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Comparison of induction and recovery characteristics of propofol and sevoflurane in day care adult tonsillectomies

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***Abstract*---**Ambulatory anaesthesia is a rapidly growing subspecialty. Although its history is as old as the history of general anesthesia itself, it has emerged as a recognized concept and is evolving over the past couple of decades. Propofol and Sevoflurane have increased the ability of the anaesthesiologist to provide a successful day-care experience. The aim of the study was to compare the induction and recovery characteristics of Propofol and Sevoflurane when they are used as single induction and maintenance anaesthetic agent in adult day care tonsillectomies. This was a randomized prospective study carried out after obtaining ethical committee and institutional

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approval. 60 patients were randomly allocated to either the Propofol or the Sevoflurane group by lots. Each group had 30 patients and was named 'P' for Propofol and 'S' for Sevoflurane. Their age ranged from 13 to 40 years. All the patients were assessed and those with normal clinical, biochemical, radiological and haematological parameters were selected. Despite the low blood gas solubility of Sevoflurane, inhalation induction of anaesthesia was slower than intravenous induction with Propofol. Though the incidence of induction complications was more with Sevoflurane group, it did not compromise tracheal intubation or haemodynamics except for bradycardia observed in three patients. Equal incidence of apnoea in both groups is attributable to the enhancement of the ventilatory depressant effect of Propofol and Sevoflurane by the opioid Fentanyl. Shorter emergence time in the Sevoflurane group did not translate into a shorter hospital study. Increased incidence of PONV and pain did not affect the time for home readiness. Sevoflurane is found to be a useful alternative for elective procedures of short duration.

***Keywords*---**sevoflurane, propofol, haemodynamic, elective procedures.

Introduction

Ambulatory anaesthesia is one administered for elective surgical procedures performed on carefully selected patients, which is undertaken with all its constituent elements (admission, surgery and discharge home) on the same day. It is also referred to as day case, day care or outpatient anaesthesia and more recently: office-based anaesthesia. Ambulatory anaesthesia is a rapidly growing subspecialty. Although its history is as old as the history of general anaesthesia itself, it has emerged as a recognized concept and has evolved over the past couple of decades. In the United States, it comprises 70% of anaesthesia services provided. In the United Kingdom, the NHS plan published recently predicts that 75% of elective surgical procedures will soon be conducted as day cases. Anaesthetic agents today have been designed and marketed to meet the specific niche criteria for ambulatory anaesthesia. Among the agents available in India, Propofol and Sevoflurane have increased the ability of the anaesthesiologist to provide a successful day-case experience. The present study compares the induction and recovery characteristics of these two anaesthetic agents and their usefulness in ambulatory anaesthesia.

Materials and Methods

This was a randomized prospective study was carried out in the ENT theatre, Gandhi Hospital, Secunderabad after obtaining ethical committee and institutional approval. The aim of the study was to compare the induction and recovery characteristics of Propofol and Sevoflurane when they are used as single induction and maintenance anaesthetic agent in adult day care tonsillectomies. Sixty patients undergoing tonsillectomy were selected for the study. Their age ranged from 13 to 40 years. All the patients were assessed and those with normal

clinical, biochemical, radiological and haematological parameters were selected. Informed written consent was obtained from all the patients and parents in case of minor. Each patient was randomly allocated to either the Propofol or the Sevoflurane group by lots. The groups were named 'P' for Propofol and 'S' for Sevoflurane.

Inclusion criteria

- Age group between 13 to 40 years
- ASA physical status I & II with normal biochemical and haematological parameters
- Airway- MPC I & II
- Undergoing tonsillectomy
- Surgery lasting around one hour
- Patients normally able to ambulate well
- Educated attender who can understand and carry out instructions

Exclusion criteria

- ASA class III and above
- Patients with H/O drug or egg allergy
- Anticipated difficult airway
- H/O serious adverse experience with anaesthesia,
- Severe CVS/RS/CNS/ Metabolic disease
- Any case with excessive primary/reactionary/secondary haemorrhage

Equipment

- Anaesthesia machine with Sevoflurane vaporizer
- Appropriate drugs in labelled, preloaded syringes
- Syringe pumps
- Functioning Laryngoscope with appropriate size blades
- Appropriate sized endotracheal tubes
- Equipment and drugs for resuscitation

Preoperative preparation

Patients were assessed pre-operatively. Procedure was explained to the patient, informed consent obtained and overnight NPO status confirmed. They were assessed with particular attention to any contraindications. The tests for recovery and the importance of strictly following instructions were emphasized. The patients were not given any IM premedication. Routine IV pre-medication was given. All patients were pre-oxygenated. On arrival of the patient in the operating room, monitors like pulse-oximetry, NIBP and ECG were connected and baseline values of HR, BP and SpO_2 were recorded. An intravenous access was obtained on the non-dominant arm and an infusion of Lactated Ringer's solution was started. All emergency drugs were kept ready. 2% IV Lignocaine 1cc was given before induction to both the groups. Although Lignocaine was given as

prophylaxis against pain on injection of Propofol, it was administered to both groups of patients because of possible effects on haemodynamic variables and to make it a constant.

