Preemptive Oral Gabapentin and Pregabilin for Post-Operative Pain Management after Surgery under Spinal Subarachnoid Block.

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ABSTRACT

Background: Pregabalin has been used and found effective in preventing neuropathic component of acute nociceptive pain during and after surgery. We conducted a study to compare the effect of oral gabapentin and pregabalin on different block characteristics. **Methods:** A total of 90 ASA grade I and II patients posted for elective surgeries were randomized into 3 groups (groups A, B and C 30 patients each). One hour before entering into the operation theatre the blinded drug selected for the study was given with a sip of water. Group A – received identical placebo capsule, Group B-received 600 mg of gabapentin capsule and Group C- received 150 mg of pregabalin capsule. Spinal anaesthesia was performed at the L3-L4 interspace. 3.5 ml of 0.5% bupivacaine heavy injected over 30 sec through a 25 G spinal needle. VAS score at first rescue analgesia, mean time of onset of analgesia, level of sensory block at 5 min and 10 min interval, onset of motor block, total duration of analgesia and total requirement of rescue analgesia were observed. Hemodynamics parameters and side effects were recorded in all patients. **Results:** A significantly longer mean duration of effective analgesia in group C was observed compared with other groups ($p<0.001$). The mean duration of effective analgesia in group C was 535.16 ± 32.86 min versus 151.83 ±16. 21 minutes in group A and 302.00 ± 24.26 minutes in group B. The mean numbers of doses of rescue analgesia in the first 24 hours in group A, B and C were 4.7 ± 0.65, 4.1 ± 0.66 and 3.9 ± 0.614 respectively. (P value <0.001). **Conclusion:** We conclude that pre-emptive use of gabapentin 600mg and pregabalin 150 mg orally significantly reduces the postoperative rescue analgesic requirement and increases the duration of postoperative analgesia in patients undergoing elective surgeries under spinal anaesthesia.

Keywords: Gabapentin, pregabalin, spinal anaesthesia.

INTRODUCTION

The relief of postoperative pain is the prime concern of patients after surgery.[1,2] Many drugs such as local anaesthetics, opioids, non-steroidal anti-inflammatory drug, cyclooxygenase-2 inhibitor, gabapentin, pregabalin, clonidine and dexmedetomidine have been used as preemptive analgesics.[3]

Gabapentin is a structural analog of gamma amino butyric acid. Large placebo controlled, double-blind trials have confirmed their efficacy in relieving neuropathic pain.[4-7]

Pregabalin has been also used in the treatment of neuropathic pain as well as postoperative pain with good results.[8-11]We compared the effect or oral gabapentin 600 mg and oral pregabalin 150 mg with the control group for post-operative analgesia in elective surgeries performed under spinal anaesthesia.

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MATERIALS AND METHODS

This study was carried out at SCB Medical College & Hospital, Cuttack after obtaining approval from the Hospital Ethical Committee and written informed consent from the patients from July 2014 to Feb. 2015. Ninety ASA grade I or II patients of either sex, aged 18 to 60 years, weighing 50 to 90 kg and with a height of 150 cm to 180 cm, scheduled for elective surgery under spinal anaesthesia were included in the study.

Patients with contraindications to spinal anaesthesia or major neurological, cardiovascular, metabolic, respiratory, renal disease or coagulation abnormalities were excluded. In the operating room, the concept of a visual analog scale (VAS)[12] [Table 1] was introduced to the patient.

Randomization was carried out by chit in box method. Patients were divided into three groups (group A, B and C). In each group, there were 30 patients. The study drug was given with a sip of water. Group A- Received identical placebo capsule; Group B – Received 600 mg of gabapentin capsule; Group C – Received 150 mg of pregabalin capsule. Intravenous (IV) line was secured by using 18 Gauge cannula. Preoperative vitals (pulse,BP, respiratory rate, SpO_2) were recorded. Preloading was done with ringer lactate at the rate of 15 ml/kg/h.

