Section: Anaesthesiology

Original Research Article

COMPARISON OF TWO GABAPENTIN PREMEDICATION DOSES ON EMERGENCE AGITATION AND POSTOPERATIVE PAIN IN CHILDREN: A RANDOMIZED CONTROLLED TRIAL

Sateesh Verma[1], Ankur Choukan[2], Manoj Chaurasiya[3], Jyotsna Agrawal[4], Sarita Singh[5]

[1]Additional Professor, Department of Anaesthesiology, King George's Medical University, Lucknow, Uttar Pradesh, India.
[2]Ex Senior Resident, Department of Anaesthesiology, King George's Medical University, Lucknow, Uttar Pradesh, India.
[3]Associate Professor, Department of Anaesthesiology, King George's Medical University, Lucknow, Uttar Pradesh, India.
[4]Ex Professor, Department of Anaesthesiology, King George's Medical University, Lucknow, Uttar Pradesh, India.
[5]Professor, Department of Anaesthesiology, King George's Medical University, Lucknow, Uttar Pradesh, India.

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Corresponding Author:
Dr. Sateesh Verma,
Email: sateeshverma24@gmail.com

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ABSTRACT

Background: Postoperative emergence agitation (EA) is a common problem in paediatric patients recovering from general anaesthesia. Primary objective study of this was to measure effect of two different doses of gabapentin premedication on postoperative delirium in children after general anesthesia. Secondary objectives were to evaluate effect of gabapentin on postoperative pain, emergence time and hemodynamic parameters. **Materials and Methods:** A total of 96 pediatric patients were randomly divided into three groups: group-A received oral gabapentin 5mg/kg dose, group-B received oral gabapentin 10mg/kg dose, and group-C received 5ml placebo syrup two hours before surgery. In early postoperative period, we evaluated emergence agitation using the pediatric anaesthesia emergence delirium (PAED) scale and WATCHA scale and also assessed postoperative pain using the FLACC scale. **Result:** Group B (gabapentin 10mg/kg) reported lowest PAED and WATCHA agitation scores recorded at 5, 10, 20, 40, 60 minutes postoperatively after extubation. Emergence time were higher in patient given gabapentin (473 second in group B and 329 second in group C). Extubation time was also higher in patient given gabapentin (376 second in group B and 286 second in group C) However, FLACC pain score were comparable in all three groups. Intraoperative heart rate and systolic blood pressure were also similar in all three groups. **Conclusion:** Gabapentin in a dose of 10mg/kg was more effective in reducing emergence agitation score. Although it was associated with some increase in emergence time and extubation time which was clinically insignificant.

INTRODUCTION

Emergence agitation is a common and significant problem for children waking up from general anesthesia. It is a state of confusion where the child becomes irritable, uncooperative, and cries inconsolably.[1] This condition is far more frequent in children—occurring two to three times more often than in adults. Symptoms usually appear right after the anesthetic wears off and last for about 15-30 minutes.[2] Notably, sevoflurane, one of the most common anesthetics for children, is a major contributor to this high rate of postoperative agitation.

While various pharmacological agents, including opioids, benzodiazepines, and alpha-2 agonists, have been used to manage emergence agitation, their efficacy is inconsistent and often accompanied by undesirable side effects.[3-7] Gabapentin, a structural analogue of gamma-aminobutyric acid (GABA), has emerged as a promising alternative. It acts by binding to the alpha-2-delta subunit of voltage-gated calcium channels, which inhibits the release of excitatory neurotransmitters.[8] This mechanism provides both analgesic and anxiolytic effects, making gabapentin a compelling option for preventing postoperative pain and agitation with a more favorable side-effect profile than traditional agents. Supporting this, studies have shown that gabapentin premedication

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effectively attenuates emergence agitation and reduces 24-hour analgesic requirements following sevoflurane anesthesia.[9]

The primary aim of this study was to compare the efficacy of two different doses of gabapentin premedication on reducing emergence agitation, as assessed by the PAED and WATCHA scales. Secondary objectives included the evaluation of postoperative pain scores using the FLACC scale, recovery characteristics such as time to emergence, time to extubation, intraoperative hemodynamic stability, and the incidence of any adverse events.

