Original Article

Perioperative role of oral gabapentin as an analgesic in paediatric patients: A randomised controlled trial

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Abstract

Background and Aims: Surgical procedure commonly performed in the advanced pediatric age group includes urogenital surgery, adenotonsillectomy, etc., Aim: The aim of this study is to determine the effect of single-dose gabapentin 15 mg/kg on acute pain in the immediate postoperative period in patients aged 8–14 years undergoing surgeries under general anesthesia.
Material and Methods: After the approval from the institutional ethical committee, 60 American Society of Anesthesiologists (ASA) I and II patients aged 8–14 years undergoing urogenital surgeries (orchidopexy/urethroplasty) under general anesthesia were included in this study. The patients were assigned into one of the two treatment groups. Patients in group I received oral gabapentin 15 mg/kg dissolved in 5 mL of honey 2 h before surgery, while patients in group II received 5 mL honey orally 2 h before surgery.
Results: A total of 60 patients participated. Patients in group I had lower consumption of fentanyl perioperatively (intraoperatively: 1.36 ± 0.70 mcg/kg; postoperatively: 2.36 ± 0.795 mcg/kg) than group II (intraoperatively: 1.8 ± 0.6 mcg/kg; postoperatively: 2.9 ± 0.47 mcg/kg). The differences in the two groups were significant. The time to first rescue analgesia was greater in group I (3.03 ± 0.60 h) than in group II (2.26 ± 0.57 h). There was an increase in sedation score in the treatment group.
Conclusion: Our clinical study demonstrates that a 15 mg/kg single preemptive oral dose of gabapentin might reduce the requirement of analgesics perioperatively in pediatric urogenital surgery but might also be associated with undesirable effects such as increased sedation.

Keywords: Adolescent, gabapentin, opioid, perioperative period

Introduction

Surgical procedures commonly performed in advanced pediatric age group include urogenital surgery, adenotonsillectomy, etc., Pain management in such surgeries includes a multimodal approach, including regional anesthesia (caudal), iv opioids, acetaminophen, and non-steroidal anti-inflammatory drugs.

Lately, gabapentin, a structural analog of gamma-aminobutyric acid (GABA), is being used as an analgesic in the immediate post-operative period in various surgeries such as hysterectomy, cholecystectomy, and spinal surgeries.[1-7] Most of these studies are on adult patients, with very few trials on pediatric patients.[8-11] Therefore, the aim of this study is to determine the effect of a single preoperative dose of gabapentin on acute pain in the immediate postoperative period in patients aged 8–14 years undergoing surgeries under general anesthesia. This study was conducted in accordance with the declaration of Helsinki.

Material and Methods

This prospective randomized double-blinded study was conducted over a period of 14 months from November 2018 to January 2020 in our institute. This was done after clearance

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Access this article online

Quick Response Code:

Website: https://journals.lww.com/joacp

DOI: 10.4103/joacp.joacp_503_21

How to cite this article: Sinha C, Kumar A, Kumar A, Kumari P, Kumar A, Kumar B. Perioperative role of oral gabapentin as an analgesic in paediatric patients: A randomised controlled trial. J Anaesthesiol Clin Pharmacol 2023;39:539-43.

Submitted: 11-Nov-2021 **Revised:** 30-Dec-2021
Accepted: 24-Jan-2022 **Published:** 24-May-2023

from the institutional ethical committee and registration in Clinical Trials Registry-India (CTRI/2018/10/016208). Sixty American Society of Anesthesiologists (ASA) I and II patients aged 8–14 years undergoing urogenital surgeries (orchidopexy/urethroplasty) under general anesthesia were included in this study. Written and informed consent for publication was obtained from the parents preoperatively. The day before surgery, the study protocol, including the use of the patient-controlled analgesia (PCA) pump for administration of analgesics and to score pain on numerical rating score (NRS) and Ramsay sedation scores (RSS), was explained to all patients. Exclusion criteria included patients who were ASA III or more, had a known allergy to gabapentin, preexisting neurological disease or spinal anomalies, and patients undergoing surgery under regional anesthesia. Patients not exhibiting adequate skills to operate PCA pumps were also excluded from the study. Consent for study and publication was taken from the parents. A computer-generated randomization table was used to assign the children in either of the two groups—30 in each group—as shown in Figure 1. The code was maintained in sequentially numbered opaque sealed envelopes, which were opened by the nurse on the morning of surgery.

