A Comparative Study Between Oral Pregabalin and Gabapentin in Prolongation of Postoperative Pain Relief after Spinal Anaesthesia

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Abstract

Background: Management of pain and its complications in postoperative period still a major challenge. Generally, the pathophysiology and treatment of postoperative pain and neuropathic pain have been considered as separate and distinct, though, there is considerable overlap in their pathophysiology.

Materials & Methods: The present study was designed as randomized, double blinded, parallel group, open label trial to compare the efficacy of pregabalin and gabapentin as preemptive analgesics in surgery below umbilicus under spinal anaesthesia. This study was conducted under the Department of Anesthesiology, in the R.G. Kar Medical College & Hospital, Kolkata. Sixty two patients, aged between 20-50 yrs, ASA grade I and II, scheduled to undergo infra umbilical surgery, were randomly divided into 2 groups. In group G (n=31) they received 1200 mg gabapentin, in group P (n=31) they received 300 mg pregabalin capsules, orally with sips of water, 1 hour before the induction of anesthesia. Spinal anesthesia was instituted with 3 ml of 0.5% bupivacaine (15 mg) at L³ – L⁴ / L⁴ – L⁵ level.

Results: All the groups were comparable in respect to demographic data, ASA physical status, the mean duration of surgery and the type of surgeries performed between them. In the 24 hrs of post-perative period the mean VAS scores at rest of Groups P was always significantly lower than those of Group G. The time to first dose of rescue analgesic was compared between the groups, as in Group G (gabapentin group) rescue analgesic was given after 9.41±1.84 hrs, while in Group P (pregabalin group) rescue analgesic was required after 15.38±3.52 hrs. Hence, as comparison of pregabalin and gabapentin could be made for these parameters, and it was possible to come to a conclusion as the superiority of pregabalin over gabapentin.

Conclusion: In conclusion, a single oral dose of pregabalin given preoperatively provides better postoperative
pain control and decreases postoperative rescue analgesic consumption compared to single dose of gabapentin, based on lower mean VAS scores at rest.

**Keywords:** Pain, postoperative pain, neuropathic pain, spinal anesthesia, pregabalin, gabapentin, VAS score

**Introduction**

Pain, which is often inadequately treated, accompanies the more than 23 million surgical procedures performed each year and may persist long after tissue heals. Postoperative pain is not purely nociceptive in nature, and may consist of inflammatory, neurogenic and visceral components. Surgical stimulation leads to sensitization of dorsal horn neurons, which are associated with augmentation of pain.

Pre-emptive analgesia, an evolving clinical concept, involves the introduction of an analgesic regimen before the onset of noxious stimuli, with the goal of preventing sensitization of the nervous system to subsequent stimuli that could amplify pain. Surgery offers the most promising setting for preemptive analgesia because the timing of noxious stimuli is known. When adequate drug doses are administered to appropriately selected patients before surgery, intravenous opiates, local anesthetic infiltration, nerve block, subarachnoid block and epidural block offer benefits that can be observed as long as one year after surgery. The most effective preemptive analgesic regimens are those that are capable of limiting sensitization of the nervous system throughout the entire perioperative period. Anticonvulsants and tricyclic antidepressants were conventionally used for neuropathic pain.

Gabapentin, a structural analogue of gamma amino butyric acid (GABA), introduced in 1994 as an antiepileptic drug and later used for chronic pain conditions like neuropathic pain, diabetic neuropathy, post herpetic neuralgia, complex regional pain syndrome, exerts its effects by binding with alpha 2 delta sub unit of presynaptic voltage gated Ca\(^{2+}\) channels and has antinociceptive, antihyperalgesic and antiallodynic properties.

Several studies have shown the effectiveness of gabapentin as an agent for acute postoperative pain relief resulting in reduced postoperative analgesic requirement in abdominal hysterectomy, spinal surgery, radical mastectomy and laparoscopic cholecystectomy.

Pregabalin, another analogue of gamma amino butyric acid, sharing some characteristics with its predecessor gabapentin, however with superior pharmacokinetic profile, introduced in 2004, already has an established role in treatment of peripheral neuropathic pain associated with diabetes mellitus and post herpetic neuralgia. On review of recent literatures pregabalin is showing evidence that it might be efficacious in relieving acute pain similar to gabapentin, although there is a relative paucity of studies comparing them.

