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Original Article

Recovery Profile After General Anaesthesia in Paediatric Ambulatory Surgeries: Desflurane Versus Propofol

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Abstract

Objective: Paediatric ambulatory surgeries warrant a speedy recovery of patients without compromising their safety. Short-acting agents such as propofol and desflurane help facilitate these objectives. In this prospective, randomised study we compared the recovery profile in paediatric patients undergoing ambulatory surgeries who received entropy guided general anaesthesia (GA) using desflurane and propofol as maintenance anaesthetics.

Methods: We enrolled 80 children (3-10 years of age), ASA I and II, scheduled for elective surgeries of <60 minutes duration requiring GA between March 2015 and June 2016. We used entropy to monitor adequate depth of anaesthesia and to ensure equipotency of anaesthetic administration in both groups. The state and response entropy was maintained between 40 and 60 by titrating the anaesthetic agents and opioid analgesics. The time of awakening, perioperative haemodynamics, postoperative recovery profile, adverse events and comparative cost of anaesthetic agents were analysed.

Results: The mean heart rate in the desflurane group was significantly higher. There was no difference between the blood pressure, end tidal carbon dioxide, or oxygen saturation in the two groups. There was a trend towards faster awakening, spontaneous respiration and extubation, quicker time to achieve a fast track score >12 and shift out of the post-anaesthesia care unit in the desflurane group, but the difference was not statistically significant. There were no serious adverse events. The mean cost of desflurane was significantly higher than propofol.

Conclusion: Desflurane and propofol provided similar recovery profiles in children receiving GA for ambulatory surgeries. However, propofol was more cost effective compared to desflurane.

Keywords: Desflurane, entropy, paediatric ambulatory surgery, propofol

Introduction

Ambulatory surgeries are on the rise because they decrease the risk of nosocomial infections and are cost effective both for the patient and the health care system. Children are good candidates for such surgeries because they have assured postoperative care providers and are usually bereft of comorbidities. However, paediatric patients are not just small adults, and they are more prone to hypoxia, acidosis, hypercarbia and anaesthetic agent-induced myocardial depression (1). Hence, optimal paediatric anaesthetic regimens are required to allow a clear-headed recovery and to minimise postoperative pain, nausea, vomiting, hospital stay and other adverse events without compromising the safety of these patients.

The short-acting anaesthetic drugs such as propofol, sevoflurane and desflurane have the ability to deliver safe and effective anaesthesia with minimal side effects and a rapid recovery (2, 3). The literature describes faster awakening time with desflurane compared to propofol in adult patients, but it was associated with higher nausea and vomiting (4). Propofol was found to be more expensive than desflurane for maintenance of general anaesthesia (GA) (5, 6). Evidence comparing desflurane to propofol for maintenance regarding recovery characteristics in paediatric patients is scant. There are very few trials comparing anaesthetic agents in the paediatric population with doses titrated according to the depth of anaesthesia, and most of them have used the bispectral index. Recently, entropy has been introduced as a safe and non-invasive technique for measuring the depth of anaesthesia in children above the age of 2 years. This prevents

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drug overdose and facilitates safer and more cost effective anaesthesia practice (7). Volume-controlled ventilation with nitrous oxide in oxygen 60:40 with fresh gas flow 1.5 L min^{-1} was used. Neuromuscular blockade was achieved with atracurium besylate 0.5 mg kg^{-1}, and repeated boluses of 0.1 mg kg^{-1} were given for maintenance of neuromuscular blockade. The patient's lungs were ventilated with a facemask for three minutes to allow for full relaxation of the jaw before introduction of an appropriately sized endotracheal tube. After induction, patients were randomised to either of the two groups as per group allocation:

Group D (desflurane group): GA using desflurane 2%-8% inhalation titrated to entropy values of 40-60.

Group P (propofol group): GA using propofol infusion 100–150 µg kg^{-1} min^{-1} and titrated up and down at 25-50 µg $kg^{-1}min^{-1}$ titrated to entropy values of 40-60.

