INTRODUCTION

Although recently approved for use in the United States on June 7, 1995, Sevoflurane has a relatively long history when compared to the currently used inhalational anesthetics. First synthesized in the late 1960’s by Drs. Wallin, Regan, and Napoli while working for Baxter-Travenol Laboratories, the agent saw limited activity for development at this time. Although given excellent clinical reviews in studies done on volunteers [1], the further development of sevoflurane was not undertaken at this time. This was predominantly due to two reasons. First, Baxter-Travenol Laboratories did not have a strong interest at the time for developing new inhaled anesthetics. The second and more important reason for the lack of interest in further development was that sevoflurane possessed two characteristics which, at the time, caused some clinical safety concerns. The first concern related to sevoflurane and fluoride ion metabolism. Methoxyflurane with its associated fluoride ion nephrotoxicity became a major issue for clinicians during the late 1960’s and early 1970’s. As newer inhalational agents were developed that could also generate fluoride ions through metabolism, such as ethrane, isoflurane, and sevoflurane, any possible effects on renal function had to be fully assessed. The second concern related to sevoflurane’s ability to react in the presence of strong bases such as carbon dioxide absorbents. All of today’s currently used inhalational anesthetic agents react with CO₂ absorbents resulting in the formation of agent-specific compounds. Sevoflurane produces a vinyl ether commonly referred to as compound A. Halothane produces a similar chemical entity, referred to as compound B, C, D, F, E. Desflurane, ethrane, and isoflurane can produce carbon monoxide in the presence of CO₂ absorbents. Any significant clinical relevance to patients from any of these inhalational agent byproducts has never been proven. In 1988, Maruishi Pharmaceuticals in Japan renewed the interest in sevoflurane by beginning an in-depth research and development program for clinical use of the inhalational agent. Their efforts led to clinical approval of the agent in Japan in 1990. During the first three
years of clinical use in Japan, sevoflurane has become the most popular halogenated inhalational anesthetic agent. In 1992, Abbott Laboratories licensed sevoflurane from Maruishi Pharmaceuticals. FDA approval for use in the United States, based on large scale safety and efficacy studies conducted by Abbott Laboratories, was granted in June, 1995. Sevoflurane is presently approved in 56 countries worldwide. To date, more than 20 million sevoflurane anesthetics have been given worldwide. Clinical experience has shown the agent to offer many favorable characteristics. In addition, the worldwide clinical safety record of the agent has been excellent and shown the early concerns related to renal toxicity to be unfounded.

1. CLINICAL BENEFITS

As with isoflurane, halothane, and enflurane, sevoflurane is used with a conventional vaporizer. When addressing the needs of the ambulatory surgical environment, an ideal anesthetic would provide rapid, smooth, and pleasant induction of anesthesia, allow for quick, safe adjustments in anesthetic depth, result in a rapid and safe emergence and recovery period, and should be void of unpleasant side effects. The recent introduction of some of the newer anesthetic agents have moved us closer towards this goal. The physical characteristics of sevoflurane allows for rapid induction and emergence of the patient. Awakening time was shown to be approximately half that of isoflurane for comparable surgical procedures [2], but slightly slower than that of desflurane in the ambulatory environment [3]. In comparisons with propofol, studies have found conflicting results in emergence times. Fredman et al [4] found similar emergence times, patients’ subjective feelings, and psychomotor performance scores when sevoflurane was compared to propofol. Others have found a more rapid emergence and recovery profile with sevoflurane when compared to propofol. Wandel, et al. found that patients receiving sevoflurane were extubated faster. They noted that in the sevoflurane group, times to eye opening and hand squeezing were also shorter. Modified aldrete scores were higher in the sevoflurane group within the first hour after anesthesia when compared to the propofol group [5]. Emergence data should be viewed with caution as many of these studies fail to show differences in hospital discharge times for these patients. This may be explained by numerous reasons, including variations in discharge criteria or pain medication requirements with associated side effects. Study results reported by Jeff Apfelbaum, M.D. at the 1997 Annual Meeting of the ASA related to the short acting fast emerging (SAFE) agents’ study have shown economic benefits related to improved discharge times with the newer agents. Also, recent clinical study data has indicated that sevoflurane may have a reduced incidence of nausea and vomiting over desflurane in certain ambulatory surgical procedures [6]. Further studies are needed to better define these effects on recovery and discharge times.

