

ORIGINAL ARTICLE

To compare the efficacy of Gabapentin with Paracetamol for Preemptive Analgesia in children undergoing TonsillectomyANUM ZEB¹, MUHAMMAD MUAZZAM BUTT², AQEEL AHMAD³, RIFAH ZIA⁴, ABAID-UR-REHMAN⁵, DAWOOD AHMAD KHAN⁶¹Senior Registrar Anesthesia, Lahore General Hospital Lahore²Assistant professor of Anesthesia, Punjab Institute of Neuroscience/PGMI/ Lahore General hospital, Lahore.³Assistant Professor Anaesthesiology, PGMI, Quetta⁴Senior Registrar, Doctors Hospital, Kaul Associates, Lahore⁵Associate Professor Anesthesiology, Lahore Medical and Dental college/Ghurki Teaching Hospital Lahore⁶Senior Consultant, Anesthesia & ICU. Lahore General Hospital/PGMI

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ABSTRACT**Aim:** To compare the mean time for first rescue analgesia after preemptive gabapentin versus paracetamol for pain control after tonsillectomy in children.**Method:** This random controlled trial was conducted by Anesthesia team in ENT OT in Jinnah Hospital, Lahore from January 1, 2018 to June 30, 2018. After taking informed consent, 60 patients fulfilling the selection criteria were recruited and after obtaining demographic information, two groups were formed using lottery method Group G and Group P each having 30 patients. Patients were given oral Paracetamol 20 mg/kg and oral Gabapentin 10 mg/kg 120 minutes before induction of anesthesia in Group P and Group G respectively. Post-operatively, patients' pain was monitored with VAS after every 30 minutes. When VAS exceeded 3, it marked the demand of first post-operative rescue analgesia was given and time was noted. Injection Ketorolac 0.5mg/kg was given as rescue analgesia. Mean time of first rescue analgesia was compared in between 2 groups via SPSS 19**Results:** There were no significant differences for variables such as age and BMI in between two groups. The main result of study is that mean time for first rescue analgesia in group G and group P found to be 468.00± 57.14 & 377.00±51.47 minutes respectively. The calculated p-value was P < 0.0001 proving significant difference in duration for first analgesia in between two groups.**Conclusion:** There is significant difference in mean time for first rescue analgesia after preemptive gabapentin versus paracetamol for pain control after tonsillectomy in children.**Keywords:** Preemptive Analgesia, Gabapentine, Paracetamol, Post-operative pain control**INTRODUCTION**

Central sensitization is described as a response to intraoperative tissue injury leading to intensification of long term postoperative pain¹. Analgesia before incision, better known as pre-emptive analgesia, is an approach in which we give analgesia before surgical cut to prevent pain from happening by blocking central sensitization and stopping the pain cycle before it starts². Preemptive analgesia not only decreases post-operative pain, but also significantly decreases post operative opioid consumption³. Different drugs have been used as preventive analgesia such as dezocine, tramadol, paracetamol, pregabalin, gabapentine, non-steroidal anti-inflammatory drugs (NSAIDs) etc⁴⁻⁶. In one of local studies, Khan MA, Siddiqi KJ, Aqeel M. found that intensity of pain in the group G (gabapentin) was significantly lower when compared with the placebo group⁷. Sabry M. Amin and Yasser M. Amr found that time required for first analgesia was significantly more in group gabapentin than paracetamol group⁸.

After so many years of research, we have yet to establish an ideal drug for preemptive analgesia. In this regard, a local study has been already conducted on gabapentin but it does not compare it with any other analgesic. The aim of this study is to compare gabapentin with paracetamol for preemptive analgesia in patient undergoing tonsillectomy. By finding a better drug, if any, it will decrease post-operative opioids utilization thus decreasing hospital stay and side effects of opioids such as respiratory depression, constipation.

The objective of the study was to compare the mean time for first rescue analgesia after preemptive gabapentin versus paracetamol for pain control after tonsillectomy in children.

