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Original Research Article

To Compare Oral Gabapentin and Oral Pregabalin as Preemptive Analgesia under Spinal Anaesthesia for Abdomino-Pelvic Surgeries

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Abstract:

Background: Various adjuvants both orally (clonidine) and intrathecally (opiods, neostigmine, alpha 2 agonist) have been used to prolong the postoperative analgesia of intrathecal bupivacaine. Gabapentin and Pregabalin and a structural analogue of gamma- amino butyric acid given orally, has been found to prolong the analgesia of intrathecalbupivacaine.

Objective: To compare the effects of 150mg of oral Pregabalin and 300mg of oral Gabapentin given90mins before on duration of postoperative analgesia in patients posted for elective Abdomino-pelvic surgeries under subarachnoid block.

Methods: Hundred patients of either sex in ASA I and II aged between 18-65 years postedfor elective Abdomino-pelvic surgeries under subarachnoid block were selected and divided into 2 equal groups of 50 each –Group P(Pregabalin) and Group G(Gabapentin)and the drug was given 90mins before induction of spinal anaesthesia. All patients weregiven 3ml of bupivacaine heavy intrathecally for the surgery.

Results: Mean of Total duration of postoperative analgesia in group P was 270.30 ± 25.07min and in group G was 260.04 ± 23.90min which was statistically significant. VAS score was low at 1st, 2nd,3rd and 4th hour in group P than group G but was statistically insignificant however the VAS score at 5th, 6th and 7th hour in group P was lower than group G and was statistically significant.

Conclusions: A preoperative oral dose of Pregabalin 150mg is more effective than 300mg ofGabapentin for reducing postoperative pain in patients undergoing Abdomino-pelvic surgeries. Pregabalin 150mg produce a prolonged postoperative analgesia compared toGabapentin 300mg.

Keywords: Abdomino-pelvic surgeries; Bupivacaine 0.5%; Oral pregabalin 150mg and gabapentin 300mg; Ramsay sedation score, Spinal Anaesthesia.

Introduction

Anaesthesia as a subject by itself originated in an endeavor to offer pain relief to the patient during surgical procedures. But acute pain following surgery has been managed inadequately because of wide variety of myths and fears. The incidence of post-operative pain has been found to be between 25%-76%.

This uncontrolled pain in postoperative period has some adverse physiologic responses and effects like delayed recovery and chronic pain. [1] Postoperative pain may be considered as a transient type of "neuropathic" pain. The concept of pre-emptive analgesia involves initiating an analgesic regimen before the onset of the noxious stimulus to prevent this central sensitization and limit the subsequent pain experience. [2] Spinal anaesthesia is the preferred technique for most of lower abdominal and lower limb surgeries. It allows the patient to remain awake and minimizes or completely avoids the problems associated with airway management. The technique is simple to perform and the onset of anaesthesia is more rapid, allowing the surgical incision to be made sooner and also provides postoperative analgesia. Spinal anaesthesia with cocaine was initially produced inadvertently by Leonard J Corning in 1885 and first used deliberately by August Bier in 1898. [3]

Gabapentin and Pregabalin are the structural derivatives of the inhibitory Neurotransmitter γ-aminobutyric acid. Their main site of action is α2-δ (α2-δ) ligand that has analgesic, 4 anticonvulsant, 5 anxiolytic6 and sleep-modulating activities.

Pregabalin binds potently to the α2-δ subunit of calcium channels, resulting in a reduction in the release of several neurotransmitters, including glutamate, noradrenaline, serotonin, dopamine, and substance P4. Pregabalin is several times more potent than gabapentin. It is rapidly absorbed orally and achieves peak plasma levels within one hour. [4]The analgesic property of pregabalin has been successfully used by various authors as oral premedication to prolong the postoperative analgesia of local anaesthetics given intrathecally. [7,8] Pregabalin has fewer side effects with the most common events being dizziness and somnolence. [4] Gabapentin is being used since 1994 and pregabalin is a relatively new drug and not many studies have been done regarding its use as oral adjuvant for intrathecal analgesia. It has been used in various doses of 75mg, [9,10] 150mg, 300mg and 600mg [10] orally to prolong the postoperative analgesia. Since there is a difference of opinion regarding the effective dose of pregabalin to be used as oral premedicant for spinal anaesthesia, as 75mg was inadequate [11] and 600mg produced more side effects, [12] a study was required to know the optimal dose of pregabalin before spinal anaesthesia for prolongation of postoperative analgesia. Hence this present study was aimed at comparing 150mg and 300mg of oral pregabalin given as premedicant one hour before Bupivacaine spinal anaesthesia for elective lower abdominal surgeries.