Group I received oral gabapentin 15 mg/kg dissolved in 5 mL honey 2 h before surgery.

Group II received 5 mL honey orally 2 h before surgery.

The pharmacist not involved in the collection or analysis of the data mixed the appropriate dose of gabapentin with honey.

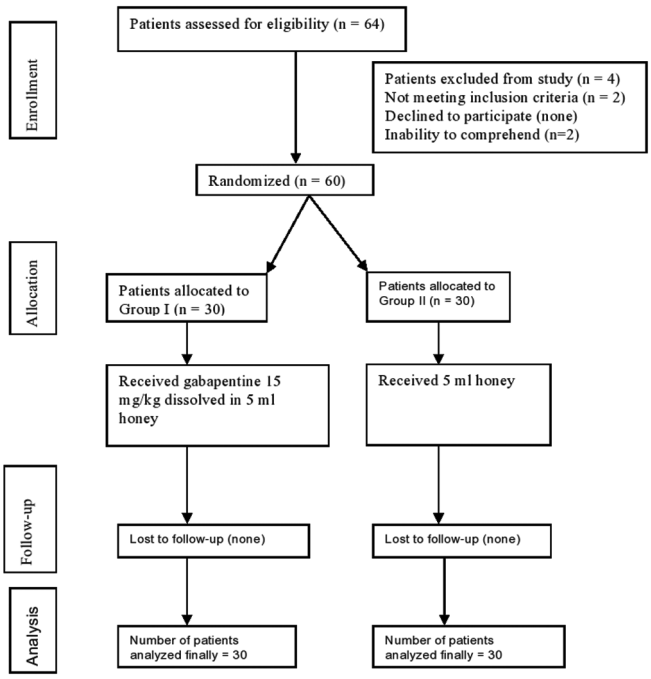

Figure 1: Consort Flowchart

The author who participated in premedication of patients and analysis of data was blinded for the study.

The patients were administered anesthesia in a standardized manner (propofol 2 mg/kg, atracurium 0.5 mg/kg, fentanyl 2 mcg/kg). Sevoflurane in air was used to maintain a MAC of 1. Bispectral index monitoring was done to maintain a value between 40 and 60. Any increase in HR/MAP of more than 20% intraoperatively was treated with additional fentanyl doses of 0.5 mcg/kg. At the end of the surgery, the patients were shifted to the postoperative ward, where they were connected to the PCA pump with the following drug regime (fentanyl bolus dose of 0.5 mcg/kg every 5 min till NRS <3, maximum dose 5 mcg/kg/h or till RR <12). No basal infusion was allowed.

Patients of both groups received intravenous paracetamol (iv PCM) 15 mg/kg every 8 h. No local anesthetic was used by the surgeon for infiltration in either of the groups. A resident blinded to the group allocation assessed the pain score: NRS and RSS at 0, 1, 4, 8, 16, and 24 h at rest. The total fentanyl consumption was noted in both groups. Any adverse effects such as nausea, vomiting, sedation, and respiratory depression (SP02 <90%) were documented.

The primary outcome measurement was total fentanyl consumption within 24 h postoperatively. Secondary outcome measures included time to first rescue analgesia, pain intensity scores at rest, incidence of nausea, vomiting, pruritus, sedation, presence of persisting pain symptoms, and patient satisfaction.