Group P

The patients were induced with Propofol 2mg/kg IV and intubated with 1.5mg/kg Succinylcholine. After confirming and securing the endotracheal tube in position, they were connected to the closed circuit with Nitrous Oxide and Oxygen in 2L: 1L ratio. Immediate post intubation, this group of patients received a continuous infusion of Propofol 6-12mg/kg/hr (100-200 µg/kg/min) to maintain an adequate depth of anesthesia as judged by clinical signs and haemodynamic responses to surgical stimuli. Throat packing was done. Ventilation was controlled with Vecuronium 0.8 mg/kg as the loading dose and one fourth of the loading dose as top up dose. Inj. Paracetamol 1gm IV was given towards the end of surgery.

Group S

The patients were induced with Sevoflurane 4% by patient controlled inhalation induction i.e. spontaneous ventilation in Nitrous Oxide and Oxygen in 4L:2L ratio and intubated with 1.5mg/kg of Succinylcholine. After confirming and securing the endotracheal tube in position, they were connected to the closed circuit with Nitrous Oxide and Oxygen in 2L:1L ratio with Sevoflurane 1-2.5% to maintain adequate depth of anaesthesia. Throat pack was placed. Ventilation was controlled with Vecuronium 0.8mg/kg as loading dose and one fourth of the loading dose as top up dose. This group also received Paracetamol 1gm IV towards the end of surgery. Throughout the procedure, HR, ECG and SpO_2 were monitored continuously and NIBP was monitored every 5 minutes. Upon completion of the surgery, residual neuromuscular block was reversed with Neostigmine 50µg/kg IV and Glycopyrrolate 10µg/kg IV and anaesthesia was discontinued. The patients' lungs were ventilated with 100% O_2 at a flow rate of 8L/min until tracheal extubation. The time of discontinuing the agent was taken as 'time zero' to calculate the recovery time. Inj. Ondansetron 0.15mg/kg IV was used as rescue anti-emetic and Inj. Diclofenac IM was the rescue analgesic post-operatively in both groups.

Parameters assessed

- Time to loss of consciousness
- Induction complications (desaturation, coughing, laryngospasm and patient movement)
- Incidence of apnoea
- Haemodynamic changes
- Time to phase in recovery (This is the time taken from discontinuation of Propofol or Sevoflurane to the time when Aldrete score is ≥ 9)
- Time to phase II recovery (This is the time taken from discontinuation of Propofol or Sevoflurane to the time when the PADSS score is ≥ 9. It is also taken as the time to home readiness.)

Statistical analysis

The descriptive statistics of the variables studied are represented as two-way tables. The categorical factors are represented by the number and frequency (%) of cases. The continuous variables are represented by measures of central frequency (like mean, median) and deviation (say, standard deviation and range.) The differences in the properties are tested for statistical significance using non-parametric Chi-square test for variables measured on nominal scale. For variables measured on a continuous scale, when testing for two groups, Student "t" test is used to test for statistical significance in the differences of the two means.

Results

The mean age was observed to be greater in Group P than Group S but not statistically significant. A female preponderance was forthcoming in Group P and equally distributed in Group S. The difference was not statistically significant. All the cases from both groups were identically classified as Grade I on ASA. Hence, there are no differences in ASA between the two groups. Although there were more Grade I cases in Group S than Group P, the distribution of cases by MPC in the two groups was not statistically significant.

Table1
Distribution of cases by MPC and groups

MPC	Group P		Group S		P values
Pre- OP	Actual	Difference from references	Actual	Difference from references	
Mean	92.5	-	94.5	-	0.3
SD	9.4	-	7.9		
At induction					
Mean	81.3	-11.2	86.9	-7.6	0.08
SD	11.3		13.1		
Post -OP					
Mean	92.6	0.1	93.2	-1.3	0.8
SD	9.2		13.0		
At discharge					
Mean	90.5	-4.3	92.8	-1.7	0.17
SD	5.8		7.1		

The actual mean MAP values were generally lesser in Group P than Group S at all points in time. The differences in the mean values of MAP at induction, post-op and at discharge compared to the pre-operative reference value between the two groups were observed to be statistically insignificant.