Materials and Methods: This prospective study was undertaken in Khaja Banda Nawaz Teaching and general hospital Kalaburagi during the period of 01/12/2017 to 30/06/2019. The study was undertaken after obtaining ethical committee clearance as well as informed written consent from all patients.

100 patients of either sex, scheduled for abdomino-pelvic surgeries belonging to ASA class I or II were included in the study. The study population was randomly divided into two groups each group containing 50 patients each.

1. Group P (n=50): will receive oral 150mg of pregabalin 90mins preoperatively
2. Group G (n=50): will receive oral 300mg of gabapentin 90mins preoperatively

Inclusion criteria:

- Patients belonging to ASA grade I and II
- Consented patients undergoing Elective Abdomino-Pelvic surgery under SpinalAnesthesia.
- Anticipated duration of surgery between 90 to 120 minutes.
- Age group between 18 and 65 years of both sex

Exclusion criteria:

- Pregnant & Lactating patients.
- Patients on Sedatives, Hypnotics, Antidepressants, Corticosteroids and drugswith effects on the nervous system.
- Patients with Chronic pain syndrome & patients who have taken NSAID in last6 hrs.
- Patients having absolute contraindication for spinal anaesthesia.
- Patients already taking oral Gabapentin, oral Pregabalin.
- Patients with failed or inadequate spinal anaesthesia

A routine pre-anaesthetic examination was conducted on theevening before surgery, assessing

- History and general condition of the patient
- Airway assessment by Mallampati grading.
- Nutritional status, height and weight of the patient
- A detailed examination of the Cardiovascular system, Respiratory systemand Central nervous system
- Examination of the spine

The following investigations were done in all patients

- CBC, LFT, HIV and HbsAg
- Urine examination for albumin, sugar and microscopy
- Standard 12-lead electrocardiogram
- Random blood sugar
- Blood urea and Serum creatinine.
- Informed consent was taken from the patient

Patients were asked to stay NPO for at least 6 hours prior to administering any pre medication. Patients basal pulse rate and basal blood pressure was recorded. Drugs were given 90 minutes prior to the procedure in the ward. A peripheral intravenous line with 18 gauge cannula was secured in one of the upper limbs. Patients were preloaded with 10ml/kg of Ringer lactate 30 minutes prior to the scheduled time of surgery. Upon the arrival in Operation room, Baseline Non-Invasive Blood Pressure(NIBP), Electrocardiogram(ECG), Pulse Rate (PR) and Oxygen Saturation (SpO2%) was noted & monitored, thereafter Under aseptic precautions Lumbar puncture was performed with 25 gauge Quincke's spinal needle using a midline approach with the patients in the left or right lateral decubitus position at lumbar 3-4 inter space and when a free flow of clear cerebrospinal fluid was obtained, 3ml of 0.5% hyperbaric Bupivacaine was administered. Immediately after the injection the needle iswithdrawn, the patient turned supine, onset of sensory block was assessed bilaterally by loss of pinprick sensation with a short hypodermic needle. After achieving the sensory block up to T6 dermatome level and motor block of 3 on Bromage scale, the surgery was allowed to begin. If the block was inadequate or if the spinal subarachnoid block was repeated than such patients were excluded from the

study. Measurements of blood pressure, heart rate, respiratory rate, and arterial oxygen saturation was recorded at 0, 2, 5 minutes & at every 5 minutes thereafter till 30 minutes, after spinal anaesthesia.

Postoperative Sedation scoring was done as per Ramsay sedation scale.

Visual Analog Scale (VAS):

Currently, the most commonly used method, first described by Aitken in 1966. Using a ruler, the score is determined by measuring the distance (mm) on the 10 - cm line between the "no pain" anchor and the patient's mark, providing a range of scores from 0–100. A higher score indicates greater pain intensity. Based on the distribution of pain VAS scores in post- surgical patients who described their postoperative pain intensity as none, mild, moderate, or severe, the following cut points on the pain VAS have been recommended: no pain (0–4 mm), mild pain(5- 44 mm), moderate pain (45–74 mm), and severe pain (75–100 mm).