In view of the above observations the present study was designed as randomized, double blinded, parallel group, open label trial to compare the efficacy of pregabalin and gabapentin as preemptive analgesics in surgery below umbilicus under spinal anaesthesia.

**Aims and Objectives**

1. To compare postoperative efficacy of gabapentin and pregabalin with respect to increase in duration of analgesia.
2. To compare reduction in total postoperative requirements of analgesics.
3. To compare side effects and complications of the drugs.

**Materials & Methods**

**Study Area:** Preoperative room, General Surgical operation theatre, Gynae and Obstetrics operation theatre, Orthopaedic operation theatre and postoperative care unit (POCU) of R.G. Kar Medical College & Hospital, Kolkata, West Bengal.

**Study Population:** Patient with physical status ASA-I and ASA-II undergoing infra umbilical surgery under spinal anaesthesia.

**Sample Size:** As calculated from previous study to get clinically relevant difference in duration of postoperative analgesia we need 31 patients in each group with a power of study 80% at 95% confidence interval (alpha=0.05). Total patients were 62. They were randomly allocated in two groups. Group \(G\) (n=31) received single dose of gabapentin 1200 mg
and Group –P (n=31) had received single dose of pregabalin 300 mg.

**Sample Design:** Patients of sex (male & female), age between 20-50 years, weight between 50-75 kg and ASA physical status-I &II were included.

**Inclusion Criteria:** Patients of sex (male & female), age between 20-50 years, weight between 50-75 kg and ASA physical status-I &II for infraumbilical surgery under spinal anaesthesia were included.

**Exclusion Criteria:** ASA physical status>II, patient with uncontrolled or labile hypertension, patient with allergy to the study drugs, pregnancy and lactation, patient with psychiatric illness, patient with hepatic or renal impairment, patient having any contraindication to spinal anaesthesia

**Study Design:** It was a randomized double blinded prospective study.

**Parameters studied for comparing the quality of intraoperative and postoperative analgesia and sedation:** For pain: a) Visual Analogue Scale (VAS) between 0-10cm; 0=no pain, 10=most severe pain

Time elapsed after operation when the patient needs for rescue analgesic; for sedation: Filos numerical scale[3] [scale 1 = awake and nervous; scale 2 = awake and relaxed, scale 3 = sleepy but easy to awake and scale 4 = sleepy and hard to awake]

**Parameters studied for comparing adverse effects:** Dizziness/ somnolence, diplopia, vomiting (the severity of PONV was graded on a four-point ordinal scale; 0=no nausea / vomiting; 1=mild nausea; 2= moderate nausea; 3= severe nausea with vomiting)); confusion (was assessed by asking time, place, person); urinary retention in a non catheterized patient; and respiratory depression [defined as ventilatory frequency <8 bpm and oxygen saturation < 90% without oxygen supplementation.

**Study Technique:** After approval from the institutional ethics committee the study was started. Sixty two consenting patients schedule for surgery below umbilicus were selected in this study. They were randomly allocated to one of the two groups [Gr-G & Gr-P] of thirty one each by allocating the patients alternatively to either group during preanaesthetic assessment (for this study). Patient in group–G (n=31) were received single dose of gabapentin 1200 mg, where as in the group–P (n=31), patient were administered pregabalin 300 mg per oral 1 hour prior to administration of spinal anesthesia. No other premedication was instituted. A day before the scheduled operation the patients were visited pre-operatively in their wards for preanaesthetic check up. A thorough clinical history was obtained. They were physically examined, laboratory investigations were reviewed and a detail about VAS (0-10cm) was explained on the day before operation. The patients were also explained about the procedures of spinal anaesthesia and post-operative pain relief and all queries and doubts were answered to get their confidence and support.

**Procedure:**

In the group G, the bag contained four 300mg hard gelatin capsules of gabapentin belonging to one particular pharmaceutical company, in the group P the bag contained four 75 mg hard gelatin capsules of pregabalin belonging to the same pharmaceutical company (size, shape looked similar). The medication was given to the patient by an anaesthesiologist not involved in the study 1 hour before the induction of anaesthesia. Routine monitoring in the form of NIBP, pulse oxymetry and ECG were instituted on arrival in Operation Theatre. All patients were preloaded with 10 ml/kg lactated Ringer’s solution before being administered spinal anaesthesia. Spinal anaesthesia was instituted with 3 ml of 0.5% bupivacaine (15 mg) at L3-L4/ L4-L5 level. Fluid administration was continued intraoperatively and hypotension, if any was treated with fluid replacement.