Ventilation was adjusted to maintain normocarbia (target $ETCO_2$ 35-40 mmHg), and haemodynamics were maintained within 20% of baseline values. Intraoperatively, bolus doses of fentanyl 1-2 µg kg^{-1} were administered if required. All patients received IV paracetamol 15 mg kg^{-1} for analgesia and IV ondansetron 0.1 mg kg^{-1} as antiemetic prophylaxis. Fluid administration was given at maintenance rate after fluid deficit was recovered using Holiday-Segar formula. After completion of surgery, all anaesthetics were stopped and patients received 100% oxygen. Residual neuromuscular blockade was antagonised with neostigmine methyl sulphate 0.05 mg kg^{-1} and glycopyrrolate 0.01 mg kg^{-1}. The trachea was extubated when the patient had adequate ventilation and SE >80. The time of awakening was defined as the time from stoppage of anaesthetics to the time of eye opening. In the post-anaesthesia care unit (PACU), children were assessed for postoperative nausea vomiting (PONV), rescue analgesics and time taken to be ready to discharge. IV dexamethasone 0.1 mg kg^{-1} was given as rescue antiemetic. Pain assessment was done using the Wong-Baker faces score (8). Children reporting a score of 2 or more were given rescue analgesic in the form of IV fentanyl 1-2 µg kg^{-1}. Children were ready to be discharged from the PACU when the Fast track score was >12 (9).

Statistical analysis

The primary variable being compared between the two agents was the time of awakening from discontinuation of anaesthetics. Assuming a 30% difference in awakening time as significant, the sample size calculated per group to achieve a power of 90%, α error of 0.05, and confidence interval of 95% was 38. To compensate for possible dropouts, 40 children were enrolled per group. Secondary variables included haemodynamic variability, cost comparison, and comparison of immediate postoperative complications.

The data were explored for any outliers, typing errors, or missing values. All quantitative variables were estimated using measures of central location (mean, median and mode), measures of dispersion (standard deviation and standard error), and 95% confidence intervals. Normality of the data was checked using graphics (histograms, box and whisker plots, Q-Q plots) and statistically by measures of skewness and kurtosis. The chi-square test was used to determine any statistical association between categorical variables. Student's independent t-test and the Mann-Whitney U test were used to compare various quantitative variables between the two groups. Pearson's correlation coefficients were also calculated between different quantitative variables. All tests were two-tailed, and a p value <0.05 was taken as significant.

Results

Over a period of 15 months (March 2015 to June 2016), 90 children aged 3–10 years were screened. Out of these, 10 children were excluded as per the exclusion criteria (Figure 1). Baseline characteristics were comparable between both groups. There were more boys than girls in both groups because some surgeries such as herniotomies are more commonly done in males. The type of surgery, duration of anaesthesia, and surgical time were comparable in both groups (Table 1).

The baseline heart rates in both the groups were comparable. It was observed that the heart rate of patients in the desflurane group was significantly higher than the propofol group. This difference was witnessed from the time of start of maintenance agent until extubation. The difference in heart rate was statistically significant during the majority of the surgical time (p value between 0.00 and 0.02 for heart rate recorded every 5 minutes for the first 30 minutes) (Figure 2). Other intraoperative parameters including non invasive blood pressure, SpO_2, $ETCO_2$, SE and RE were all comparable.

The time taken for the child to spontaneously open their eyes after stoppage of all anaesthetic agents and delivery of 100% oxygen was 7.61 (SD 3.15) min in the propofol group and 6.36 (SD 2.52) min in the desflurane group. While there was a trend towards shorter awakening time in the desflurane group, it was not statistically significant (p=0.54). There was no statistical difference between the two groups regarding the intraoperative respiratory adverse events (p=0.47). The time to spontaneous respiration, tracheal extubation, time to achieve Fast track score >12, and discharge from PACU were similar in both groups (Table 2).