Statistical Analysis: The Student's Unpaired 't' test was used to assess the differences of VAS for pain in two groups and the changes of them over time in each group. The Statistical software namely SAS 9.2, SPSS 18 for Windows (SPSS Inc., Chicago, Illinois)., Stata 10.1, MedCalc 9.0.1, Systat and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been usedto generate graphs, tables.

Results

Maximum number of patients i.e 27 patients (27%) in both the groups belong to the age group of 31-40 followed by 18 patients (18.0%) in the age group of 41-50. But there was no statistical significant difference of age between the groups P (Oral Pregabalin) and group G (Oral Gabapentin) (P>0.05)

Table 1: Age wise distribution of patients

Age in years	Group P		Group G		Total	
	No.	%	No.	%	No.	%
≤ 20	8	16.0	4	8.0	12	12.0
21-30	7	14.0	10	20.0	17	17.0
31-40	12	24.0	15	30.0	27	27.0
41-50	11	22.0	7	14.0	18	18.0
51-60	8	16.0	9	18.0	17	17.0
≥ 61	4	8.0	5	10.0	9	9.0
Total	50	100.0	50	100.0	100	100.0
Mean ± SD	39.22 ± 14.5		40.74 ± 13.56		39.84 ± 13.85	
t-test value P-value	t = 0.538			P = 0.592	NS	

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant

Table 2: Gender wise distribution of patients

Gender	Group P		Group G		Total	
	No.	%	No.	%	No.	%
Males	29	58.0	33	66.0	62	62.0
Females	21	42.0	17	34.0	38	38.0
Total	50	100.0	50	100.0	100	100.0
X^2-test value P-value	X^2 = 0.679			P = 0.832	NS	

Table 2 shows that, Male patients were dominant i.e. 62 (62.0%) in both groups P and G and female patients were 38 (38.0%). But there was no statistical significant difference of gender between the groups P and G (P>0.05)

Table 3: Weight wise distribution of patients

Weight in Kg	Group P		Group G	
	No.	%	No.	%
51-60	23	46.0	18	36.0
61-70	24	48.0	30	60.0
71-80	3	6.0	2	4.0
Total	50	100.0	50	100.0
Mean ± SD	61.58 ± 5.97		63.12 ± 5.19	
t-test value P-value	t = 1.431		P = 0.105	NS

Table 3 shows that, the mean weight of patients in Group P was 61.58 ± 5.97 and the mean weight of patients in Group G was 63.12 ± 5.19. There wasno statistical significant difference of weight between the groups P and G (P>0.05)

Table 4: ASA Grades wise distribution of patients in both the groups

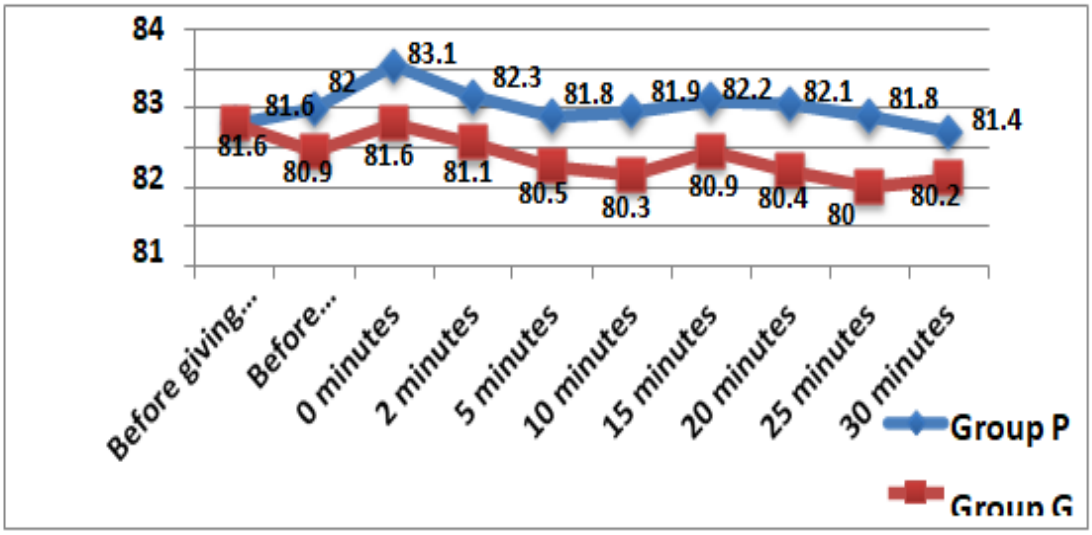
ASA Grades	Group P		Group G	
	No.	%	No.	%
Grade I	34	68.0	35	70.0
Grade II	16	32.0	15	30.0
Total	50	100.0	50	100.0
Chi-Square test P-value	**$X^2 = 0.047$**		**P = 0.983**	**NS**