METHODS

This was a randomized controlled trial conducted by anesthesia team/department in ENT Theatre, Jinnah hospital Lahore from 01.01.2018 to 30.06.2018 i.e. 6 months. Sample size of 60 cases; 30 cases in each group is calculated with confidence level = 95%, power of test = 80% and assuming time to first request for

analgesia in gabapentin group 7.95±2.06 hours and paracetamol

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group 5.85±1.87 hours⁸. Patients aged 5-12 years of either gender with status American Society of anesthesiologists (ASA) I & II going for tonsillectomy for recurrent tonsillitis were included in study and any patient's parent/guardian who refused to give informed consent, were having previous treatment with analgesic (such as opioids or NSAIDs), or any surgery that was performed for more than 60 minutes, were excluded from study. After taking approval from ethical committee and taking informed consent, 60 patients fulfilling the selection criteria were recruited for the study from operation theatres of Jinnah Hospital, Lahore. After taking informed consent, demographic information like name, age, sex, height, weight and contact were acquired. Two groups were formed using lottery method. Group P and Group G. Patients were given oral Paracetamol 20 mg/kg and oral Gabapentin 10mg/kg 120 minutes before induction of anesthesia in Group P and Group G respectively in preoperative room by a post-graduate trainee. After securing intravenous line and starting ringer lactate 12 drops per minute achieving 5ml/kg, nalbuphine 0.1mg/kg, propofol 2mg/kg were administered IV and for facilitation of intubation 0.6 mg/kg atracurium was given. Maintenance was done with isoflurane at 1.5% with O₂ at 3 liters/minute. After the surgeon completed the operation, neuromuscular blockade was negated with neopyrolate combination i.e. neostigmine 0.05 mg/kg and glycopyrolate 0.01mg/kg. Oro-pharyngeal suction was done under direct laryngoscopy and extubation was done once patient was respiring adequately. Patient's was shifted to post-anesthesia care unit (PACU) and pain was monitored by doctor who was not present in operation theatre, with VAS after every 30 minutes. When VAS exceeded 3, rescue analgesia was given and time was noted. Injection Ketorolac 0.5mg/kg was given as rescue analgesia. All the information was collected in a structured proforma. The data was entered & analyzed in SPSS version 19.0. Quantitative variables like, time for rescue analgesia, age and BMI was measured in the form of mean ± SD. Qualitative variables like

gender and status was measured in the form of frequency and percentages. Both groups were compared by using independent sample t-test taking p-value <0.05 as significant. Data was stratified for BMI, age and gender. Post-stratification t-test was applied taking p-value ≤0.05 as significant.

RESULTS

After IRB permission, all the enrolled 60 patients completed the study from 01.01.2018 to 30.06.2018 making the study period 6 months. Patients were divided into two groups i.e. "G" and "P". The mean age in group "G" was 7.733±2.12 years and in group "P" was 7.67±2.29 years. The independent t-test was applied and p-value resulted in p=0.91 proving that there was no significant difference in mean age between two groups. Mean BMI in group G was 17.31±1.81kg/m² and in group P was 17.20±2.14kg/m² and p-value was 0.83 hence no difference in mean BMI as well. Group G had 20 males (66.67%) while Group had 18(60%) males and female were 10(33.33%) and 12(40%) in group G and Group P respectively. The main result of the study i.e. mean time for first rescue analgesia in group G and group P found to be 468.00±57.14 & 377.00±51.47 minutes respectively. The calculated p-value was P<0.0001 proving that there is significant difference. All the data was stratified according to age, gender and BMI groups. All stratified data show some significant difference of mean time for first rescue analgesia. All demographic data is summarized in Table 1 and Table 2 shows mean time for rescue analgesia

Table 1: Demographic details

Demographic Data	Gabapentine group (n=30)		Paracetamol group (n=30)		p-value
Male	20	66.67%	18	60%	0.59
Female	10	33.33%	12	40%	
Age	7.733 ± 2.12 years		7.67 ± 2.29 years		0.91
BMI	17.31 ± 1.81kg/m ²		17.20 ± 2.14 kg/m ²		0.83

Chi-square test was applied and it showed P value is 0.59 showing that there was no significant difference in gender distribution between 2 groups. T-test was applied for age and BMI and it proved no significant difference for age or BMI.

Table 2: Mean time for first rescue analgesia

	Time in minutes
Gabapentine group	468.00 ± 57.14
Paracetamol group	377.00 ± 51.47
P value	P < 0.0001

After applying independent student's t-test, it was found that there was significant difference in mean time for first rescue analgesia in both groups.