Table 1: VAS

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 imaginable pain
Pain scoring-visual analog scale	

Spinal anaesthesia was instituted at L3-L4 inter space and a volume of 3.5 ml of 0.5% bupivacaine heavy injected over 30 s through a 25 Gauge spinal needle. The patient was placed in the supine position with a 15^0 head down tilt immediately after spinal injection to achieve the level of the block of T5-T6.

The level of sensory block was assessed using a 26 gauge needle and recorded as loss of sensation to pin prick. Motor block was recorded according to the Bromage scale[13] [Table 2]. Routine monitoring of pulse, BP, SpO2, ECG was done intra-operatively. Fluid administration was continued intra-operatively. Decrease in mean arterial pressure greater than 30% below the pre-anaesthetic baseline value was treated with incremental doses of injection ephedrine 5 mg IV. A decrease in heart rate below 50 beats/min was treated with incremental doses of atropine 0.6 mg IV.

Table 2: Intensity of motor block- Modified Bromage score

Score	Criteria
1	Complete block (unable to move feet or knees)
2	Almost complete block (able to move feet only)
3	Partial block (just able to move knees)
4	Detectable weakness of hip flexion while supine (full flexion of knees)
5	No detectable weakness of hip flexion while supine
6	Able to perform partial knee bend

In post-operative period pain assessment was carried out by VAS and duration of motor block was assessed by Bromage scale. Intravenous paracetamol (1 gm) was given as rescue analgesic on demand. The patient was kept under observation for a total period of 24 h to observe for the total number of doses of analgesic required and any side-effects.

Statistical analysis was performed with the SPSS, version 16.0. Categorical data, i.e., ASA grade, type of surgery and the incidence of adverse events (hypotension, bradycardia, respiratory depression, nausea and vomiting) were presented as numbers and proportion of these data were compared in all three groups and the difference in proportion was analysed by Chi-square test. Demographic data (age, weight), duration of surgery, VAS score, total duration of analgesia and requirement of rescue analgesia were expressed as mean ± standard deviation and these data were compared in all three groups. Difference in means was inferred from analysis of variance (ANOVA) test of significance. For significance P value ≤0.05 was considered as significant for both types of data.

RESULTS

A total of 90 patients was enrolled in the study. All groups were comparable with respect to age, gender, weight, ASA status, type of surgery and duration of surgery [Table 3]. The mean time of onset of analgesia was 9.83 ± 1.55, 9.96 ± 1. 97 and 9.96 ± 1.24 min in group A, group B and group C, respectively. There was no significant difference in the onset of sensory analgesia in between group A and B, group A and C and group B and C. (p>0.928).

Table 3: Demographic profile of groups

Observation	Group A	Group B	Group C	P value
	n=30	n=30	n=30	
ASA grade (I/II)	19/17	15/15	20/17	p>0.378
Age (year)	44.4±4.74	42.7±5.17	41.0±5.34	p>0.86
Weight (kg)	58.33±3.32	55.5±3.77	56.2±3.31	p>0.611
Duration of Surgery (min)	55.8±7.7	58.2±11.0	57.8±9.1	p>0.610

In group A, B and C, the mean time of onset of motor block was 14.06 ± 1. 57, 14.6 ± 1.54 and 14.7 ± 1.23 min. (p value = 0.20). There was no significant difference in the onset of motor block in

between group A and B, group A and C and group B and C.

A significantly longer duration of effective analgesia in C group was observed compared with other groups ($p<0.001$). The mean duration of effective analgesia in group C was 535.16 ± 32.86 min versus 151.83 ± 16.21 min in group A and 302.00 ± 24.26 min in group B [Table 4].

Table 4: Characteristics of sensory and motor block.

