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EFFECTS OF TWO DIFFERENT DOSES OF PREOPERATIVE ORAL GABAPENTIN ON SPINAL ANAESTHESIA: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY

Anaesthesiology

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ABSTRACT

Background: Preemptive analgesia prevents the altered processing and is effective in reducing postoperative pain. Antinociceptive treatment using multimodal analgesic regimen is highly effective and gabapentin is becoming essential part of it by preventing neuropathic component of acute nociceptive pain of surgery. We aimed to evaluate the effects of preoperative oral gabapentin 300 mg and 600 mg on duration of postoperative analgesia after spinal anaesthesia. **Methodology:** This was a prospective, randomized, controlled, single(observer) blind study conducted at tertiary care public hospital comprising 90 patients of ASA 1and2. Patients were given oral 300mg(300G) or 600mg(600G) gabapentin or nothing(C)one hour prior to surgery followed by standard spinal anesthesia. Duration of anesthesia (sensory& motor block), hemodynamic parameters, sedation scores, duration of postoperative analgesia & complications were assessed. **Results:** The VAS scores were significantly greater in C than 300G & 600G ($p<0.05$) at various time intervals in the postoperative period. Total duration of analgesia(min) was significantly greater in patients of 300G(320±18) & 600G(328±22) than C(172.6±14), ($P<0.001$). Dizziness was observed more in 600G. **Conclusion:** Preemptive use of oral gabapentin (300mg & 600 mg) single dose decreased postoperative pain and delayed the requirement of rescue analgesia. In patients undergoing elective surgeries under spinal anesthesia 300mg can be considered safely and effectively for extended duration of postoperative analgesia.

KEYWORDS

Gabapentin, spinal anaesthesia, multimodal analgesia, Preemptive analgesia

INTRODUCTION

Pain is an unpleasant sensory and emotional experience which is very distressing in the postoperative period. The relief of post operative pain is of paramount importance as it affects recovery from surgery and anaesthesia and postoperative outcome. [3,4] Pre-emptive analgesia is an antinociceptive treatment that prevents the establishment of altered central processing of afferent input, thus decreasing the magnitude of postoperative pain, hyperalgesia and allodynia after surgery [5, 6]. Preemptive analgesia which is given before the beginning of pain using multimodal analgesic (MMA) regimen is highly effective and gabapentin is becoming essential part of it by preventing neuropathic component of acute nociceptive pain of surgery. Various medications which are used in different combinations as part of MMA are nonsteroidal anti-inflammatory drug(NSAIDs), paracetamol, local anaesthetics like lidocaine, ketamine, opioids, gabapentin, pregabalin, clonidine, dexmedetomidine, magnesium sulphate etc. They have been used as pre-emptive analgesics in various anaesthesia techniques including spinal, epidural, general anaesthesia etc. However, opioids and NSAIDI use is limited by associated side effects [7, 8].

Gabapentin, a structural analogue of gamma-amino butyric acid, is an anticonvulsant and antinociceptive drug acts on the CNS to reduce sensitization of dorsal horn neurons [11]. It is a commonly used drug for relieving neuropathic pain and is being used increasingly perioperatively as adjuvant analgesic agent [9,10]. Studies mention its analgesic and opioid sparing effect are used to reduce postoperative pain and can be included in a multimodal analgesic schedule due to synergistic action. [2] It has been successfully used along with spinal anesthesia however different studies mention different dose regimen and no standard dose for perioperative use has been confirmed yet. [1,2]

Hence, we aimed to evaluate the effects of Preoperative oral Gabapentin 300 mg and 600 mg on duration of postoperative analgesia after spinal anaesthesia. We also compared postoperative VAS scores and requirement of rescue analgesia, intraoperative & postoperative, hemodynamic effects, duration of analgesia, sedation scores, the side effects & complications.