Pain was assessed postoperatively by visual analogue scale[1] in immediate postoperative period and every two hourly thereafter which was explained to the patient during preoperative visit. When patient was shifted to the ward one 1st year anaesthesiology post graduate trainee, unaware of the premedication was responsible for charting the pain score by VAS scale[1]. Pain charting was done separately and anaesthetic chart was not attached with the case sheet, so the observer was not find out to which group patient belong. Any patient with VAS score of more than three was received diclofenac 1 mg/Kg intramuscularly. Time since spinal anesthesia to first dose of analgesic and total dose of analgesic
in first 24 hours was recorded. Any complications like dizziness, somnolence, diplopia, vomiting, confusion, respiratory depression, pain and urinary retention was recorded in first 24 hours postoperative period. Data were analysed using simple proportion, average (mean), standard deviation, independent ‘t’ test and chi-square test, Odds ratio (OR) with its 95% confidence interval (CI). For this purpose, SPSS 19 and Epi info 3.4.3 version were utilized.

Results

Data derived from altogether 62 patients i.e. 31 in each arm were considered for analysis.

Table 1: Distribution of demographic and clinical parameters among participants as per groups (N=62)

<table>
<thead>
<tr>
<th>Attributes</th>
<th>Group P (n=31)</th>
<th>Group G (n=31)</th>
<th>Chi-square, df, p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age groups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 yr</td>
<td>7 (22.58)</td>
<td>10(32.26)</td>
<td>0.79, 2</td>
</tr>
<tr>
<td>20-40 yr</td>
<td>10(32.26)</td>
<td>8(25.81)</td>
<td></td>
</tr>
<tr>
<td>&gt;40 yr</td>
<td>14(45.16)</td>
<td>13(41.94)</td>
<td>0.674</td>
</tr>
<tr>
<td>Age (yr) (mean±SD)</td>
<td>38.42±9.77</td>
<td>36.61±9.19</td>
<td>0.750, 0.456</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13(41.94)</td>
<td>13(41.94)</td>
<td>0.00, 1</td>
</tr>
<tr>
<td>Female</td>
<td>18(58.06)</td>
<td>18(58.06)</td>
<td>1,00</td>
</tr>
<tr>
<td>BMI in kg/M² (mean±SD)</td>
<td>21.61±1.79</td>
<td>21.99±1.91</td>
<td>0.813, 0.420</td>
</tr>
<tr>
<td>Duration of surgery in minutes (mean±SD)</td>
<td>62.09±23.48</td>
<td>60.81±20.13</td>
<td>0.232, 60, 0.817 (unpaired t, p at df=60)</td>
</tr>
</tbody>
</table>

Table 1 shows that maximum number of participants was belonged to the age group of 40 years and above. No statistically robust difference could be observed in the age group distribution between the groups. Majority of the study subjects were in the age range of forty years and above. There was no significant difference in gender distribution of study subjects among two groups. As a whole, there were 41.94% male, being 41.94% in each arm. The male-female ratio was 1:1.38. The average age between two groups didn’t show statistically sound difference. The mean body mass index had a uniform distribution in both the groups and no significant difference could be explored. The groups didn’t vary in respect of the average time required for the surgical maneuver [Table 1].

Table 2: Distribution of participants as per the time elapsed after of surgery when VAS score was more than 3 (N=62)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time (hrs) after OT when VAS was &gt;3 (mean±SD)</th>
<th>Unpaired t, df, p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr. P (n=31)</td>
<td>15.38±3.52</td>
<td>8.364,60, 0.000</td>
</tr>
<tr>
<td>Gr. G (n=31)</td>
<td>9.41±1.84</td>
<td></td>
</tr>
<tr>
<td>Total (N=62)</td>
<td>12.39±4.09</td>
<td></td>
</tr>
</tbody>
</table>