Table 2
Distribution of cases by groups and heart rate

MPC	Group P		Group S		P values
Pre- OP	Actual	Difference	Actual	Difference	

		from references		from references	
Mean	92.8	-	96.4	-	0.29
SD	12.6		13.6		
At induction					
Mean	105.8	13	86.4	10.0	0.0006
SD	15.0		13.1		
Post -OP					
Mean	91.2	-2.25	95.9	-0.5	0.07
SD	14.4		16.2		
At discharge					
Mean	89.3	-4.2	92.5	-3.9	0.17
SD	9.2		11.2		

The actual mean heart rate values were generally lesser in Group P than Group S at all points in time except at induction. The differences in the mean values at induction, post-op and at discharge compared to the pre- operative reference value between the two groups *was* observed to be statistically significant at induction and not at other points in time. (p value = 0.00006)

Table 3
Time to Loss of Consciousness (LOC) by groups

Time to LOC	Group P	Group S	P-value
Mean	40.1	74.7	<0.001
SD	15.8	24.0	
Median	35	75	
Range	20-90	20-140	

The mean time to LOC was observed to be lesser in Group P than Group S and the *difference was found to be statistically significant* (p<0.0000001)

Table 4
Distribution of cases by induction complications

Induction complications	Group P		Group S		P-value
	No	%	No	%	
Nil	25	83.3	18	60	0.02
Yes	5	16.6	12	40	
Complication type					
Patient movement	5		5		
Desaturation	0		4		0.08
Bradycardia	0		3		

The number of cases with induction complications was more among Group S than Group P and difference was statistically significant (p= 0.02) No coughing or laryngospasm occurred in both the groups.

Table 5

Distribution of Phase I recovery (in minutes) by groups*

Phase I Recovery profile	Group P	Group S	P-value
Mean	12.2	11	
SD	2.6	2.2	0.05
Median	11	10	
Range	8-17	8-17	
Phase I Recovery profile			
Mean	106	101	
SD	10.7	12.4	0.09
Median	105	100	
Range	85-130	80-130	

The distribution of Phase I recovery profile between Group P and Group S is not statistically significant. The distribution of Phase II recovery profile between Group P and Group S is not statistically significant.

Table 6

Distribution of cases incidence of apnoea, post operative nausea

incidence of apnoea	Group P		Group S		P-value
	No	%	No	%	
No	7	23.3	7	23.3	0.5
Yes	23	76.6	23	76.6	
Post operative nausea/vomiting					
No	20	66.6	14	46.6	0.1
Yes	10	33.3	16	53.3	
post operative pain					
No	21	70	19	63.3	0.2
Yes	9	30	11	36.6	

*Not statistically significant

The difference in distribution of apnoea was not statistically significant. Although the distribution of post operative nausea/vomiting and post operative pain was less in Group P, it was found to be statistically insignificant.

Discussion

Intravenous agents are used commonly for induction of anaesthesia followed by inhalational agents for maintenance. A problem with this technique is the transition phase from induction to maintenance. The rapid redistribution of the intravenous agent could lead to lightening of anaesthesia before an adequate depth is attained with the inhalational agent. This has promoted the rediscovery of “single agent” anaesthesia, which avoids problems associated with a transition

phase.[3] Propofol is a short acting general anaesthetic agent used widely for total intravenous anaesthesia because of its favorable recovery profile and low incidence of side effects. Propofol infusions are also becoming increasingly popular for maintenance of anaesthesia. It is particularly well-suited for anaesthesia in patients undergoing ambulatory and neurosurgery where rapid psychomotor recovery are of upmost importance.[2] TIVA with Propofol is an attractive option with the benefit of minimal pollution to the operating room environment. However, use of Propofol is associated with pain on injection, cardiovascular and respiratory depression and it requires an intravenous drug delivery system.[4,5]

Sevoflurane is a safe and versatile inhalational anaesthetic compared with the currently available agents. Sevoflurane is useful in adults and children for both induction and maintenance of anaesthesia in inpatient and outpatient surgery. Of all the currently used anaesthetics the physical, pharmacodynamic, and pharmacokinetic properties of Sevoflurane come closest to that of the ideal anaesthetic. These characteristics include its inherent stability, low flammability, non-pungent odour, lack of irritation to the airway, low blood: gas solubility allowing rapid induction of and emergence from anaesthesia, minimal end-organ effects, minimal effect on cerebral blood flow, low reactivity with other drugs and a vapour pressure and boiling point that enables delivery using standard vapourisation techniques. The availability of this agent makes it an alternative option for volatile Induction and Maintenance Anaesthesia (VIMA) [6].