MATERIALS AND METHODS

Study design and patient inclusion criteria: Our prospective, randomized, comparative study, approved by institutional ethical Committee with approval number (956/Ethics/2020). It was conducted at a tertiary health care centre in India.

It involved 96 paediatric patients aged 3-10 years with ASA physical status I and II, who were scheduled for elective urogenital surgeries like hypospadias repair, herniotomy and orchiopexy. Exclusions criteria were patients with mental retardation, developmental delay, epilepsy, psychiatric or neurological diseases, current use of gabapentin and psychotropic drugs, and those with liver and/or kidney diseases or hypersensitivity to drugs.

Randomization, concealment and group allocation: Statistician generated random number sequence by using the RAND function in Microsoft Excel (version 2010, Microsoft Corp.) and it was used to randomize the recruited patients into one of three groups with a 1:1:1 allocation ratio.

The randomization results were kept in sealed envelopes for concealment and were opened at morning of planned surgery. Healthcare personal who opened sealed envelope and given drug to child in form of syrup was not involved with data collection and data analysis. Both the patient and the attending anesthesiologist responsible for data collection were blinded to the nature of drug intervention.

Based on group allocation, patients received following intervention- Group A: oral gabapentin 5mg/kg mixed in 5ml multivitamin syrup, Group B: oral gabapentin 10mg/kg mixed in 5ml multivitamin syrup or Group C: received 5ml of multivitamin syrup without gabapentin 2 hours before surgery.

Anaesthesia and intraoperative management: In the operating theatre, standard monitor including ECG, non-invasive blood pressure, pulse oximetry was used. Inhalational induction was started with 8% sevoflurane in oxygen, once child was sedated intravenous access was secured. After that intravenous fentanyl 2 microgram/kg and atracurium 0.6 mg/kg were administered, and after 4 minutes, endotracheal intubation was done with direct laryngoscopy. Anaesthesia was maintained with sevoflurane (titrated approximately 1 mac) in O2 and air, along with injection atracurium 0.1 mg/kg boluses and fentanyl 1 microgram/kg boluses. We also administered intravenous paracetamol 15mg/kg for pain management intraoperatively as well as postoperatively. After surgery was completed, the inhalational anaesthetic agent was closed. Once patients started making spontaneous breathing efforts, neostigmine in dose of 0.05mg/kg and glycopyrrolate in dose of 0.005mg/kg was given for reversal. Patients were extubated once they demonstrated adequate respiratory effort and protective airway reflexes. For post-operative pain management, intravenous paracetamol at a dose of 15mg/kg was administered every 6 hours, and tramadol was given at 1mg/kg every 12 hours. We assessed emergence agitation using the paediatric anaesthesia emergence delirium (PAED) scale and WATCHA score at 5, 10, 20, 40, 60 minutes after extubation. Pain assessment was conducted using the FLACC scale at the 2 hours, 6 hours, 12 hours, 18 hours, and 24 hours post-extubation.

Sample size estimation and statistical analysis: Sample size estimation was based on a previous study by Salman AE et al.[10] Its calculation was done by assuming 0.05 level significance, and 80% power of study. Obtained numbers were rounded to 32 patients in each group.

All collected data were analysed with help of SPSS software (version 20.0, SPSS Inc., USA). The findings were expressed as mean (SD) or percentages. Chi-square statistical analysis was done for categorical data, and for continuous data student's t-test and Kruskal-Wallis Test were performed. The ANOVA test was used to compare the within group and between group variances amongst the study groups.

