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Original Research Article

THE EFFECT OF DEXMEDETOMIDINE AND PROPOFOL ON SEVOFLURANE RELATED EMERGENCE DELIRIUM IN CHILDREN UNDERGOING ADENOTONSILLECTOMY

Manasa.G.[1], Darshan M. S.[2], Sridevi S.[3]

[1]Assistant Professor, Department of Anaesthesiology, Chamarajnagar Institute of Medical Sciences, Karnataka, India.
[2]Associate Professor, Department of Anaesthesiology, Chamarajnagar Institute of Medical Sciences, Karnataka, India.
[3]Associate Professor, Department of Anaesthesiology, Chamarajnagar Institute of Medical Sciences, Karnataka, India.

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Corresponding Author:
Dr. Manasa.G.,
Assistant Professor, Department of Anaesthesiology, Chamarajnagar Institute of Medical Sciences, Karnataka, India.
Email: manasagopal555@gmail.com

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ABSTRACT

Background: The occurrence of emergence delirium in children after sevoflurane anaesthesia is common, with a reported incidence up to 80%1. In children sevoflurane is associated with delirium upon recovery from anaesthesia, cause is not clear. It is called emergence delirium or emergence agitation. This is usually seen in first thirty minutes, but this short term episode can cause harm to patient or damage to surgical site and dissatisfaction to parent. This study was conducted to compare the effect of dexmedetomidine and propofol for preventing the emergence delirium in paediatric patients undergoing adenotonsillectomy under general anaesthesia.
Aim and objective: To compare the effect of dexmedetomidine and propofol in prevention of emergence delirium in paediatric patients undergoing adenotonsillectomy under general anaesthesia.
Materials and Methods: This was a prospective comparative study conducted in a tertiary care hospital among the 70 pediatric patients. American Society of Anesthesiologists (ASA) grade 1 and 2 patients undergoing elective adenotonsillectomy surgeries and receiving general anesthesia were included in this study. The incidence of emergence delirium (ED) was evaluated using Aono's four point scale. The effect of dexmedetomidine and propofol in prevention of emergence delirium was evaluated. The severity of ED was evaluated using paediatric anesthesia emergence delirium (PAED) scale. The incidence and severity of ED were measured at different time intervals. Both pulse and MAP were recorded at PACU on arrival, then at 5mins and 10 minutes then every ten minutes until the patients were discharged to ward. The duration of surgery, duration of sevoflurane anesthesia and duration of extubation assessed. Data was analyzed by descriptive statistics and chi-square test.
Results: Among total 70 patients, the Aono's four point scale score was 1 for 34 (48.6%) of the patients of which 20 (58.8%) were in Dexmedetomidine group and 14 (41.2) in Propofol group. Pediatric anesthesia emergence delirium (PAED) scale score was 6 among the 24 (34.3%) patients immediately after surgery. At 5 minutes, 25 (35.7%) of the patients showed PAED scale score 6. At 30 minutes, 6 (8.6%) of the patients showed PAED scale score 6. The time taken extubation was less in Dexmedetomidine group as compared that in Propofol group.
Conclusion: Dexmedetomidine is effective in reducing the emergence delirium (ED) in the patients underwent adenotonsillectomy with sevoflurane anesthesia.
Keywords: Dexmedetomidine, Propofol, Sevoflurane, adenotonsillectomy, Emergence delirium.

INTRODUCTION

The occurrence of emergence delirium in children after sevoflurane anaesthesia is common, with a reported incidence up to 80%.[1] Sevoflurane is a fluoromethyl trifluoro-1-ethyl ether. It is a clear, colourless volatile, nonirritating liquid widely used in day care surgery particularly in paediatric surgery because of its rapid recovery and non irritation to airway. But in children sevoflurane is associated with delirium upon recovery from anaesthesia, cause is not clear. It is called emergence delirium or emergence agitation.[2]

Emergence delirium is characterised by a period of restlessness, agitation, inconsolable crying, disorientation, delusion, hallucination and cognitive changes with memory impairment.[3] This is usually seen in first thirty minutes and it is self limiting, without any long term sequelae.[2]

But this short term episode can cause harm to patient or damage to surgical site and dissatisfaction to parent. Various drugs have been evaluated for reducing this episode i.e. ketorolac, clonidine, midazolam, ketamine, propofol and α adrenoreceptor agonists.