Lack of airway irritation makes Sevoflurane almost ideal for inhaled induction, which may be especially desirable in children and needle-phobic adults. [7] Moreover, rapid increases in inspired concentration are well tolerated, facilitating control of anesthetic depth. [8] Therefore, in our present study we compared the induction and recovery characteristics of these two anaesthetic drugs and their usefulness in ambulatory anaesthesia. Day-care surgery is believed to reduce the average unit cost of treatment by up to 70% as compared to inpatient surgery. With more than 20% of the world's disease burden, India only has 6% of the world's hospital beds. Hence, there is an immense opportunity for expansion in day-care surgery in India to ensure faster and safer, cost- effective patient turnover. [9]

The American Society of Anesthesiologists (ASA) endorses and supports the concept of Ambulatory Anesthesia and Surgery. ASA encourages the anesthesiologist to play a leadership role as the peri-operative physician in all hospitals, ambulatory surgical facilities and office-based settings, and to participate in facility accreditation as a means for standardization and improving the quality of patient care 10. The purpose of this study was to compare and contrast the common properties of “early onset and early offset” of both these drugs and to determine if they had any effect on patient recovery, and ultimately, the length of hospital stay. Tonsillectomy procedures were chosen in our study because tonsillectomy with or without adenoidectomy is a long practiced and one of the most frequently performed surgical procedures in paediatric age group worldwide. [11]

The most common indication for adult tonsillectomy was chronic infection and tonsillar hypertrophy.[12] The surgery is most commonly carried out under General Anaesthesia with a duration usually less than 60 minutes. Hence, daycare tonsillectomy is safe as long as the patient is carefully selected. This was similarly concluded by *Wong HT, Sien Hui T, Chong AW.* in their study. [13] *Anton A. van den Berg, FRCA, Dudley A. Chitty, MD, Ramoun D. Jones, MD, Mir S. Sohel, MD and Ali Shahen, MD* in their audit on preoperative patient preferences for induction of anaesthesia in adults found that 33% selected IV induction, 50% chose inhaled induction and 17% patients were undecided. [14] They conclude that where manpower and facilities permit and in the absence of risk of regurgitation or airway difficulty, it is suggested that enquiry may be made of healthy adults presenting for elective ambulatory surgery as to their preferred route for the induction of anaesthesia. The inhalation induction done in our study was based on the above study.

A. *Thwaites, S. Edmends and I. Smith* in their study of inhalation induction with Sevoflurane versus intravenous induction with Propofol conclude that induction of anaesthesia with Sevoflurane was significantly slower compared with Propofol, but was associated with a lower incidence of apnoea and a shorter time to establish spontaneous ventilation.[15]. The results of our study confirm the slower induction with Sevoflurane. The time to Loss of Consciousness in Sevoflurane group was found to be 74.7 ± 24.0 seconds which is significantly higher than that for Propofol induction (40.1 ± 15.8 seconds) with a p value of <0.0000001. The incidence of apnoea however, was found to be equal in both the groups. This may be attributed to the opioid premedication given as a part of our protocol. *Brain Fredman, MH. Nathanson, I. Smith, J. Wang, K. Klein and PF*. White in their study of Sevoflurane versus Propofol found that intravenous induction was significantly faster than inhalation induction with Sevoflurane and there were no significant difference in the incidence of coughing, airway irritation or laryngospasm during induction of anaesthesia. [16]

In our study, we found that induction with Sevoflurane took longer and was associated with more complications. This is in concurrence with the study done by *W. Scott Jellish, Cynthia A. Lien, H. Jerrel Fontenot, and Richard Hall*, which compared the induction and maintenance of anaesthesia in adult patients with Sevoflurane and Propofol. They found that induction of anaesthesia is shorter with Propofol. And side effects involving airway excitement were more during mask induction with Sevoflurane as compared to Propofol.[17] This explains the greater incidence of desaturation observed in the Sevoflurane group. The patient's movements during intubation were slight movements of the hands or feet which did not compromise tracheal intubation or haemodynamics.The observation of increase in the incidence of patient movement during induction with Sevoflurane is supported by the study done by *J.K. Moore, E.W. Moore, R.A. Elliott, A.S. St. Leger, K. Payne and J. Kerr* on comparing the induction and recovery characteristics of Propofol and Sevoflurane. [18]