METHODOLOGY

This was a prospective, randomized, single blind study conducted after Institutional ethics committee approval and valid written informed consent from each patient. Inclusion criteria was patients belonging to ASA I & II, age group between 18-60 years of either sex who were undergoing elective surgery that can be done under spinal anesthesia. Patients falling into any of the following categories were excluded from the study. Patient refusal; pregnant patient, allergy to any of the drugs to be used; treated with analgesics, α2 agonists, CCB, antipsychotics; clinically significant CVS, CNS disease, renal insufficiency, hypothyroidism; H/O OSA, APD, drug abuse; C/I to Intrathecal anesthesia; uncooperative patients, inability to understand VAS score, or the study protocol; obese with BMI > 35 kg/m2

Sample size was calculated using assuming alpha error of 0.05 and the power of the study 80%, which was total of 90 patients who will be divided into three equal groups. [2] Total 90 patients were randomly distributed into one of the three groups using computer generated random numbers as follows.

1. **Group B:** nothing preoperatively
2. **Group 300G**: preoperative oral gabapentin 300 mg one hour prior to spinal anesthesia.
3. **Group 600G**: preoperative oral gabapentin 600 mg one hour prior to spinal anesthesia.

Observer was blinded to the group allocated. Preoperatively Written Informed Consent, History, ASA Grade, necessary investigations & hemodynamic parameters were checked. A visual analog scale (VAS) was explained to all the patients in the preoperative area. [Table 1] With blinding of observer and group distribution by randomization, patient was given oral 300 mg or 600 mg gabapentin or nothing one hour prior to surgery. This was followed by standard spinal anesthesia procedure. After attaching standard ASA monitors, intravenous preloading was done. Patients were given spinal anaesthesia with standardized procedure with 3 cc 0.5% bupivacaine (dose was adjusted for patients age, weight, surgical requirement). Hemodynamic parameters, onset of sensory & motor block, time for two segment regression, time for regression to L1 after subarachnoid injection were assessed and noted. Motor block was assessed using the Modified Bromage Scale, Sedation was assessed with sedation score. (Table 1) We also recorded VAS scores at rest & on movement postoperatively. End point was VAS>3 when patient was given rescue analgesia. Patients were observed for any side effects or complications perioperatively, they were recorded and treated promptly.

Table 1: Pain scoring-visual analog scale, Modified Bromage Scale, sedation score

Pain scoring-visual analog scale	Modified Bromage Scale	Sedation score
Score Criteria	Score Criteria	Score Criteria
Score 0- No pain Score 1, 2, 3- Mild pain Score 4, 5, 6- Moderate pain Score 7, 8, 9 – Severe pain Score 10- worst pain	0 - no block, able to flex hips, knees, ankles 1 - able to move knees, unable to raise extended leg 2 - able to flex ankles, unable to flex knees 3 - complete motor block, unable to move any part of the lower extremities.	Grade 0: no sedation Grade 1: drowsiness Grade 2: asleep but arousable Grade 3: unarousable with loss of verbal contact

After data collection, data compilation was done in Microsoft Excel. Quantitative data (i.e., Age, time for two dermatomal sensory level regression, time for rescue analgesia, sedation score etc.) was presented with the help of Mean, Standard deviation(SD). Qualitative data (i.e., sex, ASA grade, complications etc.) was presented with the help of frequency and percentage table. Epi Info 7.2 software was used for statistical analysis. Intergroup comparison of demographic data was made by Unpaired 't' test. The three groups were compared by Mann Whitney U test for non-parametric data. Comparison was done by one way analysis of variance (ANOVA) followed by Student's t test for parametric data. Motor changes (expressed in Bromage scale values) did not follow normal distribution and were analyzed with Friedman's test. Results were expressed as mean ± standard deviation. A value of $P < 0.05$ was considered statistically significant.

