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Use of Oral Gabapentin as Preemptive Analgesia to Attenuate Post Operative Pain in Patients Undergoing Spine Surgery

KEYWORDS: Gabapentin, Post op Pain Relief, Spine Surgeries,Post op Nausea Vomitting(PONV)

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ABSTRACT **Background and aims:** Pain is a common postoperative symptom impairing the quality of postoperative recovery, delaying discharge from Post-anaesthesia care unit (PACU) or surgical centre.The aims and objectives of present study were

1. To study the safety and efficacy of preoperative single oral dose of gabapentin for post-operative analgesia after Spine surgery.

2. To study the other effects and side effects of oral gabapentin.

Methods:80 ASA (American Society of Anaesthesiologists) I or II patients aged 18-70 years scheduled for elective Spine surgery under general anaesthesia were recruited for the comparative study. The patients were assigned randomly into either of following two groups with each group including 40 patients.

Group A (gabapentin group): All patients were given Oral Gabapentin 600 mg 1 hour before surgery and Group B (control): placebo in the form of glucose capsule. Postoperative pain was analyzed by Severity of postoperative pain by Visual Analogue Score(VAS), Postoperative hemodynamic changes, Time of rescue analgesic, Post-operative complications

Results: Group A, 3(7.5%) patients required only one rescue analgesic dose in the post-operative period, 30(75%) patients required 2 doses, only 7(17.5%) patients required 3 rescue analgesic doses and No patient required 4 doses. While in Group B No patient satisfied with one rescue analgesic dose in the post-operative period, 2(5%) patients required 2 doses, 25(62.5%) patient required 3 rescue analgesic doses and 13(31%) patients required 4 rescue analgesic doses.Mean VAS score in Group A is significantly less than Group B over 24 hours of postoperative period and it is statistically significant (p value<0.005).Mean intra operative heart rate and Blood pressure in Group A is lower than Group B throughout the intra operative period after intubation with statistical significance (p<0.05).

Conclusions: Gabapentin reduced the need for additional postoperative pain treatment (PCA boluses of 50 microg of fentanyl) by 40% during the first 20 postoperative hours.Pre-treatment with gabapentin reduced the degree of postoperative nausea and incidence of vomiting/retching possibly either due to the diminished need for postoperative pain treatment with opioids or because of an anti-emetic effect of gabapentin itself.

INTRODUCTION:

Post-operative pain is not purely nociceptive in nature and may consist of inflammatory, neurogenic, and visceral components. The use of opioids by patient-controlled analgesia is popular, but limited by side-effects and by the fact that certain types of pain respond poorly to opioids. Methods used for post-operative pain relief after spine surgery include non-steroidal anti-inflammatory drugs, analgesic suppository, parenteral opioids, intermittent intramuscular injections, infiltration of local anaesthetics at incision site, antihyperlgesic drugs like gabapentin and pregabalin etc. Pre-treatment with gabapentin can block the development of hyperalgesia. Studies have demonstrated that mechanical hyperalgesia surrounding the wound in post-operative patients and experimentally, heat-induced, secondary hyperalgesia share a common mechanism - central neuronal sensitization, which may contribute to some aspects of post-operative pain.

MATERIAL AND METHODS :

Following approval by the institutional ethics committee and written informed consent, 80 ASA (American Society of Anaesthesiologists) I or II patients aged 18-70 years scheduled for elective Spine surgery under general anaesthesia were recruited for the comparative study. The patients were assigned randomly into either of following two groups with each group including 40 patients

Inclusion Criteria:

Written informed consent by the patient's relative.
ASA (American Society of Anaesthesiologists) risk I and II.

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Patients aged 18-70 years of either sex.
Patients scheduled for elective Spine surgery.

Exclusion Criteria:
Patient refusing to give consent.
Allergy to gabapentin or diclofenac.
Patient having a preexisting cardiac or neurological disease

Patients who are not able to appreciate the VAS score.
Patients under treatment by steroids, NSAIDS or opioids before surgery

Group A (gabapentin group): All patients were given Oral Gabapentin 600 mg 1 hour before surgery