Table 4 shows no statistical significant difference of ASA gradesbetween the groups P and G (P>0.05)

Table 5: Surgery wise classification of patients in both the groups

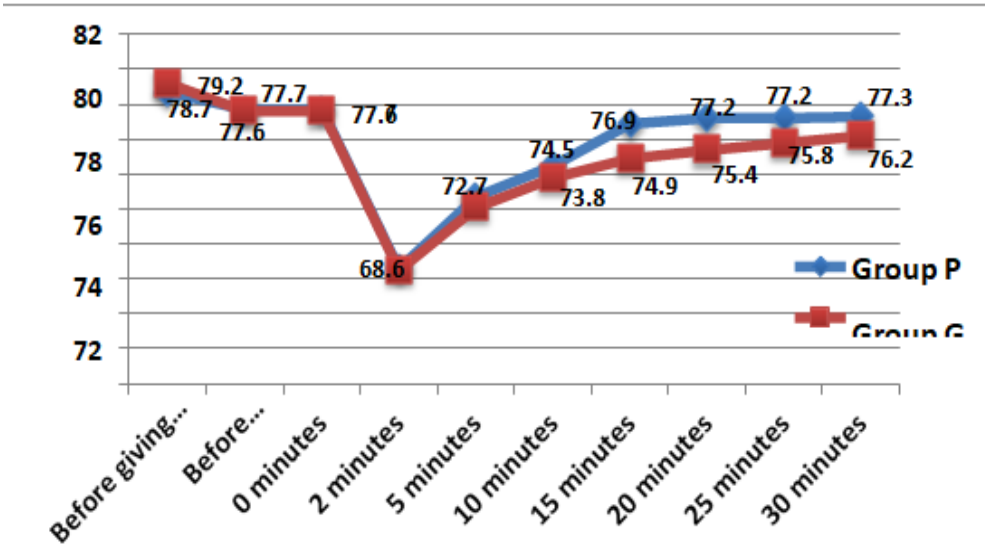
Types of surgeries	Group P		Group G	
	No.	%	No.	%
Appendicectomy	28	56.0	24	48.0
Hernioplasty	7	14,0	10	20.0
Jaboulay's Procedure	5	10.0	10	12.0
Ovarian cystectomy with tubectomy	1	2.0	0	0.0
TAH	9	18.0	6	20.0
Total	50	100.0	50	100.0
Chi-Square test, P-value	**$X^2 = 2.432$**		**P = 0.223**	**NS**

Table 5 shows no statistical significant difference of types ofsurgeries between the groups P and G (P>0.05).