Propofol is an intravenous anaesthetic agent administered as a 1% solution. It is believed to exert its sedative-hypnotic effects through γ-Aminobutyric acid type A (GABA A) receptor interaction. The quick recovery without residual sedation and low incidence of nausea and vomiting make propofol suitable for ambulatory conscious sedation techniques. Propofol also reduces postoperative sevoflurane-related ED.[4]

Dexmedetomidine is a potent, selective α2 adrenergic agonist. It can affect the brain and spinal cord α2 adrenergic receptor, inhibition of neural discharge to produce sedative, analgesic and anxiolytic effects. The Locus Coeruleus is a verified key part of the brain responsible for the regulation of arousal and sleep. Dexmedetomidine affects the brainstem locus coeruleus α 2-adrenergic receptors and produces sedative, hypnotic, and anxiolytic effects and it has also anesthetic-sparing effects without significant respiratory depression.[5]

The aim of the study is to compare dexmedetomidine and propofol in prevention of emergence delirium in pediatric patients undergoing adenotonsillectomy under general anaesthesia.

MATERIALS AND METHODS

This wass a prospective comparative study, after approval of the research protocol by the hospital ethics committee for human studies and obtaining written informed consent from patients guardians, American Society of Anesthesiologists(ASA)grade 1 and 2 patients undergoing elective adenotonsillectomy surgeries and receiving general anesthesia were included in this study. Exclusion criteria were patients who had allergy to study medications, developmental delay, mental retardation, attention deficit hyperactive disorders, use of psychiatric medications, liver, renal, cardiac or respiratory diseases. Patients were then randomly divided in two groups, group D, is a dexmedetomidine group and group P, is a propofol group.

All patients were subjected to a routine pre anaesthetic check up. On the day of surgery, all children were kept nil per oral according to ISA guidelines. In the operating room, after attaching all standard ASA monitors baseline HR, blood pressure, SpO_2 and respiratory rate were noted. General anesthesia was induced with Midazolam 0.04mg/kg, fentanyl 2mcg/kg, glycopyrrolate 0.004mg/kg and a dose of 2mg/kg propofol intravenous. An intubating dose of atracurium 0.5mg/kg was injected to all patients for muscle relaxation and oral endotracheal intubation is performed. Anaesthesia was maintained with 50% nitrous oxide and 1-2% sevoflurane. Paracetamol 15mg/kg I.V. was administered over the span of 15mins.

Just 10 min before surgery patients in group P was received propofol 1mg/kg IV and group D was received dexmedetomidine 0.3mcg/kg diluted in 10ml NaCl 0.9%. After completion of procedure sevoflurane was replaced by 100% oxygen. Muscle relaxation was reversed with neostigmine 0.05mg/kg iv and glycopyrrolate 0.01mg/kg iv. Extubation was performed when the patients gag reflex was restored and they showed facial grimaces or purposeful appearing motor movements. Children were transferred to the post operative recovery room.

The incidence of emergence delirium (ED) was evaluated using Aono's four point scale; 1=calm; 2=not calm but could be easily consoled; 3=moderately agitated or restless and not easily calmed; 4=combative, excited, or disoriented, thrashing around. Scores of one and two are considered as absence of ED, and scores of three and four are analyzed as presence of ED. The severity of ED was evaluated using pediatric anesthesia emergence delirium (PAED) scale devised by Sikich et al.[3] [Table1], a five‑point rating scale with five grades for each item.