The intraoperative and postoperative adverse events are shown in Table 3 and were comparable in both groups. None of the children had laryngospasm or airway obstruction. Six

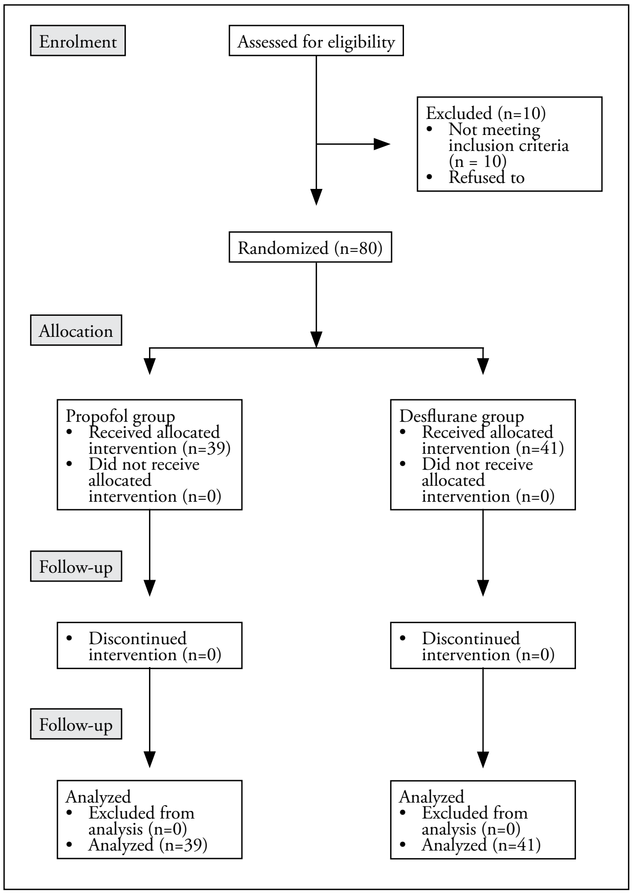

Figure 1. Consort diagram

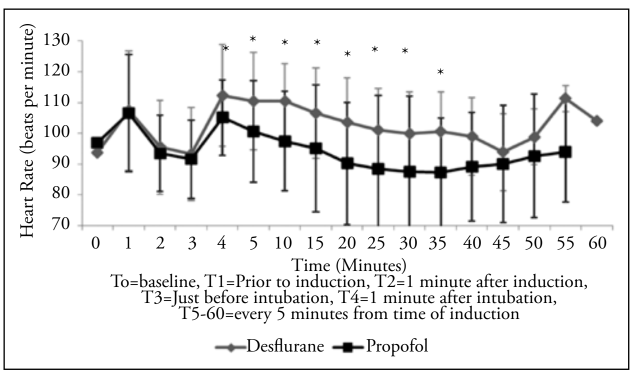

Figure 2. Variation of heart rate in peri-operative period

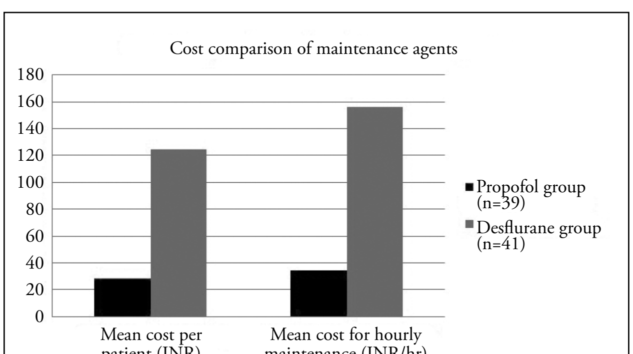

Figure 3. Cost comparison of maintenance agents

Table 1. Demographic characteristics of patients receiving desflurane or propofol during ambulatory surgeries