Table 3: Stratification of mean time for first rescue analgesia according to demographic data

Age groups	Group	Time For First Rescue Analgesia In Minutes	P value	
5-8 Years	Gabapentine group	456.67 ± 52.02	P < 0.0001	
	Paracetamol group	372.63 ± 55.06		
9-12 Years	Gabapentine group	485.00 ± 62.45	P = 0.0002	
	Paracetamol group	384.55 ± 46.12		
Gender				
	Male		P < 0.0001	
	Gabapentine group	478.50 ± 58.78		
	Paracetamol group	383.33 ± 47.77		
Female	Gabapentine group	447 ± 49.90	P = 0.0027	
	Paracetamol group	367.50 ± 57.39		
BMI				
	BMI ≤18 kg/m ²	Gabapentine group	471.82 ± 58.69	P < 0.0001
		Paracetamol group	379.50 ± 50.83	
	BMI >18 kg/m ²	Gabapentine group	457.50 ± 54.97	P = 0.0048
Paracetamol group		372.00 ± 55.14		

DISCUSSION

Preemptive analgesia is reducing post-operative costs by reducing the need of opioids for post-operative pain, thus reducing the risk of opioid induced hypoventilation and postoperative nausea and vomiting. In our study we found that by giving gabapentin as a premedication, time for first rescue analgesia is prolonged. It has longer and better effect when compared to paracetamol as a preventive medication for pain. In order to decrease post-operative cost of patient stay in hospital and utilization of analgesics such as opioids, it's better to use gabapentin as premedication to decrease the pain intensity of patient which will also help to mobilize patient sooner leading to eventually early discharge. We did not face any major side effects of gabapentin when used as preventive analgesic. In parent study the time to first analgesia was longer in the gabapentin group than paracetamol group (7.95±2.06 hours' vs 5.85±1.87 hours; P<0.0001). Our study's result strengthens the existing evidence. In our study, we measured the time in minutes and it came to be 468.00±57.14 & 377.00±51.47 minutes in gabapentin & paracetamol group respectively. Gabapentin time is roughly 7 hours and 45 minutes with standard deviation of almost one hour in our study which is nearly equal to the parent the study and in paracetamol group it's nearly 6 hours and 15 minutes which also same as in parent study.

Our results were also in concordant with metanalysis performed by Nada Alayed, Nadin Alghanaim, Xianming Tan which concluded that preemptive administration of gabapentin is effective in decreasing postoperative pain scores, narcotic consumption, and nausea, and vomiting¹⁰. Another group of researchers lead by Ezgi Erkilic don't concur with our findings. They compared the gabapentin with placebo for knee arthroscopy and inferred from their findings that VAS score was not significantly different in between both groups¹¹. Although they found that gabapentin has modulated the cytokine response by decreasing the levels of interleukin 6 for first 24 hours of postoperative period but not tumor necrosis factor. Marzieh Beigom Khezri, Nahid Nasseh and Ghodrattollah Soltanian compared pre-emptive analgesic effect of adding vitamin B complex with gabapentin for cesarean section and concluded that vitamin B complex addition helps to further reduce the intensity of postoperative pain following cesarean section¹².

Sidharth S. Routray, Nibedita Pani, Debasis Mishra, and Sunita Nayak compared placebo, gabapentin and pregablin as pre-emptive analgesic for lumbar spine surgery and found that gabapentin and pregablin, both have better profile for providing longer post-operative analgesia when compared to placebo¹³. So far only one study did not concur with our finding which might be due to the different kind of surgery i.e. knee arthroscopy which may not be related to that much cytokine release as compared to surgeries such as lumbar spine or cesarean section in which tissue handling is way more than knee arthroscopy. For limitations in our study, we did not take an account of total consumption of opioids in post-operative period, but it definitely reduced the visual analogue pain score and thus we can expect that the total consumption may have reduced in next 24 to 48 hours. There was minor difference of nalbuphine as peri-operative opioid for analgesia as in parent study they used fentanyl which is much potent then nalbuphine but have a shorter half-life i.e. 30-60 minutes as compared to nalbuphine i.e. 3-6 hours⁹. We were expecting that due to lower potency nalbuphine, our patients may require analgesia sooner but it did not affect the duration of post-operative rescue analgesia requirement. As our result for increase in time for rescue analgesia strengthens the already existing data, hence we recommend using gabapentin as premedication for preemptive analgesia instead of paracetamol as it prolongs the time for first rescue analgesia without any serious complications.

