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Pharmacology

A SINGLE PREOPERATIVE DOSE OF GABAPENTIN REDUCES POST OPERATIVE TONSILLECTOMY PAIN AND SUBSEQUENT ANALGESICS REQUIREMENT IN CHILDREN

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ABSTRACT **BACKGROUND**: Gabapentin is an antiepileptic drug used in a variety of chronic pain conditions. Increasing number of randomized trials indicate that gabapentin is effective as a post-operative analgesic. This procedure-specific systematic review aims to investigate whether a single preoperative dose of gabapentin could improve pain relief and reduce subsequent analgesic requirements during the first 24 hrs after tonsillectomy in children .**METHODS**: A Randomized, single blind prospective parallel group placebo controlled study was conducted in 59 patients who underwent tonsillectomy.30 patients received single oral dose of gabapentin in the dose of 10-15 mg/kg body weight 60 minutes before surgery. 29 patients received empty capsules .In the post operative unit, pain was assessed every three hours using Wong baker's faces pain scale for 24 hrs after surgery. **RESULTS**: The duration of post operative analgesia in the study group was 17.9± 8hrs and the same for control group was 9.1 ± 3.8 hrs. This showed a significant reduction in the postoperative pain in patients who received gabapentin as premedication. The mean pain score of study group was 1.13± 0.35 and the same of control group was 2.50± 1.41. This difference is considered to be statistically significant (p=0.0409). In the study group only 4 patients required subsequent analgesics whereas in the control group 18 patients required it. **CONCLUSION**: A single preoperative oral dose of gabapentin reduced analgesic requirements in the first 24 hrs after tonsillectomy. So the addition of gabapentin prior to tonsillectomy may have an adjunctive role in postoperative pain control.

KEYWORDS : Gabapentin, postoperative pain, tonsillectomy

BACKGROUND

Tonsillectomy is one of the most commonly performed pediatric surgeries and produces a consistent pattern and intensity of pain in the recovery period. These qualities make this surgery ideal for the investigation of pain relieving medications. Adequate analgesia for tonsillectomy in the perioperative period presents a challenge to the anesthetist because opiates, which provide the most effective analgesia, are associated with a high incidence of nausea and vomiting, respiratory depression and sedation. These effects make recovery from tonsillectomy particularly hazardous in children with obstructive sleep apnea syndrome (the primary indication for tonsillectomy or adenotonsillectomy) thus alternatives to opiates have been sought. Gabapentin is a drug with an extensive safety record in the treatment of children's seizures and chronic pain syndromes. As such it may have a role in the relief of acute pain. We hypothesize that given preoperatively as a single dose; gabapentin will reduce postoperative pain and opiate requirement in children undergoing tonsillectomy.[1]

Gabapentin is an amino acid analog of GABA that is effective against partial seizures. This drug has been approved for both anti seizure activity and for its analgesic properties.[2] In spite of its close structural resemblance to GABA; gabapentin does not act directly on GABA receptors. It may, however, modify the synaptic or nonsynapytic release of GABA.[2] It is not metabolized in humans and is excreted unchanged mainly in the urine[3]. Drug is not bound to plasma proteins. Drug-drug interactions are negligible.[2] Gabapentin was designed to be a centrally acting GABA agonist, with its high lipid solubility aimed at facilitating its transfer across the blood brain barrier. [3] It also inhibits N type calcium channels and decreases the synaptic release of glutamate in therapeutic doses. Recent evidence suggests that they also function as GABAB receptor agonist[4]. Gabapentin has antiallodynic and antihyperalgesic properties that result in decreased central sensitization which plays a vital role in acute post-operative pain.[5]

AIM: The aim of the present study is to analyze the effectiveness of a single preoperative dose of gabapentin in relieving the post operative pain and reducing the analgesic requirements during the first 24 hrs after tonsillectomy in children.

METHODOLOGY:

STUDY TYPE: Interventional

STUDY DESIGN:

Randomized, single blind prospective parallel group placebo controlled comparative study.

STUDY CENTRE:

Department of ENT surgery, Tirunelveli medical college hospital, Tirunelveli.

STUDY DURATION: 2 months

STUDY POPULATION:Children who were undergoing tonsillectomy

SAMPLE SIZE: 59

INCLUSION CRITERIA:

Children (5-12 years of age & irrespective of sex) who were undergoing Tonsillectomy and whose parents were willing to give written informed consent were included for the study.

EXCLUSION CRITERIA:

Children of age less than 5yrs and more than 12 yrs and Children whose parents were not willing to give consent were excluded from the study. Children with upper respiratory tract infection, lower respiratory tract infection, cardiovascular abnormalities, abnormal bleeding and clotting time and patients having history of allergy or renal disease were also excluded.

STUDY METHODS:

A randomized single blind study was conducted after getting approval from the Institutional Ethical Committee. A fully written informed consent was obtained from the parents of study participants. Preoperative investigations like blood sugar, urea, creatinine, complete hemogram, coagulation profile, blood grouping and typing were done. Totally 59 patients who were included for the study were randomly allocated either to gabapentin group or to the control group. Children in the control group received empty capsules preoperatively whereas those in the study group received single oral dose of gabapentin in the dose of 10- 15 mg/kg body weight 60 minutes before surgery. They were premedicated with injection Atropine 0.02mg /kg I.M and injection Midazolam 0.07 mg /kg I.M 45 minutes before surgery. Induction was done with injection Thiopentone 5 mg/kg and injection Succinylcholine1.5 mg/kg. In the post operative unit, pain was assessed in both the groups using Wong Bakers faces pain scale for every 3hrs for a period of 24 hrs after surgery.