RESULTS

Total 90 patients were analyzed with 30 in each group. The three groups were comparable with respect to demographic data, ASA physical status and duration of surgery. (Table 02)

Table 02: Demographic data and duration of surgery (mean ± standard deviation)

Variable	Control (n=30)	300G(n=30)	600G (n=30)
Age (years)	52 ± 5.2	49 ± 6.1	53 ± 5.6
Weight (kg)	58 ± 5	56 ± 4.2	60 ± 4
Height (cm)	161 ± 8.8	165 ± 7.2	159 ± 6.8
ASA status I/II	22/8	19/11	23/7
Duration of surgery(min)	118 ± 12.2	108 ± 15	116 ± 9.9

There was no difference in onset of sensory and motor block in 3 groups. Regression of the 2 segment block level time was higher in gabapentin group as compared to control but the difference was not statistically significant between the three groups. (Figure 01)

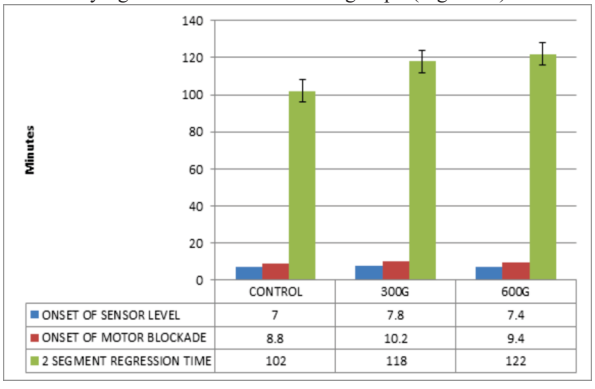

Figure 01: Distribution of sensory and motor effects among the three groups

Hemodynamic parameters including systolic blood pressure, heart rate, oxygen saturation, and respiratory rate were comparable between the groups at any of the measured time intervals. The sedation scores were also similar between the groups at all the measured time intervals. The VAS scores were significantly greater at 30, 60, 90, 120, 150 min after surgery in patients of control group than in those of 300G & 600 G ($p<0.05$). But there was no significant difference between VAS scores in patients receiving 300 mg & 600 mg gabapentin ($p>0.05$). (Figure 02) ANOVA for repeated measures confirmed that gabapentin significantly reduced postoperative pain scores.

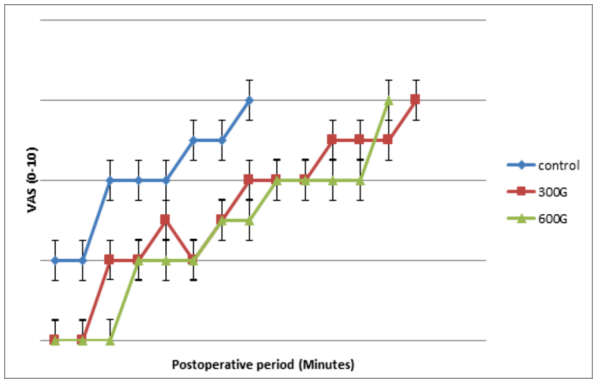

Figure 02: Distribution of VAS scores among the three groups

Various side effects or complications observed in 3 groups are detailed in table 03. All the common side effects are comparable in all the 3 groups except higher incidence of dizziness was observed in 600 mg group of gabapentin which was in 12(40%).

Table 03: Postoperative side effects among the three groups

Side-effect	Control	300G	600G
Hallucinations	0	2(6.67%)	4(13.33%)
Dizziness	0	4(13.33%)	12(40%)
Hypotension	3(10%)	2(6.67%)	3(10%)
Bradycardia	2(6.67%)	1(3.33%)	4(13.33%)
Nausea/vomiting	2(6.67%)	2(6.67%)	2(6.67%)
Somnolence	2(6.67%)	7(23.33%)	8(26.67%)
Diarrhea	0	0	1(3.33%)
Pruritis	1(3.33%)	1(3.33%)	2(6.67%)
Urinary retention	3(10%)	2(6.67%)	3(10%)
Constipation	2(6.67%)	0	1(3.33%)