Group B (control): placebo in the form of glucose capsule

All the patients were examined on previous day of surgery and were assessed for fitness of anaesthesia. All the patients were explained about VAS for pain. Routine investigations (CBC, RFTs, LFTs, serum electrolytes, chest x-ray, ECG) were carried out in all cases and specific investigations were done if indicated and required. Before taking the patient to the operation theatre, he/she was again explained the VAS (Visual Analogue Scale) for pain. Before 1 hour of surgery group A patients were given 600 mg gabapentin orally with sip of water. After arrival in operating room, routine monitors in the form of ECG, NIBP, and SpO2 were applied and 18 G intravenous catheter was inserted into a suitable vein on the dorsum of non-dominant hand. Sedation level was assessed. The patient was premedicated with Injection Glycopyrrolate (4 ug/kg), Injection Ondansetron (150 ug/kg) and Injection Fentanyl (2 ug/kg) intravenously. The patient was then pre-oxygenated through a face mask with fresh gas flow of 8 L/min oxygen for 5 min. The induction was done with Injection Propofol 2 mg/kg followed by injection Vecuronium bromide 0.1 mg/kg intravenously. The patient was intubated with a suitable size cuffed endotracheal tube.Controlled ventilation was maintained with 50% O_2, 50% N_2O, and Sevoflurane and Injection Vecuronium bromide Intravenously intermittently for muscle relaxation throughout the procedure. Intra operative monitoring included ECG, NIBP, SpO_2, $ETCO_2$ and temperature. Neuromuscular blockade was reversed with Inj. Glycopyrrolate 8mcg/kg IV and Inj. Neostigmine 0.05mg/kg IV. Extubation was done after proper oral and endotracheal suctioning. Patients were shifted to the post operative recovery room when they were breathing spontaneously and following verbal command and with stable vital parameters.

Post-operative pain was assessed at 0, 1, 2, 3, 4, 8, 12, 16, 20 and 24 hours period post operatively. Patients were asked to rate the severity of pain with a Visual analogue scale ranging from 0-10 cm where 0 cm corresponds to no pain and 10 cm corresponds to worst conceivable pain. Any time during the post-operative monitoring of pain score when the VAS (Visual Analogue Scale) was more than 4, the patients were given Inj. Diclofenac Sodium as a rescue analgesic in the dose of 2mg/kg IV slowly. The time of first analgesic dose and the total number of analgesic doses required during 24 hours in the post-operative period were recorded. Post-Operative Nausea Vomiting (PONV) score along with hemodynamic variables (Systolic blood pressure and pulse rate) were also observed post operatively. All patients were observed for minimum period of 24 hours post operatively. Patients were watched for possible complications or side effects during 24 hours post operatively.

All the data were expressed as mean +/- SD except post-operative complications which were expressed as percentage. Data analysis was done by applying independent sample t-test. Statistical significance was defined as $p<0.05$.

RESULTS:
This prospective study was carried out in 80 ASA I and II patients posted for elective Spine surgery under general anaesthesia. The study population was randomly allocated in two groups, 40 patients in each group.

Group A (gabapentin group): All patients were given Oral Gabapentin 600 mg 1 hour before surgery

Group B (control group): placebo in the form of glucose capsule

TABLE-1 DEMOGRAPHIC DATA

Group	Age (MEAN+/-SD) (Years)	Gender (M/F)	Weight (MEAN+/-SD)(kg)
A	43.6+/-5.8	7/33	55+/-6.7
B	44.1+/-7.58	8/32	54+/-6.6

TABLE-2 POST-OPERATIVE ANALGESIC REQUIREMENT

GROUP	ANALGESIC PROFILE	
	Time to first analgesic dose(hours) (Mean+/-SD)	Number of total dose (Mean+/-SD)
A	9.55+/-4.08	2.10+/-0.5
B	1.60+/-1.39	3.28+/-0.55
	p<0.0001	p<0.0001

As shown in Table-2, mean duration at which first analgesic dose was required after surgery is significantly longer in Group A than Group B and mean of total number of analgesic doses required in Group A is lesser than Group B and both are statistically significant ($p<0.05$).

TABLE-3 ANALGESIC REQUIREMENT

GROUP A	GROUP B		
No. of Doses	No. of Patients	No. of Doses	No. of Patients
1	3	1	0
2	30	2	2
3	7	3	25
4	0	4	13

As shown in above data (Table-3), in Group A, 3(7.5%) patients required only one rescue analgesic dose in the post-operative period, 30(75%) patients required 2 doses, only 7(17.5%) patients required 3 rescue analgesic doses and No patient required 4 doses. While in Group B No patient satisfied with one rescue analgesic dose in the post-operative period, 2(5%) patients required 2 doses, 25(62.5%) patient required 3 rescue analgesic doses and 13(31%) patients required 4 rescue analgesic doses.