The study groups had a significant variation in the time interval after surgery when the VAS score was found to be 3 or more signaling the need of rescue analgesic. In group P, time interval was more compared to group G [Table 2].
Table 3: Distribution of participants according to the time of administration of rescue analgesic after surgical maneuver, i.e. postoperative analgesia time after giving preemptive pregabalin or gabapentin (N=62)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time (hrs) (after operation) of administration of rescue analgesic (mean±SD)</th>
<th>Unpaired t, df, p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr. P (n¹=31)</td>
<td>15.38±3.52</td>
<td>8.364,60</td>
</tr>
<tr>
<td>Gr. G (n²=31)</td>
<td>9.41±1.84</td>
<td>0.000</td>
</tr>
<tr>
<td>Total (N=62)</td>
<td>12.39±4.1</td>
<td>…</td>
</tr>
</tbody>
</table>

The time required for the administration of the rescue analgesic postoperatively was found to be significantly earlier in case of group G compared to group P. That means pregabalin shows prolong postoperative analgesia compared to gabapentin [Table 3].

Table 4: Distribution of participants as per requirement of subsequent dose of analgesic

<table>
<thead>
<tr>
<th>Attributes</th>
<th>Group P No. (%)</th>
<th>Group G No. (%)</th>
<th>Chi-square, df, p</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subsequent dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Required</td>
<td>02(6.45)</td>
<td>03(9.68)</td>
<td>0.22,1,0.64</td>
<td>1.50 (0.27-8.36)</td>
</tr>
<tr>
<td>Not required</td>
<td>29(93.55)</td>
<td>28(90.32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>31(100)</td>
<td>31(100)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Above table 4 reveals that the groups was not significantly dissimilar in respect of the proportion of the subjects’ required subsequent dosage of rescue analgesics. Study shows that subsequent dose of rescue analgesics was required by 6.45%, 9.68% and 8.06% of the participants in group P, G, and overall [Table 4].

Table 5: Distribution of adverse events among the groups

<table>
<thead>
<tr>
<th>Attributes</th>
<th>Group P No. (%)</th>
<th>Group G No. (%)</th>
<th>Chi-square, df, p</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>7 (22.58)</td>
<td>13(41.94)</td>
<td>2.66, 1, 0.103</td>
<td>1.86 (0.86-4.02)</td>
</tr>
<tr>
<td>Absent</td>
<td>24(77.42)</td>
<td>18(58.06)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>31(100.0)</td>
<td>31(100.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

It is clear that the groups didn’t differ to the extent of statistically significant level in respect of proportion of study subjects showed adverse events [Table 5].

Table 6: Distribution of different types of adverse events among the groups

<table>
<thead>
<tr>
<th>Adverse effects</th>
<th>Group P No. (%)</th>
<th>Group G No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somnolence</td>
<td>4(12.90)</td>
<td>7(22.59)</td>
<td>11(35.48)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3(9.68)</td>
<td>6(19.35)</td>
<td>9(29.03)</td>
</tr>
<tr>
<td>Total</td>
<td>7(22.59)</td>
<td>13(41.94)</td>
<td>20(64.52)</td>
</tr>
</tbody>
</table>

The above table 6 shows adverse effects were more in gabapentin group than pregabalin group. The adverse events (AEs) were found in 22.58% and 41.94% of the study subjects in group P & G, respectively and as a whole among 32.26% of the participants [Table 6].

**Discussion**

Preemptive analgesia is a treatment that prevents establishment of the altered sensory processing that amplifies postoperative pain. The treatment should cover the entire duration of high-intensity noxious stimulation that can lead to establishment of central and peripheral sensitization caused by incisional or inflammatory injuries (during surgery and the initial postoperative period). Emphasis on the PRE versus POST design has led to a situation in which establishment of sensitization during inflammatory injuries in the initial postoperative period is excluded from consideration.

Pre-incisional analgesia has been shown to be more effective in control of postoperative pain.
by protecting the central nervous system from deleterious effects of noxious stimuli and resulting allodynia, and increased pain. Gabapentin and pregabalin have antiallodynic and antihyperalgesic properties useful for treating neuropathic pain and may also be beneficial in acute postoperative pain. Several studies have reported the usefulness of gabapentin and pregabalin in perioperative settings resulting in reduced postoperative pain, postoperative analgesic requirement, side effects, prolongation of analgesia, and higher patient satisfaction. [19-22] Gabapentin, a structural analogue of gamma amino butyric acid (GABA), introduced in 1994 as an antiepileptic drug and later it was used for chronic pain conditions, has antinociceptive, antihyperalgesic and antiallodynic properties. Several studies have shown the effectiveness of gabapentin as an agent for acute post-operative pain relief resulting in reduced postoperative analgesic requirement.