Preemptive analgesia for tonsillectomy is not in common practice in our set ups. As proved by results in local population, we recommend using gabapentin 10mg/kg as preemptive analgesic in

every patient who is undergoing tonsillectomy for recurrent tonsillitis.

CONCLUSION

There is significant difference in mean time for first rescue analgesia after preemptive gabapentin versus paracetamol for tonsillectomy in children. Gabapentin being the better drug for providing longer mean duration of time for first rescue analgesia.

Conflict of interest: Nil

REFERENCES

- Vadivelu N, Mitra S, Schermer E, Kodumudi V, Kaye AD, Urman RD. Preventive analgesia for postoperative pain control: a broader concept. *Local and Regional Anesthesia*. 2014;7:17-22.
- Katz J, Clarke H, Seltzer Ze. Preventive analgesia: quo vadimus? *Anesthesia & Analgesia*. 2011;113(5):1242-53.
- Elazzazi H, Atalla R. Evaluation of the optimum preemptive dose of gabapentin and its postoperative morphine-sparing effect after debridement of burned patient. *Ain-Shams Journal of Anaesthesiology*. 2014;7(2):138-42.
- Badawy AA, Sakka AE. Preoperative gabapentin alone or in combination with dexamethasone on postoperative pain relief after abdominal hysterectomies. A randomized controlled trial. *Egyptian Journal of Anaesthesia*. 2015;31(2):107-13.
- Costa FWG, Esses DFS, Silva PGdB, Carvalho FSR, Sá CDL, Albuquerque AFM, et al. Does the Preemptive Use of Oral Nonsteroidal Anti-inflammatory Drugs Reduce Postoperative Pain in Surgical Removal of Third Molars? A Meta-analysis of Randomized Clinical Trials. *Anesthesia Progress*. 2015;62(2):57-63.
- Zhou X, Zhang C, Wang M, Yu LN, Yan M. Dezocine for Preventing Postoperative Pain: A Meta-Analysis of Randomized Controlled Trials. *PLoS ONE*. 2015;10(8).
- Khan MA, Siddiqi KJ, Aqeel M. Effect of gabapentin on opioid requirements in patients undergoing total abdominal hysterectomy. *Anaesth Pain & Intensive Care*. 2013;17(2):131-5.
- Amin SM, Amr YM. Comparison between preemptive gabapentin and paracetamol for pain control after adenotonsillectomy in children. *Anesthesia, Essays and Researches*. 2011;5(2):167-70.
- Buchh A, Gupta K, Sharma D, Anwar U, Pandey MN, Kalra P. Comparative evaluation of fentanyl versus nalbuphine for attenuation of hemodynamic changes during airway stimulation. *International Journal of Research in Medical Sciences*. 2018 Jan 24;6(2):632-8.
- Alayed N, Alghanaim N, Tan X, Tulandi T. Preemptive use of gabapentin in abdominal hysterectomy: a systematic review and meta-analysis. *Obstetrics & Gynecology*. 2014 Jun 1;123(6):1221-9.
- Erkılıç E, Kesimci E, Sahin D, et al. Does preemptive gabapentin modulate cytokine response in total knee arthroplasty? A placebo controlled study. *Adv Clin Exp Med*. 2018;27(4):487-491.
- Khezri MB, Nasseh N, Soltanian G. The comparative preemptive analgesic efficacy of addition of vitamin B complex to gabapentin versus gabapentin alone in women undergoing cesarean section under spinal anesthesia: A prospective randomized double-blind study. *Medicine (Baltimore)*. 2017;96(15):e6545.
- Routray SS, Pani N, Mishra D, Nayak S. Comparison of pregabalin with gabapentin as preemptive analgesic in lumbar spine surgery. *J Anaesthesiol Clin Pharmacol*. 2018;34(2):232-236.