TABLE-4 POST-OPERATIVE COMPLICATIONS

COMPLICATIONS	GROUP A	GROUP B
NAUSEA	5 (12.5%)	11 (27.5%)
VOMITING	1 (2.5%)	9(22.5%)
TOTAL	6 (15%)	20 (50%)

As shown in above data (Table-4), post-operative complications like nausea and vomiting are significantly less in Group A as compared to Group B. ($p<0.05$)

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DISCUSSION:

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"; nevertheless, pain is still a poorly understood, complex phenomenon.Good postoperative analgesic management brings most gratifying smile on the patient's face, in addition to other benefits like attenuation of the neuroendocrine stress response, reduction of postoperative pulmonary and cardiac complications, an opportunity to institute early physiotherapy that will in turn promote early mobilisation and put the patient on fast track mode.Patients undergoing spinal surgery may have a large incision extending over several dermatomes. Many patients have preexisting chronic pain conditions. Ongoing, acute postoperative pain may also lead to chronic pain after surgery. Underlying mechanisms may be prolonged afferent input of nociceptive signals, originating from surgical trauma and perioperative inflammatory mechanisms, subsequently leading to central sensitization producing chronic pain.

Gabapentin is used as an adjunctive therapy for partial seizure in epileptic patients and in neuropathic pain like diabetic neuropathy. In last few years many clinical trials have suggested that it is effective for attenuation of post-operative pain and can be part of multimodal post-operative analgesia. Gabapentin binds potently to the $alpha_2$delta subunit of five subunits of voltage-gated calcium channels and modulates calcium influx at nerve terminals and thereby, reduces the release of several neurotransmitters, including glutamate, noradrenaline, serotonin, dopamine, and substance P. One of the mechanisms implicated in this effect of gabapentin is the reduction of the axon excitability measured as an amplitude change of the presynaptic fiber volley (FV) in the CA1 area of the hippocampus. This is mediated through its binding to presynaptic NMDA receptors. Other studies have shown that the antihyperalgesic and antiallodynic effects of gabapentin are mediated by the descending noradrenergic system, resulting in the activation of spinal $alpha_2$-adrenergic receptors. Gabapentin has also been shown to bind and activate the adenosine A_1 receptor.

The present study was undertaken to assess the efficacy of pre-operative oral gabapentin for post-operative analgesia after Spine surgery and to study the adverse reactions and complications if occur. Patients were divided into

Group A (gabapentin group): 600 mg gabapentin orally 1 hour before surgery

Group B (control group): control group

INTRA OPERATIVE VITALS: Mean intra operative heart rate and systolic blood pressure in Group A were lower than Group B throughout the intra operative period after intubation with statistical significance($p<0.05$). Premedication with oral gabapentin 600 mg blunted the hemodynamic response after laryngoscopy and intubation.

DURATION OF ANALGESIA Mean VAS scores in Group A were significantly less as compared to Group B upto 24 hours postoperatively and statistically significant ($p<0.005$). Mean duration at which first analgesic dose required after surgery was 9.55+/-4.08 hours in Group A while in Group B it was 1.60+/-1.39 hours. So mean duration at which first analgesic dose required after surgery was longer in Group A than Group B and it was statistically significant ($p<0.05$).

NUMBER OF RESCUE ANALGESICS IN THE FIRST 24 HOUR POST OPERATIVE PERIOD

Mean of total number of analgesic doses required in Group A (2.10+/-0.5) was lesser than Group B (3.28+/-0.55) and was statistically significant ($p<0.05$). In Group A, 3(7.5%) patients required only one rescue analgesic dose in the post-operative period, 30(75%) patients required 2 doses, only 7(17.5%) patient required 3 rescue analgesic doses and No patient required 4 doses. In Group B, No patient satisfied with only one rescue analgesic dose in the post-operative period, 2(5%) patients required 2 doses, 25(62.5%) patient required 3 rescue analgesic doses and 13(31%) patients required 4 rescue analgesic doses.

POST OPERATIVE VITALS:

Mean post operative heart rate and systolic blood pressure in Group A were lower than Group B throughout the post operative period with statistical significance ($p<0.05$).

CONCLUSION:

We concluded that preoperative single oral dose of gabapentin 600 mg reduces pain and rescue analgesic requirement in the early post-operative period after Spine surgery. It is easy, safe and effective method for reducing post-operative pain after Spine surgery without any complications.

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