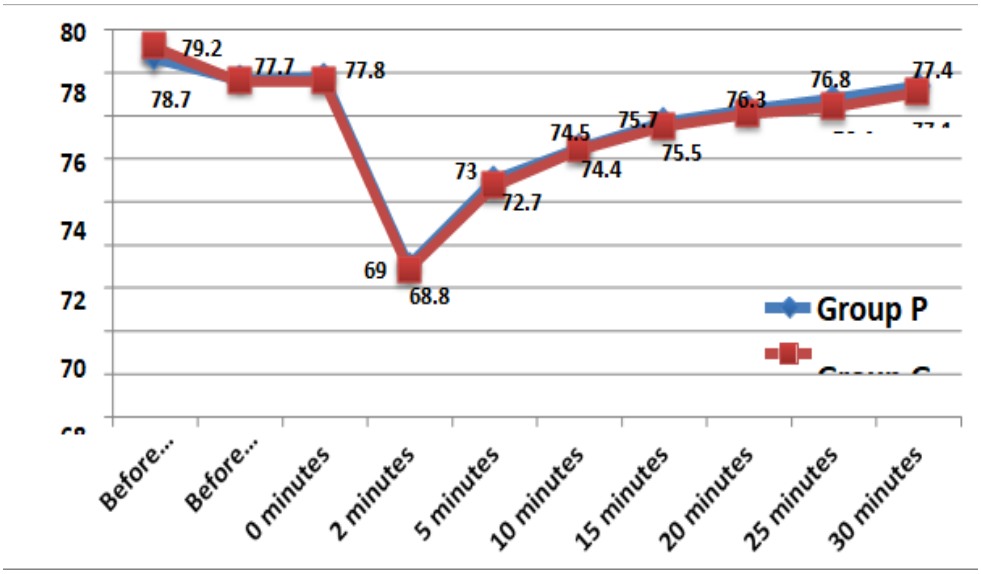


Graph 1: Line diagram represents mean heart rates in both the groups

Graph 1 shows no statistical significant difference of mean heart rate between the groups at before giving drug orally, before subarachanoid block and after subarachanoid block at 0 minute, 2 minute, 5 minute, 10 minute, 15 minute, 20 minute, 25 minute and 30 minute (P>0.05). Graph 2 shows no statistical significant difference of mean systolic BP between the groups at before giving the drug orally, before subarachanoid block and after subarachanoid block at 0 minute, 2 minute, 5 minute, 10 minute,15 minute, 20 minute, 25 minute and 30 minute(P>0.05)



Graph 2: Line diagram represents mean systolic BP in both the groups



Graph 3: Line diagram represents mean diastolic BP in both the groups

Graph 3 shows no statistical significant difference of mean diastolic BP between the groups at before giving the drug orally, before subarachanoid block and after subarachanoid block at 0 minute, 2 minute, 5 minute, 10 minute, 15 minute, 20 minute, 25 minute and 30 minute between the groups (P>0.05)

Table 6: Comparison of Spo2% in both the groups

Time period	Group P	Group G	t –test value	P- Value & Significance
	Mean ± SD	Mean ± SD		
Before Subarachanoidblock	98.20 ± 0.72	98.18 ± 0.66	t = 0.86	P= 0.391, NS
After Subarachanoidblock				
0 minutes	98.32 ± 0.65	97.34 ± 0.73	t = 1.15	P= 0.254, NS
2 minutes	97.48 ± 0.73	97.34 ± 0.74	t = 0.95	P= 0.347, NS
5 minutes	97.78 ± 0.64	97.62 ± 0.72	t = 1.63	P= 0.248, NS
10 minutes	97.40 ± 0.69	97.28 ± 0.70	t = 0.85	P= 0.394, NS
15 minutes	97.80 ± 0.69	97.72 ± 0.72	t = 0.56	P= 0.557, NS
20 minutes	97.80 ± 0.76	97.76 ± 0.77	t = 0.89	P= 0.245, NS
25 minutes	97.92 ± 0.68	97.73 ± 0.63	t = 0.04	P= 0.884, NS
30 minutes	97.91 ± 0.61	97.34 ± 0.63	t = 0.18	P= 0.784, NS

Table 6 shows no statistical significant difference of mean Spo2% between the groups at before giving the drug orally, before subarachnoid blockand after subarachnoid block at 0 minute, 2 minute, 5 minute, 10 minute, 15 minute 20 minute, 25 minute and 30 minute between the groups

Discussion:

In our study mean total duration of analgesia in group P was 270.30 ± 25.07 min, and in group G was 260.03 ± 24.19 min. In our study Pregabalin group in comparison with Gabapentin had significantly lower VAS score at 5th, 6th and 7th after surgery ($p<0.05$) and total diclofenac consumption in group P was 87.02 ± 27.77 and in group G it was 100.50 ± 35.88. There was statistical significant difference in duration of analgesia, VAS score and total diclofenac consumption between the groups ($P<0.05$)

Duration of analgesia was significantly higher in group P as compare to group G. VAS score was significantly lower in group P as compare to group G Total diclofenac consumption was significantly low in the group P as compareto group G

Our study concurs with the study conducted by Saraswat V et al [7] who observed that total duration of analgesia in 1200mg of gabapentin it was 538 minutes and in 300 mg of pregabalin group was 857 minutes and which was highly significant.

Our study also concurs with the study done by Kohli M et al [13] where the duration of analgesia in 300mg pregabalin group was 202.42 minutes and in 150mg pregabalin group was 175.38 minutes which was statistically highly significant.