Both Propofol and Sevoflurane produce dose dependent depression of ventilation and produce apnoea. Opioids given as premedication enhance this ventilatory depressant effect.This explains the increased and equal incidence of apnoea observed in both groups. Though MAP decreased during induction of anaesthesia

in both groups, the fall in MAP is more with induction of anaesthesia with Propofol. We found that MAP fell by 11.2 ± 1.9 mmHg on induction with Propofol, whereas the fall in MAP was 7.6 ± 5.2 in the Sevoflurane induction group. This finding is also in line with the study by *Bharti N, Chari P, Kumar P* who concluded that Mean Arterial Pressure was better maintained with Sevoflurane compared with Propofol. Though the difference may be of limited significance for healthy patients, it may be advantageous in elderly patients with coronary artery disease.[19]

This finding was also supported by the study of *Husedzinovic et al.* who compared the effect of Sevoflurane and Propofol anesthesia on myocardial contractility using transesophageal echo-Doppler and found that stroke volume was significantly higher in the Sevoflurane than in the Propofol group ($p<0.05$) after induction of anesthesia.[20]. HR increased during induction of anaesthesia in both groups. This was probably due to the administration of Glycopyrrolate prior to induction.The differences in the mean values at induction, post-op and at discharge compared to the pre-operative reference value between the two groups was observed to be statistically significant only at induction and not at other points in time. The occurrence of bradycardia in three patients during induction of anaesthesia with Sevoflurane could be explained by the direct Sevoflurane induced inhibition of the beta adrenoceptor system.

Though statistically not significant, phase I recovery i.e. emergence from anaesthesia is shorter with Sevoflurane than with Propofol. This is in concurrence with the study done by *A. Thwaites, S. Edmends and I. Smith* comparing the induction of anaesthesia and recovery with Sevoflurane and Propofol.[15] In our study, we found that the phase II recovery time after induction and maintenance of anaesthesia with Propofol (106.0 ± 10.7 minutes) and Sevoflurane (101 ± 12.4 minutes) were comparable. This finding concurs with that of *Fredman B, Nathanson MH, Smith I, Wang J, Klein K, White PF.* [16] The same results were obtained in studies involving the Paediatric population. The incidence of postoperative nausea and vomiting was more with Sevoflurane anaesthesia (53.3%) and the number of patients complaining of pain were more with Sevoflurane anaesthesia (36.6%). This observation is supported by the studies done by Brian Fredman et al., [16] Cynthia A Lien et al.,[17] Reader. J et al.,[21] Hanna Viitanen et al.,[22] and V. Picard et al.,[23] The same conclusion was drawn from the meta-analysis by Joo HS, Perks WJ. [24]

PONV is a major cause of patient dissatisfaction with day care surgery. Patients in the Propofol group showed a lower incidence of PONV, a finding supported by the work of Siddik-Sayyid SM et al.[25] This may be related to the “intrinsic” antiemetic property of Propofol. The shorter time for requiring postoperative analgesics in the Sevoflurane group probably reflects its rapid recovery profile and lack of tissue solubility and accumulation. It has been speculated- but not substantiated- that Propofol may have some analgesic effects. Studies have been conducted to explore possible anti-nociceptive mechanisms of Propofol and its potential role as an analgesic clinically. In animal studies, Propofol has been shown to directly depress the dorsal horn neurons in the spinal cord,inhibit the phosphorylation of N-methyl-D- aspartate receptor NR_1 subunit,and inhibit the Cannabinoid CB_1 and CB_2 receptors. In human volunteers, hypnotic doses of Propofol at 3.5 mcg/ml

decreased pain-related regional blood flow to the thalamus and anterior cingulate cortex. Propofol has been shown to be anti-inflammatory, both in vitro and in human studies, which may play an essential role in post-operative analgesia.

Conclusion

On comparing the induction and recovery characteristics of Propofol and Sevoflurane in adult tonsillectomies, it was found that induction with Sevoflurane is slower and with more complications and incidence of apnoea is equal in both groups. Phase I & II recovery times were comparable between both groups Sevoflurane anaesthesia was associated with high PONV and postoperative pain rate, but was not statistically significant.

Limitations of the study

Small sample size, hence the results cannot be generalized for a larger population. As only ASA Grade I and II patients were included in the study, we cannot predict outcomes in patients who are > ASA Grade II. This study did not include extremes of age group. Hence, the outcomes in paediatric and geriatric populations cannot be predicted. End-point of induction was based on clinical observation of the loss of verbal response and not Bispectral Index. The concomitant use of opioid premedication and Nitrous Oxide in the breathing mixture may have contributed to the higher incidence of post-operative nausea and vomiting. The surgical technique was not standardized.

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