition sevoflurane is pleasant smelling and relatively non-irritant to the airways permitting a high delivered concentration to be inhaled without side effects or discomfort.\textsuperscript{15}

Although inhalational induction is the route of choice for anaesthetising neonates and children but under certain situations like needle phobias and
potential difficult airways, inhalational induction is desirable even in adults. Halothane has been the agent of choice till recently but with the introduction of sevoflurane in anaesthesia practice, inhalational induction seems more favourable with sevoflurane owing to its pleasant smell and low blood:gas solubility. Keeping this in background we studied the induction characteristics of sevoflurane with or without N\textsubscript{2}O in adults and compared it with the most prevalent intravenous induction agent propofol.