RESULTS

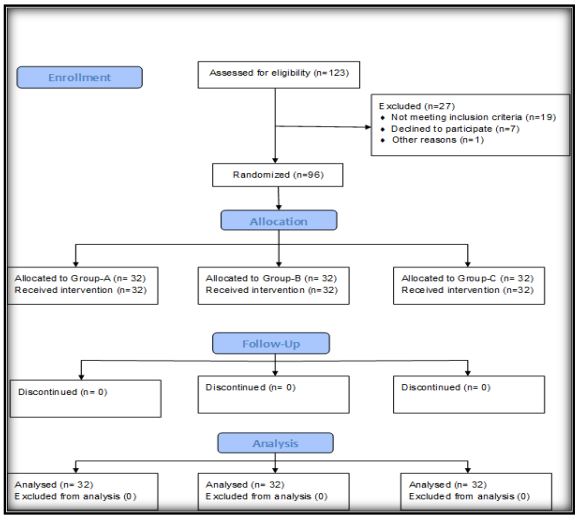

Figure 1: CONSORT flow diagram of study participants

In our study, 123 paediatric patients were assessed for eligibility and 27 were excluded based on

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inclusion/exclusion criteria. Thus 96 patients were enrolled and randomised equally in three groups as shown in [Figure 1].

All three group were comparable for age, gender and weight. Mean age in group A was 4.87±1.69 years, in group B was 4.76±1.87 years and in group C it was 5.72±2.20 years. Mean weight in group A was 16.41±5.06 kg, in group B 14.52±4.25 kg and group C it was 17.03±4.78 kg as shown in [Table 1].

Table 1: Demographic parameters of enrolled children.

Demographic parameters	Group A (n=32)	Group B (n=32)	Group C (n=32)	P-value
Age in years n (%)				
Mean±SD	4.87±1.69	4.76±1.87	5.72±2.20	F=3.65, p=0.098
<5 year	16 (50.0%)	19 (59.4%)	13 (40.6%)	$\chi2$=3.747, p=0.441
5-7 year	13 (40.6%)	9 (28.1%)	12 (37.5%)	
>7 year	3 (9.4%)	4 (12.5%)	7 (21.9%)	
Gender n (%)				
Female	13 (40.6%)	11(34.4%)	9 (28.1%)	$\chi2$=3.747, p=0.441
Male	19 (59.4%)	21 (65.6%)	23 (71.9%)	
Weight	16.41±5.06	14.52±4.25	17.03±4.78	F= 2.477, p= 0.090

Extubation time in group B was 376.25±123.17 seconds while in group A and C it was 338.56±114.25 and 286.06±100.09 seconds respectively. Emergence time in group B was 473.53±147.07 second while in group A and C it was 406.06±144.23 and 329.22±110.68 seconds. Duration of surgery and duration of anesthesia were also comparable in all groups [Table 2].

Table 2: Emergence and extubation time parameters.

Parameter	Group A(n=32) Mean±SD	Group B (n=32) Mean±SD	Group C(n=32) Mean±SD	ANOVA	
				F	P
Extubation Time (second)	338.56±114.25	376.25±125.17	286.06±100.09	5.085	0.008*
Emergence Time (second)	406.06±144.23	473.53±147.07	329.22±110.68	9.165	0.005*
Duration of Surgery (min)	103.41±14.97	101.03±16.71	105.32±13.50	0.559	0.574
Duration of Anaesthesia (min)	115.15±12.14	118.62±15.83	114.06±13.82	1.467	0.236

Agitation/delirium score measured at 5 min, 10 min, 20 min, 40 min and 60 min interval after extubation. These scores were consistently lower in group that received gabapentin group A and B) in comparison to placebo group with p-value lying between 0.017 to 0.041. Among group A and B, PEAD score was lower in group B where larger dose of gabapentin was given. Similar trend was found when WATCHA score was used for agitation measurement. Post-operative pain measured by the FLACC scale, at 2 hrs, 6 hrs, 12 hrs, 18 hrs and 24 hrs intervals. These scores were similar in all group, p-value ranging from 0.535 to 0.829, as shown in [Table 3].