The sample size was calculated based on a pilot study of 10 patients. The requirement of fentanyl postoperatively in the gabapentin group was 2.3 mcg/kg, whereas that of the placebo group was 3 mcg/kg. Assuming the alpha error as 0.05 and power 90%, the sample size calculated was 26 in each group. We took a sample size of 30 to compensate for any dropouts. Statistical analysis was performed using IBM SPSS Statistics version 20 (IBM, Armonk, New York, USA). Continuous variables are expressed as means ± standard deviation, and categorical variables as proportions (%). We compared patient characteristics and the differences of variables among two groups by using unpaired student *t* test. *P* values < 0.05 were statistically significant.

Results

Figure 1 shows the consort flow diagram of study participants. There was no significant difference between the two groups in terms of demographic parameters [Table 1]. The total fentanyl consumption in 24 h was lower

in group I (intraoperatively: 1.36 ± 0.70 mcg/kg; postoperatively: 2.36 ± 0.795 mcg/kg) than in group II (intraoperatively 1.8 ± 0.6 mcg/kg; postoperatively: 2.9 ± 0.47 mcg/kg). These differences between the two groups were statistically significant [Table 2]. The time to first rescue analgesia was greater in group I (3.03 ± 0.60 h) than in group II (2.26 ± 0.57 h). These differences between the two groups were highly statistically significant ($P = 0.001$) [Table 2].

Numerical Rating Score for pain at rest in the postoperative period for 48 h was lower in group I than in group II. This difference in pain scores was significant ($P < 0.05$) only during the first 4 postoperative hours [Table 3]. Ramsay Sedation Score (RSS) was used for detection of sedation as side effects during the first 24 postoperative hours. Patients in group I were more sedated ($P < 0.05$) in the initial postoperative period [Table 4].

Frequent side effects such as nausea, vomiting, dry mouth, somnolence (RSS >3), pruritis, and headache were noted in the postoperative period during the first 24 h [Table 5]. None of the patients in either group developed respiratory depression.

Table 1: Demographic parameters

Variant	Mean±SD		P*
	Group I (*n*=30)	Group II (*n*=30)	
Age (years)	9.83±2.13	9.07±1.43	0.10
Sex (male/female)	26/4	25/5	0.72
Duration of surgery (minutes)	67.5±24.52	66.66±6.68	0.86
Type of surgery (orchidopexy/urethroplasty)	10/20	6/24	0.38

*SD - Standard deviation, *P<0.05=significant*

Table 2: Analgesic requirements in 24 h

Variant	Mean±SD		P*
	Group I (*n*=30)	Group II (*n*=30)	
Intraop fentanyl consumption (mcg/kg)	1.36±0.70	1.8±0.6	0.01
Postop fentanyl consumption (mcg/kg)	2.36±0.795	2.9±0.47	0.002
Time of first analgesic requirement (hours)	3.03±0.60	2.26±0.57	0.001

*SD - Standard deviation, *P<0.05=significant*

Table 3: Numerical rating pain score in 24 h

Time (h)	Mean±SD		P*
	Group I (*n*=30)	Group II (*n*=30)	
0	1.27±0.57	1.80±0.40	0.001
1	1.93±0.44	2.23±0.42	0.01
4	2.56±0.84	3.17±0.69	0.004
8	2.63±0.65	2.43±0.49	0.18
16	1.97±0.48	2.23±0.67	0.08
24	2.10±0.51	2.26±0.44	0.12

*SD - Standard deviation, *P<0.05=significant*

Table 4: Ramsay sedation score

Time (h)	Mean±SD		P*
	Group I (*n*=30)	Group II (*n*=30)	
0	2.56±0.55	1.73±0.51	0.001
1	2.50±0.56	2.00±0.25	0.001
4	1.96±0.31	1.93±0.35	0.72
8	1.93±0.57	1.73±0.51	0.153
16	1.80±0.40	1.77±0.42	0.75
24	1.90±0.18	1.97±0.18	0.159

*SD- Standard deviation, *P<0.05=significant*

Table 5: Side effects

Side Effects	Group I (*n*=30)	Group II (*n*=30)	P*
Nausea	4	6	0.72
Vomiting	3	2	0.64
Dry mouth	2	1	0.35
Pruritus	1	1	1.00
Respiratory depression	0	0	1.00

*SD - Standard deviation, *P<0.05=significant*

Discussion

Urogenital procedures commonly performed in childhood include orchidopexies and urethroplasties. Our study revealed that a single dose of gabapentin 15 mg/kg administered 2 h before surgery decreases the perioperative fentanyl consumption and pain scores in pediatric urogenital surgeries. Postoperative sedation was an unwanted side effect in patients receiving gabapentin.