	Groups		
Characteristics	**Propofol group (n=39)**	**Desflurane group (n=41)**	**p**
Age (yr)	6.69 (2.47)	6.51 (2.21)	0.73
Gender			
Male	28 (71.79%)	27 (65.85%)	0.57
Female	11 (28.2%)	14 (34.15%)	
Weight (kg)	20.17 (7.38)	19.78 (5.69)	0.79
ASA physical status			
ASA I	38 (97.43%)	40 (97.56%)	0.97
ASA II	1 (2.56%)	1 (2.44%)	
Cooperation scale			0.76
1	1 (2.56%)	0	
2	20 (51.28%)	23 (56.1%)	
3	13 (33.33%)	13 (31.7%)	
4	5 (12.82%)	5 (12.19%)	
Types of surgeries			0.67
ENT	4 (10.26%)	7 (17.07%)	
Eye	18 (46.15%)	15 (36.59%)	
General Surgery	14 (9%)	14 (34.15%)	
Orthopaedics	3 (7.69%)	5 (12.19%)	
Duration of anaesthesia (min)	49.28 (12.44)	47.76 (12.12)	0.58
Duration of surgery (min)	35.89 (11.05)	35.73 (10.87)	0.94

Data are presented as mean (SD) or numbers

children had bronchospasm intraoperatively and were managed with metered-dose levosalbutamol and a single dose of intravenous steroid. The pulse oximetry showed oxygen saturation of less than 94% for approximately 10 minutes in three children. All patients had an uneventful tracheal extubation. Six patients in the propofol group and twelve patients in the desflurane group suffered from coughing postoperatively, but this difference was not statistically significant (p=0.14). On shifting patients to the PACU, 14 patients in the propofol group and 17 in the desflurane group had a saturation of less than 90%. Oxygen supplementation was given to all patients, and there were no severe lasting adverse effects. Emergence delirium was assessed using the PAEDS score. The mean PAEDS score was comparable in both groups as were the number of children who required rescue analgesics.

Table 2. Comparison of recovery variables at end of surgery in patients receiving desflurane or propofol during ambulatory surgeries

	Groups		
Variable	**Propofol group (n=39)**	**Desflurane group (n=41)**	**p**
Awakening time (min)	7.61 (3.15)	6.36 (2.52)	0.54
Recovery of spontaneous respiration (min)	6.87 (2.80)	5.97 (2.33)	0.12
Time to extubation (min)	9.28 (3.68)	8.24 (2.68)	0.15
Time to reach Fast track score >12 (min)	16.15 (8.82)	15.48 (8.38)	0.73
Time to discharge from PACU to ward (min)	22.56 (10.87)	20.65 (9.64)	0.41
Children requiring rescue analgesic dose			
Intraoperative	23	26	0.68
Postoperative	10	7	0.35

Data presented as mean (SD) or numbers. PACU: post-anaesthesia care unit

Table 3. Respiratory adverse events in patients receiving desflurane or propofol during ambulatory surgeries

	Groups		
	Propofol group (n=39)	**Desflurane group (n=41)**	**p**
Intraoperative respiratory adverse events			
Bronchospasm	4	2	0.31
O_2 saturation <94%	1	2	0.52
Total children affected	4	3	0.47
Postoperative respiratory adverse events			
Coughing	6	12	0.14
Excessive secretion	3	2	0.60
Bronchospasm	1	1	0.97
SpO_2 < 90%	14	17	0.61
PAEDS score	7.36 (3.81)	6.51 (3.48)	0.45
PONV	0	1	0.32

Data presented as mean (SD) or numbers. PAEDS: Paediatric Anaesthesia Emergence Delirium Score; PONV: postoperative nausea and vomiting

The total cost of anaesthetics in the two groups was calculated by adding the cost of maintenance drug and the rescue analgesics (Table 4, Figure 3). Propofol used in the study was Nirfol 1% (Aculife Healthcare Pvt. Ltd., Sachana, Gujarat, India) at a cost of INR 1.90 per mL. The total cost of propofol incurred in this study was INR 1,026.08. The rescue analgesic used intraoperatively and postoperatively was fentanyl available as Verfen (Verve Healthcare Ltd, Delhi, India). The cost of maintenance was calculated to be INR 34.31 per hour. The total consumption of desflurane was 174.04 mL as calculated by the Dions formula (10). Desflurane is available as Suprane (Baxter Healthcare Corporation, Puerto Rico, USA) containing 240 ml of desflurane and costs INR 28.88 per ml. The total cost of desflurane was INR 5,025.30. The difference between the mean cost per patient and hourly cost was highly statistically significant (p<0.001).