The incidence and severity of ED were measured upon admission to the PACU (T0) and in the PACU at 5 min (T5), at 15 min (T15) and at 30 min (T30). Children were considered severely agitated if they had a PAED scale of 15/20 or higher. Postoperative pain was assessed using objective pain score [table 2]. The observer scored pain every 5 min(none/insignificant pain 1-3, moderate pain 4-6, severe pain 7-10).[6] Patients with pain score 4 were treated with additional dose of fentanyl.

Both pulse and MAP were recorded at PACU on arrival, then at 5mins and 10 mins, then every ten mins until the patients were discharged to ward. The incidence of adverse events such as hypotension,

bradycardia, laryngospasm, bronchospasm and oxygen desaturation, were noted.

The following time intervals were recorded: The duration of surgery (from the time of mouth opening to the completion of the procedure), duration of sevoflurane anesthesia(from mask induction to the discontinuation of the inhaled anesthetic), duration of extubation (from the discontinuation of sevoflurane to the removal of endotracheal tube), time of emergence (from discontinuation of sevoflurane to the first response to a simple verbal command).

Table 1: Pediatric anesthesia emergence delirium

Behavior	Not at all	Just a little	Quite a bit	Very much	Extremely
Make eye contact with caregiver	4	3	2	1	0
Actions are purposeful	4	3	2	1	0
Aware of surrounding	4	3	2	1	0
Restless	0	1	2	3	4
Inconsolable	0	1	2	3	4

Table 2: Objective pain scale for postoperative pain

Parameter	Finding	Point
Systolic blood pressure	Increase <20% of preoperative blood pressure	0
	Increase 20–30% of preoperative blood pressure	1
	Increase>30% of preoperative blood pressure	2
Crying	Not crying	0
	Responds to age-appropriate nurturing (tender loving care)	1
	Does not respond to nurturing	2
Movements	No movements relaxed	0
	Restless (moving about in bed constantly)	1
	Thrashing (moving wildly)	2
	Rigid (stiff)	2
Agitation	Asleep or calm	0
	Can be comforted to lessen the agitation (mild)	1
	Cannot be comforted (hysterical)	2
Complains of pain	Asleep	0
	States no pain	0
	Cannot localize	1
	Localizes pain	2

RESULTS

This study was conducted among the 70 children undergoing adenotonsillectomy. These 70 patients were randomly allocated in to dexmedetomidine group (35 patients) and Propofol group (35 patients).

Table 1: Age group wise distribution of children underwent adenotonsillectomy (N=70)

Age group (In years)	Children underwent adenotonsillectomy		Total (%)
	Dexmedetomidine group (%)	Propofol group (%)	
6 to 8 years	8 (47)	9 (53)	17 (24.3)
9 to 11 years	15 (48.4)	16 (51.6)	31 (44.3)
12 to 14 years	12 (54.5)	10 (45.5)	22 (31.4)
Total	**35**	**35**	**70**

Table 2: Duration of adenotonsillectomy surgery in Dexmedetomidine group and Propofol group (N=70)

Duration of surgery (hours)	Children underwent adenotonsillectomy		Total (%)
	Dexmedetomidine group (%)	Propofol group (%)	
1 hour	15 (50)	15 (50)	30 (42.8)
1hour 10minutes	0	2 (100)	2 (2.8)
1hour 15minutes	9 (47.4)	10 (52.6)	19 (27.2)
1hour 20minutes	6 (46.1)	7 (53.9)	13 (18.6)
1hour 30minutes	5 (83.3)	1 (16.7)	6 (8.6)
Total	**35**	**35**	**70**

Table 3: Duration of sevoflurane administration among the Dexmedetomidine group and Propofol group during the adenotonsillectomy surgery in children (N=70)

Duration of sevoflurane administration	Children underwent adenotonsillectomy		Total (%)
	Dexmedetomidine group (%)	Propofol group (%)	
1 hour 5 minutes	15 (50)	15 (50)	30 (42.8)
1 hour 15 minutes	0	2 (100)	2 (2.8)
1 hour 20minutes	9 (47.4)	10 (52.6)	19 (27.2)
1 hour 25minutes	6 (46.1)	7 (53.9)	13 (18.7)
1 hour 35minutes	5 (83.3)	1 (16.7)	6 (8.5)
Total	**35**	**35**	**70**