2. IDEAL AGENT FOR MASK INDUCTION

Sevoflurane has been shown to be non-pungent and non-irritating to the respiratory tract. These unique respiratory characteristics, combined with it’s rapid induction characteristics, make it an ideal agent for mask induction in the pediatric and adult patient populations. In volunteers, sevoflurane has been shown to result in less respiratory irritation than halothane, enflurane, or isoflurane [7]. Because of these qualities, renewed
interest in adult mask induction techniques, including the use of vital capacity single
breath techniques, has started to occur since the release of sevoflurane [8]. Studies
comparing the clinical benefits and cost-effectiveness of mask induction in adult patients
have also recently been published [9]. Besides being very cost-effective, mask induction
in adults offers several clinical advantages in certain patient populations. In patients
with difficult airways, a mask induction technique allows for the continuation of
spontaneous ventilation throughout the induction period, alleviating fears of apnea and
an inability to ventilate the patient. The ability to maintain spontaneous ventilation during
the induction period also offers clinical advantages when a laryngeal mask airway (LMA)
is going to be used. The use of sevoflurane for LMA insertion was recently reported by
Muzi, et al [9]. Additionally, mask induction can allow for an alternative approach in
patients with difficult IV access or a phobia to needles. Based on these studies, patient
acceptance of a mask induction technique with sevoflurane has been excellent and equally
comparable to an intravenous induction.

3. PEDIATRIC ANESTHESIA

The clinical characteristics of sevoflurane offer many advantages in the pediatric patient
population. When used for mask induction, the agent is well tolerated by infants and
children [10, 11]. Coughing is rarely seen. Breath holding, laryngospasm and
bronchospasm also occur very infrequently. The low solubility and rapid wash-in
characteristics of the agent combined with the relative lack of respiratory irritation can
allow for faster induction times over halothane when higher concentrations (8 %) are
used. Transient involuntary movements of the extremities may be seen during mask
induction with sevoflurane. The occurrence of these involuntary movements is minimized
by the use of nitrous oxide and higher sevoflurane concentrations during the induction
period.

4. TOLERANCE

Hemodynamically, sevoflurane has been shown to be very user friendly in children.
Although all volatile inhalational anesthetics are dose dependent cardiac depressants,
sevoflurane has been shown to depress myocardial contractility less than halothane during
induction of anesthesia in children [12]. In a comparison study with halothane, heart rate
with sevoflurane increased before tracheal intubation. During maintenance of anesthesia
with sevoflurane, heart rate and systolic blood pressure did not change when compared
to baseline. In the halothane group, heart rate did not change throughout the study, but
systolic blood pressure remained significantly below control values throughout both
induction and maintenance of anesthesia [13]. Arrhythmias are uncommon under
sevoflurane anesthesia and the agent has significantly less epinephrine sensitization of
the myocardium to arrhythmias than that seen with halothane.

5. ANALGESIA

Pre-emptive analgesia has become an important consideration in pediatric anesthesia.
As with other rapid emergence type agents, sudden awakening under sevoflurane
anesthesia can produce an excitement state that may, on occasion, be difficult to control.
Recovery can be so rapid that some form of pain management (e.g. opioids, caudal or
field block) should be administered before emergence when pain is anticipated. Numerous other techniques have also proved successful in reducing or eliminating this occurrence. Finally, like all inhalational anesthetic agents, sevoflurane can be a triggering agent for malignant hyperthermia.

REFERENCES BIBIOGRAPHIQUES