Our study also concurs with the study done by Rahmawy G E et al. [14] in which duration of analgesia in pregabalin (150mg) group was 248.6±57.8min.

Our study also concurs with the study done by Sahu S et al. [15] in which duration of analgesia in pregabalin (300mg) group was 480min which was significant. Studies done under general anaesthesia by Jokela R et al [9] (150mg pregabalin), Agarwal A et al [16] (150mg), Ghai A et al [17] (300mg), wichai I et al [18] (300mg pregabalin) and Balaban F et al [19] (150 and 300mg pregabalin) observed that there was delay in requirement of first rescue analgesic, decreased requirement of total dose of analgesics and decreased VAS scores during the postoperative period in pregabalin groups compared to the control groups, which suggests prolongation of duration and quality of analgesia in pregabalin group.

Our study also concurs with the study done Dr. Barun Ram et al2 in which Diclofenac Consumption was lowest in pregabalin (300mg) group, as comparison to group C (control) and gabapentin (900mg) group. The mean of diclofenac Consumption in group C was 186.33±38.54, in group G was 174.66±38.79 and in group P was 103.00±20.36. These findings were both clinically and statistically highly significant. ($P < 0.001$).

Sedation score

In our study sedation score was assessed by Ramsay sedation score. Ramsay Sedation score in group P was 2 in 12 patients (24%) and 3 in 38 patients (76%) suggesting that more number of patients were awake and responding to commands. In group G, sedation score was 1 in 3 patients (6%) 2 in 31 patients (62%), 3 in 16 patients (32%) suggesting that more number of patients were awake and responding to commands.

In a study by C K Pandey et al [7] in patients undergoing laproscopic cholecystectomy, it was found that there was higher incidence of sedation (33.98%) in gabapentin group of patients. Ghai et al [20] compared effects of 300 mg Pregabalin and900 mg Gabapentin in 90 patients undergoing hysterectomy. They reported that the incidence of somnolence was 33% in Gabapentin group compared to control. In the study by Rajendran et al, it was found that both pregabalin had slightly higher sedation scores than gabapentin upto 6 hours postsurgery whereas in this study the sedation scores were similar in pregabalin and gabapentin groups.

Our study concurs with the study done by Kohli M et al [8] who observed higher sedation score in group P150 (27/50 patients having score >3) and in P300 (38/50 patients having score >3) than the control with 38/50 patients having sedation score of 1 and 2 which was statistically significant.

Our study also concurs with the studies done by Yucel A et al [21] and Rahmawy GE et al [14] who observed that sedation score was more in pregabalin group than control group and was more with higher doses of pregabalin.

VAS Scores

In our study Pregabalin group in comparison with Gabapentin had significantlylower VAS at 5th, 6th and 7th after surgery ($p<0.05$).

The VAS pain scores at measured times 1st, 2nd, 3rd & 4th hr were lower in the Pregabalin group than the Gabapentin group. The difference was not consideredsignificant ($p>0.05$).

Patients who were premedicated with Pregabalin showed better pain tolerancecompared to those who had been given Gabapentin.

A study conducted by Agarwal et al [16] evaluated the effectiveness of a single dose of Pregabalin 150 mg pre operatively in patients undergoing laparoscopic cholecystectomy. Patients receiving pregab-

alin showed significant reduction in VAS scores in the first 24 hrs post-surgery which is similar to the results obtained in this study.

In a study conducted by A. Turan et al [1] in patients undergoing abdominal hysterectomy, gabapentin produced significantly lower VAS scores both during rest and movement at 1,4, 8, 12, 16, 20 and 24 hours. A meta-analysis of 22 studies conducted by Tiipana et al [22] revealed that in patients 73 receiving pre-operative gabapentin and pregabalin there was a significant reduction in pain scores during the first 24 hours post-surgery.

In our study there was no significant difference among groups in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure measuredat various intervals which concurs with the study done by Sahu S et al [15] and FassoulakiA et al [8].

Conclusion:

Oral pregabalin 150mg given 90mins before surgery was more effective in reducing postoperative pain in patients undergoing lower abdominal surgeries under spinal anaesthesia compared to Gabapentin 300mg group and 150mg dose of pregabalinwas more effective than 300mg Gabapentin in prolonging the postoperative analgesia.

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