Parameters	Group A	Group B	Group C	P value
Sensory level (pinprick)				-
5 min	T_9 (T_7-T_9)	T_9 (T_7-T_{10})	T_9 (T_7-T_9)	-
10 min	T_6 (T_5-T_7)	T_6 (T_5-T_7)	T_6 (T_5-T_7)	**>0.05**
Mean time of onset of analgesia (min)	9.83±1.55	9.96±1.79	9.96±1.24	**>0.05**
Total duration of Analgesia (min)	151.8±16.2	302±24.2	535.1±32.8	**>0.05**
Onset of motor block (min)	14.06± 0.57	14.6±1.54	14.7±1.23	-

The mean numbers of doses of rescue analgesia in the 1st 24 h in group A, B and C were 4.7 ± 0.65, 4.1 ± 0.66 and 3.9 ± 0.614 respectively. The p value between these groups in <0.001 [Table 5].

In all three groups, patients were hemodynamically stable in intra-operative and post-operative period. There were no significant differences between groups regarding intra or post-operative side effects [Table 6].

Table 5: VAS = Visual analog sale

Number of rescue analgesics given within 24 h	Group A		Group B		Group C		P<0.001
	Number of patient	%	Number of patients	%	Number of patients	%	
3	0	0	5	17	6	20	
4	11	37	17	56	20	67	
5	16	53	8	27	4	13	
6	3	10	0	0	0	0	
VAS score at first rescue analgesic	2.8±0.6		2.4±0.5		2.3±0.7		P<0.005

Table 6: Intra-operative side effects.

Side effects	Group A	Group B	Group C
Nausea	1	2	3
Hypotension	4	3	2
Bradycardia	4	2	2
Vomiting	1	1	0
Respiratory depression	0	0	0

DISCUSSION

Duration of analgesia got prolonged in gabapentin and pregabalin group as compared to control group. The rescue analgesic requirement in 24 hours was less in gabapentin and pregabalin groups. This benefit was not associated with significant hemodynamic variation and other side effects.

Pre-emptive analgesic modalities have been used as single drug and in combination.[14] A meta-analysis conducted by Cliff K.S. Ong, et al.[15] demonstrated the ability of preemptive analgesic interventions to attenuate postoperative pain, decrease supplemental postoperative analgesic requirement, and prolong time to first rescue analgesic request. Using these outcome measures, pre-emptive analgesia showed an overall beneficial effect after epidural analgesia, local wound infiltration, and systemic nonsteroidal anti-inflammatory drug administration. Preemptive analgesia has been shown to be more effective in control of post-operative pain by protecting the central nervous system from deleterious effects of noxious stimuli. Gabapentin and pregabalin have antiallodynic and antihyperalgesic properties useful for treating neuropathic pain and is beneficial in acute post-operative pain management.[10,16]

Gabapentin is structurally related to the neurotransmitter gamma-aminobutyric acid (GABA). It acts by decreasing the release of neurotransmitter glutamate.[17] Oral gabapentin as an adjunct to epidural analgesia and have been found to decrease pain and analgesic consumption.[18,19] Hurley et al[20] in a meta-analysis of 896 patients concluded that the preoperative use of oral gabapentin is a useful adjunct for the management of post-operative pain. M, Christophe et al[21] have shown that premedication with 1200 mg gabapentin reduced preoperative anxiety, provided better postoperative analgesia, and early knee mobilization after arthroscopic anterior cruciate ligament repair under general anaesthesia.

Pregabalin is claimed to be more effective in preventing neuropathic component of acute nociceptive pain of surgery and perioperaive anxiety.[22]

Saraswat and Arora[11] studied preemptive gabapentin for acute post-operative pain after surgery under spinal anaesthesia. In their study, patients received a single dose of gabapentin 1200 mg (group G) or pregabalin 300 mg (group P). The

total post-operative analgesic time was 8.9 hours in-group G whereas 14.17 hours in-group P (highly significant, P<0.001). Similarly in our study, a significantly longer duration of effective analgesia in-group C was observed in comparison with other groups (p<0.001).

CONCLUSION

Both gabapentin and pregabalin can be used safely for preemptive analgesia. Preemptive pregabalin resulted in more effective prolongation of post-operative analgesia in comparison to gabapentin..

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