Table 3: Emergence delirium and pain scales at different post-operative time intervals

Scales	Post-op time	Group A(n=32) Mean ±SD	Group B(n=32) Mean±SD	Group C(n=32) Mean±SD	Kruskal-Wallis Test	
					H	P
PAED scale	5 min	5.8±1.0	4.2±1.3	6.8±1.1	26.38	0.033
	10 min	4.6±0.8	3.1±1.0	5.9±1.0	8.050	0.041
	20 min	3.4±0.9	2.7±1.3	4.5±0.7	9.479	0.018
	40 min	2.1±0.3	1.7±1.3	3.3±0.6	4.954	0.029
	60 min	1.0±0.7	0.6±0.2	2.1±0.3	9.696	0.017
WATCHA scale	5 min	1.8±0.7	1.1±0.9	2.5±0.6	15.384	0.021
	10 min	1.5±0.6	0.7±0.5	1.9±0.5	7.761	0.033
	20 min	1.2±0.5	0.3±0.2	1.1±0.6	2.125	0.046
	40 min	0.3±0.1	0.2±0.1	0.6±0.3	1.657	0.087
	60 min	0.3±0.1	0.1±0.1	0.4±0.2	4.536	0.104
FLACC scale	2 hrs	4.1±1.3	3.8±1.5	4.9±1.2	29.209	0.535
	6 hrs	3.5±1.2	3.1±1.1	3.5±1.3	13.451	0.829
	12 hrs	2.5±1.5	2.1±1.2	2.7±1.1	8.018	0.731
	18 hrs	2.1±1.1	1.9±0.7	2.3±0.9	3.958	0.591
	24 hrs	1.9±0.5	1.8±0.8	2.3±0.6	1.251	0.535

Heart rate and systolic blood pressure trend were similar in all group with no significant difference as shown in [Table 4]. No incidence of adverse events was recorded in any groups.

Table 4: Intraoperative haemodynamic parameters

Intra-op Interval	Group A (n=32)	Group B (n=32)	Group C (n=32)	ANOVA	
				F	P
Heart rate beats per minute mean± SD					
Baseline	111.3±10.4	110.3±14.5	113.9±12.8	0.686	0.506

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15 min	118.4 ±11.2	117.9±14.6	120.9±11.9	0.511	0.602
30 min	112.0±10.0	109.3±13.8	115.6±11.2	2.319	0.104
60 min	110.8±12.1	108.7±14.8	113.1±11.7	0.945	0.392
90 min	112.6±10.7	108.8±14.5	113.3±11.4	1.195	0.307
Systolic blood pressure in mmHg mean± SD					
Baseline	97.6±6.4	96.8±5.6	99.1±7.2	0.984	0.378
15 min	105.2±8.8	100.8±9.2	105.4±10.8	2.349	0.101
30 min	102.8±10.1	97.8±8.7	100.8±9.2	2.251	0.111
60 min	98.3±7.6	97.3±7.5	99.3±8.9	0.470	0.627
90 min	99.1±7.2	98.7±6.9	102.7±9.3	2.482	0.089

DISCUSSION

In the present study, all three groups were comparable in demographic characteristics, as there was no statistically significant difference regarding the age and weight of children in the three groups. In our study, the baseline heart rate and systolic blood pressure were similar indicating that gabapentin premedication doesn't cause hemodynamic changes at these doses. Furthermore, intraoperative heart rate and systolic blood pressure were also similar among gabapentin and control group.

Using the WATCHA and PAED scales to measure emergence agitation, our study showed that children in the gabapentin groups were having less agitation score than the control group throughout the first hour of recovery. Notably, the group receiving a higher dose of gabapentin (10 mg/kg) had the lower agitation scores, indicating a dose-dependent effect on emergence agitation. This observation supports the opinion that gabapentin premedication helps in preventing emergence agitation. Our findings align with a similar study by Salman AE et al., which also found that gabapentin effectively reduced agitation in children after surgery.[10]

Postoperative pain score as assessed through the FLACC score, was not significantly different between the gabapentin and control groups at 2, 12, 18, and 24 hours post-surgery. This finding contrasts with that of Amin SM et al,[11] who reported an effective pre-emptive analgesic effect of gabapentin in children. This discrepancy is likely attributable to key differences between the study populations. Their cohort involved older children undergoing adenotonsillectomy, whereas our study focused on younger children undergoing urogenital surgery. These variations in patient age and surgical type likely account for the different findings on postoperative pain scores.