DISCUSSION

Gabapentin is structurally similar to the neurotransmitter GABA and demonstrates antiallodynic and anti-hyperalgesia properties. It has multiple mechanism of actions but prominent being modulation of glutamate receptors in the superficial lamina of the spinal cord and decreasing the release of neurotransmitter glutamate. Gabapentin mediated analgesia has been successfully used in neuropathic pain, chronic pain and in acute postoperative pain. Preemptive analgesia prevents the altered processing and is effective in reducing postoperative pain. Antinociceptive treatment using multimodal analgesic regimen is highly effective and gabapentin is becoming essential part of it by preventing neuropathic component of acute nociceptive pain of surgery. Several studies have reported the usefulness of Gabapentin in perioperative settings resulting in reduced postoperative pain, postoperative analgesic requirement, side effects, prolongation of analgesia, and higher patient satisfaction [12] Recent studies propose that gabapentin may be useful in synergistic or additive drug in MMA in the perioperative period. We evaluated the effects of preoperative oral gabapentin 300 mg and 600 mg on duration of postoperative analgesia after spinal anaesthesia. This was a prospective, randomized, controlled, single(observer) blind study conducted on 90 patients divided as 30 each in 3 groups. Patients were given oral 300mg(300G) or 600mg(600G) gabapentin or nothing(C)one hour prior to surgery followed by standard spinal anesthesia.

Preemptive analgesic modalities have demonstrated to attenuate postoperative pain scores, and prolong time to first rescue analgesic drug, decrease supplemental postoperative analgesic requirements. [1] Gabapentin in various doses have been used for the same. [1-3] We considered comparing smaller doses of gabapentin to improve the safety profile. In the current study, total 90 patients were analyzed with 30 in each group. The three groups were comparable with respect to demographic data, ASA physical status and duration of surgery. the VAS scores were significantly greater in C than 300G & 600G ($p<0.05$) at various time intervals in the postoperative period. Total duration of analgesia(min) was significantly greater in patients of 300G(320±18) & 600G(328±22) than C(172.6±14), ($P<0.001$). Preemptive use of oral gabapentin (300mg & 600 mg) single dose decreased postoperative pain and delayed the requirement of rescue analgesia. Thus in patients undergoing elective surgeries under spinal anesthesia oral gabapentin single dose have shown safety and efficacy in

extending the duration of postoperative analgesia.

A meta-analysis by Hurley *et al*[13] have reported the usefulness of Gabapentin in perioperative settings resulting in reduced postoperative pain, postoperative analgesic requirement, side effects, prolongation of analgesia, and higher patient satisfaction. Studies also showed that gabapentin reduced the requirement of fentanyl, tramadol for postoperative pain relief and also prolonged post spinal analgesia. [14, 15]

Turan A et al studied oral gabapentin 1.2grams as an adjunct to epidural analgesia and concluded it results in decreased pain and analgesic consumption and in spite of dizziness there was increased patient satisfaction.[2] Gabapentin has few minor side effects which are well tolerated and we also did not observe any significant side effects associated with a single oral dose of gabapentin except more dizziness with 600 mg. Side effects observed were minor and comparable with other studies. [3] In the current study satisfactory duration of prolongation of post operative analgesia was observed with 300 mg of gabapentin with acceptable minimal dizziness in few patients. Increasing the dose to 600 mg did not show significant prolonged analgesia as compared to 300 mg but it did increase the incidence of dizziness. The limitation of the study might be being a single-centered study with limited number of participants hence, further studies with divided doses will be considered.

From the experience of this study, we may conclude that, preemptive use of oral gabapentin (300mg & 600 mg) single dose decreased postoperative pain and delayed the requirement of rescue analgesia without any major side effect. There was no difference in the quality or duration of analgesia offered by the two doses of gabapentin except 600 mg had increased incidence of dizziness. We may recommend 300 mg gabapentin as pre-emptive analgesia in patients undergoing elective surgeries under spinal anesthesia for extended duration of postoperative analgesia safely and effectively.

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