Pregabalin, another analogue of gamma amino butyric acid, sharing same characteristics with its predecessor gabapentin, however with superior pharmacokinetic profile, introduced in 2004, already has an established role in treatment of peripheral neuropathic pain. On review of recent literatures pregabalin is showing evidence that it might be efficacious in relieving acute pain similar to gabapentin, although there is a relative scarcity of studies comparing them. In view of the above observations the present study was designed as randomized, double blinded study to compare the efficacy of pregabalin and gabapentin as preemptive analgesics in any surgery done below umbilicus under spinal anesthesia.

This study was conducted under the Department of Anesthesiology, in the R.G. Kar Hospital and Medical College, Kolkata. Sixty two patients, aged between 20-50yrs, ASA grade I and II, scheduled to undergo infra umbilical surgery, were randomly divided into 2 groups. In group G (n=31) they received 1200 mg gabapentin, in group P (n=31) they received 300 mg pregabalin capsules, orally with sips of water, 1 hour before the induction of anesthesia.

All the groups were comparable in respect to demographic data. There was no significant difference in the mean duration of surgery between the groups (table 2), nor there was any significant difference in the type of surgeries performed between them. The recommended starting dose of gabapentin for neuropathic pain is 300 mg on day 1, 300 mg twice daily on day 2 and then 300 mg three times daily thereafter. This dose is often insufficient and doses up to 1800 mg may be required. The practice of administering a first dose of 1200 mg or 600 mg immediately before anaesthesia and surgery is clearly in contravention to this recommendation.

In a recent review of 22 RCTs, meta-regression analysis suggested that the gabapentin induced reduction in the 24-h opioid consumption was not significantly dependent on the gabapentin dose. Hence, single highest safe dose of gabapentin (1200 mg) and pregabalin (300 mg) was selected for this study, which is same as used in most of the studies. In animal models gabapentin has been reported to be more effective when given preoperatively, however, Pandey et al in their study reported that gabapentin (600 mg), given preemptively or postincision did not have significant difference in fentanyl consumption between pre and postincision groups. However, we still used gabapentin and pregabalin preoperatively as analgesic consumption was lower in preoperative regimen.

The mean VAS scores at rest in the 0-10 cm scale were recorded at the following time points: 0, 1, 2, 3, 4, 5, 6, 8, 10, 12, 16, 20 & 24 hours in the first 24 hrs of postoperative period. Analysis of table 3 shows duration after operation when rescue analgesic becomes required was 15.38±3.52 hrs in case of pregabalin and 9.41±1.84 hrs in case of gabapentin, which was statistically and significantly lower in case of gabapentin. In the study conducted by Saraswat et al, time to rescue analgesic was 8.98 ±5.38 hrs for gabapentin group, which was significantly less (p value < 0.001) than pregabalin group (14.17 ±6.67 hrs). Whereas the total dose of rescue Analgesic (mg) in 24 hours postoperative period was 62.5± 28.43mg for pregabalin being lower than 5 ± 23.99mg for gabapentin, was statistically not significant between the groups. Thus they showed that pregabalin was superior to gabapentin in the above mentioned criteria.
The requirement of subsequent number of rescue analgesic doses in the 24 hours of postoperative period between the groups (Table 4) have shown that in group G (gabapentin group) and group P (pregabalin group) it was only for 3/0/0 and 2/0/0 (1dose/2 doses/3 doses) patients respectively. Thus, pregabalin and gabapentin were both effective in reducing need for rescue analgesic in the postoperative period, however no conclusion could be derived as to the superiority of pregabalin over gabapentin in this regard. This finding is in agreement with the results of study conducted by Saraswat et al\textsuperscript{24} where the number of doses in 24h (0 dose/1 dose/2 doses) in gabapentin group was 2/26/2 and for pregabalin was 4/25/1 (no discernible difference between the two groups like ours).