There have been studies establishing the role of gabapentin as an analgesic in various surgeries in the adult population: hysterectomy, laparoscopic cholecystectomy, discectomy, and mastectomy. All of these studies have used oral gabapentin in a single dose ranging from 300 mg to 1200 mg.

In 2020, Verret *et al.*[11] completed a systematic review to assess analgesia and adverse events from perioperative gabapentinoids in adults. The authors reviewed 281 RCTs with over 25,000 patients undergoing various surgical procedures. The primary outcome was acute postoperative pain while examining statistical and clinical significance. The authors concluded that although gabapentinoids were associated with statistically lower postoperative pain intensity that narrowed over 48 h, gabapentinoids were not associated with clinically meaningfully different postoperative pain intensity. The results of their study did not support the routine use of gabapentinoids for the management of postoperative

pain in adults. We also found similar results in our study. Though our results were statistically significant (less opioid consumption and better pain scores) the clinical relevance is doubtful.

Amin *et al.*[12] used a single preoperative dose of 10 mg/kg in pediatric patients scheduled for adenotonsillectomy. Analgesic requirements for the first 8 postoperative hours were reduced for the patients in the intervention group when compared to the patients in the control group, who received paracetamol, and this difference was statistically significant. There was no increase in adverse effects including sedation and vomiting. Our results were similar in terms of analgesic requirement, but our patients suffered more sedation.

Mayell *et al.*[9] used a single dose of 600 mg preemptively in patients aged 10–17 years undergoing scoliosis surgery. A single dose did not significantly reduce opioid consumption in the patients. There was no increase in adverse effects, including nausea, vomiting, and sleepiness, in either of the groups. The authors attributed their findings to the more extensive nature of the surgery and the fixed dosing irrespective of the weight of the patient. Our study showed a decrease in 24-h opioid consumption, but the clinical significance is questionable (2.36 ± 0.795 vs. 2.9 ± 0.47) as the amount is nearly the same.

Rusy *et al.*[10] used gabapentin in spinal fusion surgeries in a similar age group (10–17 years). They used a bolus dose of 15 mg/kg preoperatively, followed by 5 mg/kg 8 h for 5 days. Gabapentin reduced the requirement of opioids in these patients.

We used a single dose of 15 mg/kg based on the various studies showing the efficacy of a single dose in the adult population. In children, a dose of 9–34 mg/kg/d is well tolerated for seizure control. After a single oral dose of 300 mg, mean maximum plasma concentrations are attained in 2–3 h.[7] Thus, we chose to administer gabapentin 2 h prior to surgery.

Gabapentin has been associated with various side effects. The voltage-gated calcium channels are richly present in the cerebellum and hippocampus. Binding to these receptors can cause dizziness, sedation, and ataxia.[11,13,14]

Our patients had higher sedation scores after surgery. This would have interacted with the reporting of pain scores. In addition, this adverse effect is not desirable in patients' undergoing surgeries such as orchidopexy, which is now done on a daycare basis. There was no decrease in effects such as vomiting despite reducing the consumption of opioids in the perioperative period. This questions the clinical significance of reduction of opioids in our patients.

Limitation: We used a single dose of gabapentin in our patients. Though the results were statistically significant, they might not be clinically significant. Thus, the use of a larger sample size with using various regimens can be planned in future trials.

Conclusion

Our clinical study demonstrates that a 15 mg/kg single preemptive oral dose of gabapentin might reduce the requirement of analgesics perioperatively in pediatric urogenital surgery but might also be associated with undesirable effects such as increased sedation.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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