Table 4: Duration of extubation time among the Dexmedetomidine group and Propofol groups of the adenotonsillectomy surgery in children (N=70)

Duration of extubation (minutes)	Children underwent adenotonsillectomy		Total (%)
	Dexmedetomidine group (%)	Propofol group (%)	
2	6 (66.7)	3 (33.3)	9 (12.8)
3	22 (50)	22 (50)	44 (62.9)
4	7 (41.2)	10 (58.8)	17 (24.3)
Total	**35**	**35**	**70**

Table 5: Assessment of emergence delirium (ED) using Aono's four point scale

Aono's four point scale	Children underwent adenotonsillectomy		Total (%)	p value
	Dexmedetomidine group (%)	Propofol group (%)		
1	20 (58.8)	14 (41.2)	34 (48.6)	0.151
2	15 (41.6)	21 (58.4)	36 (51.4)	
Total	**35**	**35**	**70**	

Note: Aono's four point scale; 1=calm; 2=not calm but could be easily consoled; 3=moderately agitated or restless; 4=combative, excited, or disoriented, thrashing around.

Among total 70 patients, the Aono's four point scale score was 1 for 34 (48.6%) of the patients of which 20 (58.8%) were in Dexmedetomidine group and 14 (41.2) in Propofol group. The scores of one and two are considered as absence of emergence delirium (ED), and scores of three and four are analyzed as presence of emergence delirium (ED). [Table 5]

Table 6: Assessment of emergence delirium using Pediatric anesthesia emergence delirium (PAED) scale among the children in Dexmedetomidine group and Propofol group (N=70)

Time period	PAED scale score	Children underwent adenotonsillectomy		Total (%)	p value
		Dexmedetomidine group (%)	Propofol group (%)		
Immediately after surgery	4	4 (50)	4 (50)	8 (11.4)	0.157
	5	12 (70.8)	5 (29.2)	17 (24.3)	
	6	12 (50)	12 (50)	24 (34.3)	
	7	7 (33.3)	14 (66.7)	21 (30)	
At 5minutes	4	5 (62.5)	3 (37.5)	8 (11.5)	0.825
	5	12 (52.2)	11 (47.8)	23 (32.8)	
	6	11 (44)	14 (56)	25 (35.7)	
	7	7 (50)	7 (50)	14 (20)	
At 15minutes	4	4 (44.5)	5 (55.5)	9 (12.8)	0.757
	5	11 (52.4)	10 (47.6)	21 (30)	
	6	15 (55.5)	12 (44.5)	27 (38.6)	
	7	5 (38.5)	8 (61.5)	13 (18.6)	
At 30 minutes	4	4 (66.7)	2 (33.3)	6 (8.6)	0.636
	5	13 (56.5)	10 (43.5)	23 (32.8)	
	6	12 (42.8)	16 (57.2)	28 (40)	
	7	6 (46.1)	7 (53.9)	13 (18.6)	

Among total 70 patients, Pediatric anesthesia emergence delirium (PAED) scale score was 6 among the 24 (34.3%) patients immediately after surgery. at 5 minutes, 25 (35.7%) of the patients showed PAED scale score 6. At 30 minutes, 6 (8.6%) of the patients showed PAED scale score 6. [Table 6]

Table 7: Means of mean arterial pressure (MAP) of the patients during intra-operative and post operative period of adenotonsillectomy (N=70)

Time intervals of intra-operative and post operative period	Means of mean arterial pressure (MAP) of the patients	
	Dexmedetomidine group (mean ± SD)	Propofol group (mean ± SD)
Baseline	72.29 ±3.40	71.86 ± 3.06
After anesthesia block	68.57 ±1.92	71.11 ±3.25
Post operative at 5 minutes	68.23 ±1.47	70.86 ± 1.28
Post operative at 15 minutes	68.34 ±1.64	70.54 ±2.24
Post operative at 30 minutes	68.29 ± 1.65	70.46 ± 2.92