Table 4. Cost analysis of anaesthetics and rescue analgesics

	Groups		
	Propofol group (n=39)	**Desflurane group (n=41)**	**p**
Total drug consumption (mL)	539.90	174.01	
Total cost of drug used (INR)	1026.08	5025.30	
Total rescue analgesic consumption (mL)	28.20	29.09	
Total cost of rescue analgesia (INR)	73.18	75.52	
Total cost of maintenance (INR)	1099.26	5100.81	
Mean cost per patient (INR)	28.19	124.41	<0.001*
Mean cost for hourly maintenance (INR/hour)	34.32	156.31	<0.001*

*Highly significant. INR: Indian rupee

Discussion

The primary objective of the present study was to evaluate the difference in awakening time between children receiving propofol or desflurane as a maintenance agent during GA in short surgical procedures. We found early awakening in children receiving desflurane compared to propofol. However, this difference was not statistically significant. The findings of the present study were similar to the results of Grundmann et al. (11) who found awakening time in desflurane group to be faster than the TIVA group (11 (SD 3.9) min versus 14 (SD 7.6) min).

In a recent meta-analysis of anaesthetics in paediatric anaesthesia, Guo et al. (12) found that desflurane administration was associated with longer time for awakening as compared to propofol, but the difference was not statistically significant (Odds ratio –3.06, 95% confidence interval 7.72-1.50).

These results are, however, derived from indirect evidence because no study included in that analysis had a direct comparison of these two anaesthetic agents. Moreover that analysis included a heterogeneous sample of different age groups as well as types of surgeries.

The heart rate in the desflurane group in our study was higher than the propofol group, and this difference was statistically significant in first 30 minutes of surgery after exposure to the intervention drugs. Pain or light plane of anaesthesia are unlikely causes for this difference because the depth of anaesthesia was monitored using SE and RE. The possible explanation is that desflurane is known to cause a transient increase in myocardial contractility as an effect of increased sympathetic stimulation when its inspired concentrations are increased rapidly (13). No arrhythmias were seen in any patient in either of the two groups. Grundmann et al. (11) compared desflurane and nitrous oxide with propofol and remifentanil (TIVA) for ENT surgeries in children, and they also observed that the desflurane with nitrous oxide group had a significantly higher heart rate intraoperatively compared to the baseline.

The time to spontaneous recovery of respiration was similar between the two groups, with a trend towards faster recovery in the desflurane group. This was similar to Grundmann et al. (11) who found more rapid recovery of respiration in the desflurane and nitrous oxide group compared to the TIVA group. The children in the desflurane group showed a faster time to extubation, though this did not differ significantly from the propofol group. This was similar to the study by Grundmann et al. (11) However, Guo et al. (12) claimed that cases using desflurane had a significantly longer time before extubation than propofol. The difference might be due to heterogeneity of the study population in the meta-analysis.

Both of our groups had a comparable time of achieving a fast track score of >12. There was also no significant difference in duration of stay in the PACU in either group. These results are similar to earlier studies (11, 12). There was no significant difference between both groups for intraoperative and postoperative respiratory adverse events. Six children had bronchospasm post intubation intraoperatively, and they were all transient and resolved upon bronchodilator therapy. The reported incidence of perioperative adverse events ranges from 2.8% to 21% (14, 15). Our study had an incidence of 7.5%, which falls within this range. Contributing factors such as airway surgeries in ENT, passive smoking exposure and a high incidence of undiagnosed atopy present in this part of the country might be present. We thus conclude that both desflurane and propofol may be safely used in children. In a meta-analysis of studies comparing sevoflurane and desflurane for paediatric surgeries, it was found that desflurane had a higher overall incidence for laryngospasm and coughing. However, that study was conducted in subjects who received GA with laryngeal mask airway as compared to the present study where the subjects were intubated with an endotracheal tube. That analysis also stated that it was limited by the presence of an asymmetric funnel plot suggesting the possibility of publication bias (16).