In 2002, Dirks et al\textsuperscript{12}, studied the effects of single-dose preemptive oral gabapentin versus placebo on post-operative pain and morphine consumption after mastectomy, while we studied on surgery below umbilicus. Our study was similar with this one as we also use 1200 mg gabapentin as they used. They concluded that in gabapentin group there was substantial reduction in movement related pain 2 and 4 hour after radical mastectomy, whereas in our study movement related pain was not recorded. 4 hour post-surgery morphine consumption was significantly lowered than control group in their study while we used diclofenac as the rescue analgesic which was required in the gabapentin group as subsequent rescue analgesic in only 9.68% cases in our study. The results differ from our study as pain at rest was reduced significantly by gabapentin, but this reduction was not statistically significant in their study.

In 2004 Pandey et al\textsuperscript{25} undertook a randomized, double blinded, placebo controlled study to investigate whether gabapentin, could reduce postoperative pain and fentanyl consumption in patients after single-level lumbar discectomy. They used gabapentin 300 mg or placebo two hours before surgery while in our study 1200 mg gabapentin was used 1 hour before the surgery which was comprised any infraumblical surgery including orthopedic surgery. After surgery, the pain was assessed on a visual analogue scale (VAS) at intervals of 0–6, 6–12, 12–18, and 18–24 hr at rest, while it was recorded more frequently in our study. Fentanyl 2 µg•kg\textsuperscript{-1} intravenously was used to treat postoperative pain on patient’s demand and total dose in 24 hours was recorded. In our study i.m. diclofenac was used as the rescue analgesic. Patients in the gabapentin group had significantly lower VAS scores at rest, at all time intervals than those in the placebo group and similar results were observed in our study. The total fentanyl consumed after surgery in the first 24 hr in the gabapentin group (233.5 ± 141.9, mean + SD) was significantly less than in the placebo group (359.6 ± 104.1; P < 0.05) whereas in our study diclofenac was required only in 9.68% cases as subsequent analgesic. They concluded that preemptive gabapentin 300 mg per oral significantly decreased the severity of pain postoperatively in patients who underwent single level lumbar discectomy which was very much similar to ours.

Turan et al\textsuperscript{26} conducted a study in 2004 comparing 1200 mg preemptive gabapentin versus placebo, given 1 hour before lumbar spine surgery under GA. All patients received postoperatively patient controlled analgesia with morphine. It was much similar to our design except 1200 mg gabapentin and diclofenac (rescue) was used in ours. They found pain scores at 1, 2, and 4 hour and total morphine consumption was significantly lower in the gabapentin group when compared with the placebo group and they concluded preoperative oral gabapentin decrease pain scores in the early postoperative period in spinal surgery patients. In our study the results were almost similar. Postoperative morphine consumption was decreased much like ours where second dose of diclofenac was used in only 9.68% cases.

Peach et al\textsuperscript{27} in 2007 conducted a study in 90 women having minor gynecological surgery involving the uterus. Patients received either oral pregabalin 100 mg or placebo approximately 1 h before surgery, whereas in our study 300 mg pregabalin was used in infraumblical surgery under spinal anesthesia. The primary outcome was pain score in the recovery unit and patients were followed for 24 h. There was no significant difference between groups for pain experienced in the recovery room or thereafter; nor for recovery room fentanyl requirement (42% Group pregabalin versus 27% Group placebo), p value=0.12) or the quality of recovery at 24 h postoperatively. This finding was different from ours as pain scores in the
pregabalin group were always significantly less than the gabapentin group. This difference may be due to a lower preemptive dose of pregabalin in their study.

Agarwal A et al in the same year, i.e. 2008 conducted study to evaluate the efficacy of a single preoperative dose of 150 mg pregabalin when given 1 hour before surgery for attenuating postoperative pain and fentanyl consumption after laparoscopic cholecystectomy compared to placebo. Ours in contrast used 300 mg dose of pregabalin and that too in infraumbilical surgery. Postoperative pain (static and dynamic) was assessed by a 100 mm visual analogue scale and the subjects received patient-controlled i.v. fentanyl analgesia during the postoperative period, while in our study only static scores were measured and diclofenac was used as rescue analgesic. Result of the study revealed that postoperative pain (static and dynamic) and postoperative patient-controlled fentanyl consumption were reduced in the pregabalin group compared with the placebo group (p<0.05) which was very much in agreement with our results where pregabalin shows more postoperative analgesia than gabapentin.