Table 8: Means of heart rate (HR) of the patients during intra-operative and post operative period of adenotonsillectomy (N=70)

Time intervals of intra-operative and post operative period	Means of heart rate (HR) of the patients	
	Dexmedetomidine group (mean + SD)	Propofol group (mean + SD)
Baseline	121.03 ± 8.86	122.31 ±7.82
After anesthesia block	91.60± 4.44	110.60 ±8.03
Post operative at 5 minutes	93.31± 4.41	108.74 ±7.60
Post operative at 15 minutes	95.80±3.38	110.03 ±8.09
Post operative at 30 minutes	103.83± 4.01	108.80 ± 6.53

Table 10: Assessment of pain intensity using objective pain scoring scale among the post operative adenotonsillectomy patients (N=70)

Time period	Pain intensity (Objective pain scoring scale)	Children underwent adenotonsillectomy		Total (%)	p value
		Dexmedetomidine group (%)	Propofol group (%)		
Immediately after surgery	Mild pain	35 (81.4)	8 (18.6)	43 (61.4)	0.001
	Moderate pain	0	27 (100)	27 (28.6)	
At 5 minutes	Mild pain	35 (92.1)	3 (7.9)	38 (54.3)	0.001
	Moderate pain	0	32 (100)	32 (45.7)	
At 15 minutes	Mild pain	29 (100)	0	29 (41.4)	0.001
	Moderate pain	6 (14.6)	35 (85.4)	41 (58.6)	
At 30 minutes	Mild pain	27 (100)	0	27 (38.6)	0.001
	Moderate pain	8 (18.6)	35 (81.4)	43 (61.4)	

Note: Fisher's Exact Test: expected count less than 5 in one or more cells. Objective pain scoring scale: score 1 to 3= mild or insignificant pain; 4 to 6= moderate pain; 7 to 10= severe pain. In this study no patients had experience sever pain in the post operative time period.

Immediately after surgery, 43 (61.4%) of the patients experienced mild pain and 27 (28.6%) patients experienced moderate pain among which, all the patients from Propofol group. At post operative 15 minutes, 29 (41.4%) developed mild pain and all 29 patients from Dexmedetomidine group. At post operative 30 minutes, 43 (61.4%) patients experienced moderate pain among which, 8 (18.6%) patients from Dexmedetomidine group and 35 (81.4%) patients from Propofol group. the difference of the occurrence of the post operative pain between these two groups was found statistically significant ($p<0.001$). [Table 9]

DISCUSSION

This study was conducted among the 70 children undergoing adenotonsillectomy. These 70 patients were randomly allocated in to dexmedetomidine group (35 patients) and Propofol group (35 patients). The mean age (mean ± standard deviation) of the total 70 patients was 10.31 ± 2.14. The age groups are equally distributed in to Dexmedetomidine group and Propofol group. Vettuvanthodi, T. et. Al,[5] conducted a randomized Clinical Study in which the mean age of the patients in group sevoflurane -dexmedetomidine (SD) was 4.19±0.78 years, and in group sevoflurane – propofol (SP) was 4.03±0.71 years. Both the groups were found to be comparable in terms of patient characteristics such as age, sex, weight, and duration of surgery.

In our study, among the total 70 patients, the time taken for extubation of the patients was 3 minutes among the 44 (62.9%) patients in which 22 (50%) were in Dexmedetomidine group and 22 (50%) were in Propofol group. According to the study conducted by Vettuvanthodi, T. et. Al[5] the significantly prolonged extubation times observed in the propofol group did not result in significantly longer stays in the Post Anaesthesia Care Unit (PACU). A study conducted by Soliman, R. et.al,[7] found that Dexmedetomidine decreased significantly the incidence of agitation with sevoflurane in pediatric patients undergoing adenotonsillectomy and it was associated with a shorter time to extubation , lower incidence of postoperative nausea and vomiting and shorter post-anesthesia care unit length of stay. Extubation time was not different between groups as per the study conducted by Tsiotou, A. G et. al.[10]