PRIMARY OUTCOME MEASURES:

Duration of post operative analgesia and subsequent analgesic requirement from the time of extubation up to 24 hrs after surgery

SECONDARY OUTCOME MEASURES

Pain scores using **visual analogue scale.**

STATISTICAL ANALYSIS:

The gabapentin and control groups were matched in respect of their age and weight by the test of significance namely student's t test. They were matched in gender by chi -square test .Duration of post-operative analgesia and mean pain score between two groups were compared using student's t test. Subsequent analgesic requirements between two groups were compared using chi-square test. The above statistical procedures were performed by the PASW Statistic (18.0) (predictive and analysis software) PACKAGE. The P-values less than 0.05 were considered as significant ($p<0.05$).

RESULTS AND OBSERVATIONS:

Table 1: Age and Weight distribution

variables	Gabapentin group			Control group			difference of mean	t	d.f	significance
	n	mean	S.D	n	mean	S.D				
Age	29	10.3yrs	2.5	30	9.6	2.8	0.7	1.053	57	P=0.3159
Weight	29	24.48kg	6.66	30	24.03	6.56	0.45	0.2612	57	P=0.7949

Table 2: Sex distribution

Groups	Gender			t	d.f	p
	male	female	total			
Gabapentin	7	22	29	2.245	1	>0.05
Control	13	17	30			
Total	20	39	59			

Table3: Comparison of duration of post operative analgesia between the two groups.

group	Duration of postoperative analgesia (hrs)		mean difference	t	d.f	P value
	mean	S.D				
Gabapentin	17.9	8.0	8.8	5.411	57	P<0.001
Control	9.1	3.8				

Table 4: Comparison of mean pain scores between the two groups.

Group	Pain score		Difference of mean between groups	t	d.f	P value
	mean	S.D				
Gabapentin	1.13	0.35	-1.37	2.252	14	P<0.05
Control	2.50	1.41				

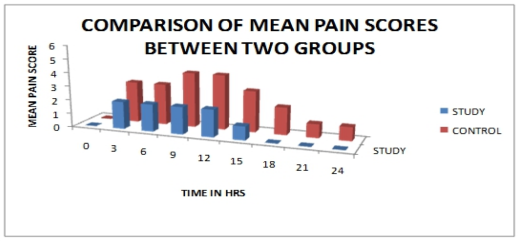
The study and control group were observed for 24 hrs after surgery and pain was analyzed as per Wong baker pain visual scale. The mean pain score of study group was 1.13±0.35 and the same of the control group was 2.50±1.41.

Table 5: Comparison of subsequent analgesics requirements between two groups.

Group	No. of patients required analgesics	Total	P value
Gabapentin n=29	4	33	<0.05
Control n=30	18	48	
59	22	81	

In the gabapentin group out of 29 patients only four patients required analgesic whereas in the control group out of 30 patients 18 patients required it. Chi-Square with age correction showed 5.148 with degree of freedom 1and two tailed p value =0.0233.

Fig: 1 Comparison of mean pain scores between two groups



This difference is considered to be statistically significant (p=0.0409).

DISCUSSION:

Baseline characters like age, weight and sex distribution showed no statistically significant difference between both the groups (Table 1 & 2). Gabapentin was given in the dose of 10-15 mg /kg body weight orally 60 minutes before surgery, which showed significant improvement in the duration of post operative pain relief between the groups (Table 3).This result is consistent with the study conducted in tonsillectomy patients in Scandinavia.[6]

A randomized double blind study conducted in Seoul, South Korea showed that patients who took single dose of 300mg of gabapentin 2hrs before surgery arthroscopic rotator cuff repair under general anesthesia without an interscalene brachial plexus block had significantly less pain during the first 12hrs after surgery but not at 24hrs when compared with placebo.[7]

The present study showed a significant reduction in pain score in gabapentin group when compared to the control group (Table 4 & figure1). A study conducted in USA showed that mean visual analogue pain score decreased from 7.3 to 5.4 in patients with neuropathic pain who took gabapentin 1200mg per day[8]

Several recent studies, meta-analysis and systematic review have demonstrated that gabapentin (300-1200 mg) given as a single preoperative dose as well as perioperatively for up to 10 days is effective in reducing post-operative pain and opioid requirements.[9] A placebo controlled randomized clinical trial conducted in Canada showed that a gabapentin –rofecoxib combination provides significant greater analgesia than single agent for post hysterectomy pain.[10] In our study even a single preoperative dose of gabapentin reduces significant postoperative tonsillectomy pain and analgesic requirements (table 5).

The most frequent adverse effects of gabapentin are sedation and dizziness which are more common with higher dose. In our study none of our patients reported any specific side effect.

CONCLUSION:

A single preoperative oral dose of gabapentin reduced analgesic requirements in the first 24 hrs after tonsillectomy. So the addition of gabapentin prior to tonsillectomy may have an adjunctive role in postoperative pain control.

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