Sahu et al in 2010 conducted a study to evaluate the role of pregabalin in reducing postoperative pain and rescue analgesic demand in patients undergoing infraumbilical surgeries under spinal anesthesia. In Group I placebo capsules 12 hour before surgery and 1 hour before surgery and in Group II-pregabalin capsules (150 mg) 12 hour before surgery and 1 hour (150mg) before surgery were used. After giving anaesthesia patients were assessed every 2 hours for 24 hours for pain score by VAS scale, BP, pulse rate, respiratory rate, rescue analgesics demand (injection tramadol IV) and side effects if any. In our study only one preemptive dose of 300 mg pregabalin or 1200 mg gabapentin was used instead of two doses at 12 hour intervals. Post-operative respiratory rate was not seen in our study and rescue analgesic used was diclofenac. Patients in pregabalin group had significantly lower mean VAS post operatively and lower rescue analgesic consumption than placebo group (I) (P<0.05) which were near similar to our results. So a conclusion was drawn by them that a 300 mg dose of pregabalin in two divided doses before surgery provided better pain control than placebo, reduce the demand for rescue analgesics. 300 mg single dose of pregabalin, used in our study also accomplished these goals.

Saraswat V et al in 2008 conducted a study on preemptive Gabapentin vs pregabalin for acute postoperative pain after infraumbilical surgery under spinal anesthesia. Patients in Group G were given single dose of gabapentin 1200mg, whereas in Group P were administered pregabalin 300mg one hour prior to administration of spinal anesthesia which was similar to our study. Pain was assessed by visual analogue scale immediate postoperatively and every two hourly thereafter, time since spinal anesthesia to first dose of analgesic (diclofenac) and total dose of analgesic in first 24 hours was recorded, similar to our study. The total postoperative analgesic time was 8.98h in Group G whereas 14.17h in Group P (HS, P < 0.001) and total dose of analgesics in first 24h was 62.5 mg in Group P and 72.5mg in Group G and was not significant (P>.05). In our study total postoperative analgesic time was 9.41±1.84 hrs in Group G whereas 15.38±3.52 hrs in Group P. From the study they concluded that gabapentin and pregabalin, both have been effective in prolongation of postspinal analgesia, but pregabalin more than gabapentin and either can be used as part of multimodal therapy if not as sole analgesic (table 3). In our study this conclusion could be derived.

Table 5 and 6 showed the comparison of the adverse effects between the study groups. In the pregabalin group incidence of somnolence and dizziness were 12.90% and 9.68% respectively, whereas in the gabapentin group incidence of somnolence and dizziness were 22.59% and 19.35%, which were lower in pregabalin group than other. Below we had compared our study with already published studies on preemptive analgesic use of gabapentin and pregabalin for their side effects.

Gajraj reviewed the pharmacology of pregabalin and found that somnolence (29.2%) and dizziness (22.2%) were the most common side effects which were similar to our study, but the % incidence was much lower (12.90% and 9.68%). The incidence of nausea and vomiting was not found in our study. Turan et al showed that the use of oral gabapentin given preoperatively in patients of spinal surgery noticed significant reduction in incidence of vomiting.
(P<0.05) compared to placebo. In 2002, Dirks et al\textsuperscript{31}, studied the effects of single-dose preemptive oral gabapentin versus placebo on post-operative pain and morphine consumption after mastectomy, while we studied on surgery below umbilicus. There was no significant difference in side effects between study groups, whereas in our study vomiting and nausea were absent in the gabapentin group.

**Conclusion**

In conclusion, a single oral dose of pregabalin given preoperatively provides better postoperative pain control and decreases postoperative rescue analgesic consumption compared to single dose of gabapentin, based on lower mean VAS scores at rest. Also, the incidence of somnolence and dizziness were less in the pregabalin group than gabapentin group and their percentage was much lower than those reported in the literature and above all, they were not distressing to the patient. So it can be postulated that pregabalin may effectively be used as a part of multimodal analgesic approach to prevent acute postoperative pain, much like gabapentin, which already has an established role. However, it may be mentioned that further studies are warranted in regard to the most suitable preemptive dose of pregabalin and comparison of pregabalin with gabapentin as preemptive analgesic in other surgeries as well.

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**References**