We observed that children who received gabapentin took slightly longer time to emerge from anesthesia and be extubated. While this delay of one to two minutes was statistically significant, a difference this small is not considered meaningful in a clinical setting.

Limitation: This study has several limitations. First, its single-center design may introduce selection bias and limit the generalizability of our findings to other clinical settings or patient populations. Second, the specificity of the agitation scales used (WATCHA and PAED) is a potential concern, as the assessed clinical signs can be confounded by other postoperative factors such as pain, hypoxia, or hypotension. To validate our promising results and address these limitations, we strongly recommend conducting large-scale, multicenter trials in this patient population.

CONCLUSION

This study evaluated the efficacy of two different doses of gabapentin premedication for preventing postoperative emergence agitation in children. We found that premedication with gabapentin significantly reduced agitation scores compared to placebo. Furthermore, a dose-dependent effect was also observed, with the 10 mg/kg dose demonstrating superior efficacy over the 5 mg/kg dose for emergence agitation score. We conclude that gabapentin premedication at a dose of 10 mg/kg is an effective strategy for mitigating emergence agitation in pediatric patients following general anesthesia.

REFERENCES

1. Vlajkovic GP, Sindjelic RP. Emergence delirium in children: many questions, few answers. Anesthesia & Analgesia. 2007 Jan 1;104(1):84-91.
2. Nair S, Wolf A. Emergence delirium after paediatric anaesthesia: new strategies in avoidance and treatment. Bja Education. 2018 Jan;18(1):30.
3. Kim J, Kim SY, Lee JH, Kang YR, Koo BN. Low-dose dexmedetomidine reduces emergence agitation after desflurane anaesthesia in children undergoing strabismus surgery. Yonsei medical journal. 2014 Mar 1;55(2):508-16.
4. Demirbilek S, Togal T, Cicek M, Aslan U, Sizanli E, Ersoy MO. Effects of fentanyl on the incidence of emergence agitation in children receiving desflurane or sevoflurane anaesthesia. European journal of anaesthesiology. 2004 Jul;21(7):538-42.
5. Isik B, Arslan M, Tunga AD, Kurtipek O. Dexmedetomidine decreases emergence agitation in pediatric patients after sevoflurane anesthesia without surgery. Pediatric Anesthesia. 2006 Jul;16(7):748-53.
6. Aouad MT, Nasr VG. Emergence agitation in children: an update. Current Opinion in Anesthesiology. 2005 Dec 1;18(6):614-9.
7. Ibacache ME, Muñoz HR, Brandes V, Morales AL. Single-dose dexmedetomidine reduces agitation after sevoflurane anesthesia in children. Anesthesia & Analgesia. 2004 Jan 1;98(1):60-3.
8. Behm MO, Kearns GL. Treatment of pain with gabapentin in a neonate. Pediatrics. 2001 Aug 1;108(2):482-4.
9. Sacha GL, Foreman MG, Kyllonen K, Rodriguez RJ. The use of gabapentin for pain and agitation in neonates and infants in a neonatal ICU. The Journal of Pediatric Pharmacology and Therapeutics. 2017;22(3):207-11.
10. Salman AE, Camkiran A, Oguz S, Donmez A. Gabapentin premedication for postoperative analgesia and emergence agitation after sevoflurane anesthesia in pediatric patients. Agri. 2013 Jan 1;25(4):163-8.
11. Amin SM, Amr YM. Comparison between preemptive gabapentin and paracetamol for pain control after adenotonsillectomy in children. Anesthesia, essays and researches. 2011 Jul;5(2):167.

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