In our study, among total 70 patients, the Aono's four point scale score was 1 for 34 (48.6%) of the patients of which 20 (58.8%) were in Dexmedetomidine group and 14 (41.2) in Propofol group. Among total 70 patients, Pediatric anesthesia emergence delirium (PAED) scale score was 6 among the 24 (34.3%) patients immediately after surgery. at 5 minutes, 25 (35.7%) of the patients showed PAED scale score 6. At 30 minutes, 6 (8.6%) of the patients showed PAED scale score 6. A study done by Ali et.al,[6] found that the incidence and severity of EA decreased significantly over time in all groups. The modified Children's Hospital of Eastern Ontario Pain Scale was significantly lower in dexmedetomidine group (group D) compared to control group (group C) and propofol group (group P).

Our study found that, at-post operative 30 minutes, the means of mean arterial pressure (MAP) were 68.29 $\pm$ 1.65 and 70.46 $\pm$ 2.92 for Dexmedetomidine group and Propofol group respectively. There is no significant change in the Means of mean arterial pressure (MAP) of the patients in the post-operative period. At post operative 30 minutes, the Means of heart rate (HR) were 103.83$\pm$ 4.01 and 108.80$\pm$ 6.53 for Dexmedetomidine group and Propofol group respectively. As the post operative period progresses from 5 minutes to 30 minutes, the mean heart rate (HR) increases to attain the normal values as in the base line readings. A study conducted by Vettuvanthodi, T. et. Al,[5] showed that there was minimal haemodynamic effects and no clinically relevant severe adverse effects in both the groups. In a study conducted by Amer. G. F. at. Al,[9] the dexmedetomidine group expressed a significant decrease in most heart rate and arterial pressure measurements. A study conducted by Huang, L et. al.[13] showed that, the value of heart rate and mean arterial pressure during emergence in Propofol group (group P) and group C were significantly ($P < 0.05$) higher than that in dexmedetomidine group (group D).

According to our study finding, at-post operative 30 minutes, 43 (61.4%) patients experienced moderate pain among which, 8 (18.6%) patients from Dexmedetomidine group and 35 (81.4%) patients from Propofol group. The difference of the occurrence of the post operative pain between these two groups was found statistically significant ($p<0.001$). Vettuvanthodi, T. et. Al,[5] showed that Dexmedetomidine was more effective than propofol in reducing the incidence and severity of EA associated with sevoflurane anaesthesia. According to the study conducted by Ali et.al,[6] dexmedetomidine was more effective than propofol in decreasing the incidence and severity of EA, when administered 5 min before the end of surgery in children undergoing adenotonsillectomy under sevoflurane anesthesia. Randomized controlled trial conducted by Amer, G. F. et. Al,[9] Emergence delirium (ED) was encountered in 5% and 27.5% of patients in the dexmedetomidine and Propofol groups respectively with significant decline in the association with dexmedetomidine. Delirium and pain scores were significantly decreased in the dexmedetomidine group throughout all times of measurements. The occurrence of the emergence delirium was less in dexmedetomidine group than in propofol group.

Sato, M. et. Al,[14] showed that, the mean pain scales in the dexmedetomidine group were significantly lower than in the saline group during the stay in the post-anesthesia care unit (PACU) ($P < 0.01$). Lee et. Al,[15] conducted a study showed that, the incidence and severity of emergence agitation (EA) were not found to be significantly different between the propofol group and saline group, but the scales in each group decreased significantly over time and it also found that, the administration of propofol 1 mg/kg at the end of surgery did not have any significant effect in reducing the incidence and severity of EA in children undergoing adenotonsillectomy under sevoflurane anesthesia.

CONCLUSION

Dexmedetomidine is effective in reducing the emergence delirium (ED) in the patients underwent adenotonsillectomy with sevoflurane anesthesia.

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