Only one child in the desflurane group had PONV similar to the results of a recent meta-analysis by Guo et al. (12), which showed that anaesthetics used in paediatric anaesthesia had no significant difference with regards to PONV. Postoperative emergence delirium was assessed using the paediatric anaesthesia emergence delirium score (17). There was no difference found between these two groups. According to Guo et al. (12) in the meta-analysis mentioned above, propofol was the best anaesthetic agent to prevent emergence agitation and desflurane had the highest rate of emergence agitation. However it is worth noting that none of the paediatric studies enrolled by the authors in their analysis had a head to head comparison of propofol and desflurane. In the study done by Grundmann et al. (11), there was also a significantly higher incidence of emergence agitation in the desflurane nitrous oxide group compared to the TIVA group (80% vs. 40%). In our study, the age profile, type of surgery, preinduction anxiety score, and pain score in both groups were similar and well controlled. Propofol was given for induction in both groups. Type of surgery, preinduction anxiety, and intraoperative pain have all been implicated as possible risk factors for emergence delirium (18). Control of these factors and well matched groups might have led to a decrease in emergence delirium post exposure to desflurane as compared to other studies. There was no significant difference between the two groups in regards to the postoperative Wong-Baker scores or fentanyl consumption for rescue analgesia.

The cost for consumption of anaesthetic agent used for maintenance and rescue agents used for analgesia, etc., was computed and compared. Because the rescue analgesic between the two groups was comparable, the difference in the costs incurred was primarily due to the maintenance agent. The cost for desflurane was found to be significantly higher than propofol. This is in contrast to the results of Kurpiers et al. (6) who found the mean propofol cost to be $31.88 (SD $14.44) compared to the mean desflurane cost of $12.99 (SD $7.61) ($p<0.05$) in 53 ASA I patients. This difference could be due to the difference in costs of the anaesthetic agents in different countries.

One of the strengths of our study was that we used entropy to monitor adequate depth of anaesthesia and to ensure the equipotency of anaesthetic administration in both groups. The state and response entropy was maintained between 40 and 60 by titrating anaesthetic agents and opioid analgesics.

Measurement of SE and RE are non invasive, objective parameters for titration of doses of anaesthetic agents to optimal levels. Studies done in children from the age of 2 years and above show that entropy correlates well with depth of anaesthesia, but a search of the available literature did not reveal any study in children while monitoring depth of anaesthesia (entropy guided) using these agents. Most studies have followed a symptom management approach to add opioids; for example, Grundmann et al. (11) used remifentanil when a 30% increase in haemodynamic parameters, movement, or sweating was observed in children. Second, we used fentanyl in both groups, both for preinduction analgesia as well as for rescue analgesia. Thus the groups in our study were well matched. Third we used fast track score to assess fitness for discharge from PACU, which has been designed specifically for ambulatory surgeries.

Study limitations

Our study has several limitations. First, we did not include very small children such as neonates and infants who might have a different response to the anaesthetic agents due to the constantly evolving physiology in the paediatric age group. Second, we only included ASA PS I and II patients. Sicker children might have different outcomes, but they are less likely to undergo ambulatory surgeries. Third, we only analysed short procedures of 60 minutes or less. The duration of surgery might impact the speed of recovery due to longer exposure time to the anaesthetic drugs. Fourth, the time to shift the child from the PACU was observed, but the actual time of discharge of the patient from the hospital was not evaluated. Finally, a larger sample size might be required to evaluate the clinical significance of respiratory and other rare adverse events.

Conclusion

Desflurane and propofol provided similar recovery profiles in ASA PS I and II children receiving GA for ambulatory surgeries. However, propofol was more cost effective compared to desflurane.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Government Medical College and Hospital (08.12.2014).

Informed Consent: Written informed consent was obtained from patients' parents who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - S.G., V.A., A.J.; Design - S.G., V.A., A.J.; Supervision - S.G., V.A.; Data Collection and/or Processing - A.J.; Analysis and/or Interpretation - S.G., V.A., A.J.; Literature Search - V.A., A.J.; Writing Manuscript - V.A., A.J.; Critical Review - S.G., V.A., A.J.

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