Pre Emptive Gabapentin Versus Pregabalin for post Operative Analgesia after Abdominal Hysterectomy under Spinal Anaesthesia

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ABSTRACT
BACKGROUND: Gabapentin and Pregabalin have been used in treatment of neuropathic pain as well as postoperative pain with gratifying results. However there is paucity of studies for comparison with each other. This study was designed to compare their efficacy with respect to increase induration of analgesia, reduction in total post-operative requirements of analgesics and side effects. Sixty patients of ASA grade I or II were randomly allocated to two groups of thirty each. Patients in Group G were given single dose of Gabapentin 600mg, Group P were administered Pregabalin 150mg one hr. prior to administration of spinal anaesthesia. The postoperative analgesic duration (time from spinal analgesia to first analgesic dose) was 4.54 hrs.in Group G, 6.26 hrs. in Group P (p<0.001), whereastotal number of Rescue analgesia given was more in Group G (mean 1.77vs.1.2 in Group P) (p=0.004) and Mean dose of analgesic given was also more in Group G (91mg vs.54.03mg). Nausea, dizziness and rigors were more common in group G. Pregabalin is more effective than Gabapentin, in prolongation of post-spinal analgesia with decreased rescue analgesic requirements and minimal side effects.

Keywords: Pregabalin, Gabapentin, Pre-emptive analgesia, Postoperative pain.

INTRODUCTION
Galen described pain as "A complex multidimensional human perception. It is divine to allay pain".1 Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Acute postoperative pain management is not only a human feeling, but it is a key aspect of postoperative care, as acute pain, regardless of its site, can adversely affect nearly every organ function, and so affects the postoperative morbidity and mortality2 Prevention and treatment of post-operative pain continues to be a major challenge in post-operative care and plays an important role in early mobilization and well-being of the surgical patients. Effective postoperative analgesia results in improvement of respiration and stress on cardiovascular system, early return of GIT motility, early ambulation and discharge from hospital.

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 ORIGINAL ARTICLE

Pre emptive gabapentin versus pregabalin for post operative analgesia after abdominal hysterectomy
pregabalin which are being used for chronic pain are also being used currently for acute pain.3

In order to minimize these side effects, to hasten the onset of sensory and motor block and to improve quality and duration of post-operative analgesia, many adjuvants have been used along with local anaesthetics. There is a need for an adjuvant which increases the duration of analgesia without increasing the duration of motor blockade, thus prolonging post-operative analgesia, reducing post-operative analgesic requirements, facilitating early ambulation, reducing the hospital stay of the patient.3

Pre-emptive analgesia is defined as an antinociceptive treatment that prevents the establishment of altered central processing of afferent input, which amplifies postoperative pain.4 The concept of pre-emptive analgesia to reduce postoperative pain was founded on a series of successful animal experimental studies that demonstrated central nervous system plasticity and sensitization after nociception.5-7 A variety of interventions have been used to achieve a pronounced pre-emptive effect, such as epidural analgesia, peripheral local anaesthetic infiltrations, systemic N-methyl daspartate receptor antagonists, systemic non-steroidal anti-inflammatory drugs and systemic opioids.8,9

Gabapentin is a structural analogue of gamma-amino butyric acid, a secondgeneration anticonvulsant, which was introduced in 1994 as an antiepileptic drug, particularly for partial seizures. Gabapentin is effective in the treatment of chronic neuropathic pain. However, a growing body of evidence suggests that perioperative administration is efficacious for preoperative anxiolysis,10 attenuation of the haemodynamic response to laryngoscopy and intubation, prevention of chronic postsurgical pain, postoperative nausea and vomiting, and delirium. Pregabalin, a structural analogue of gamma-amino butyric acid, shares some characteristics with its predecessor, Gabapentin. Its mechanism of action is probably the same as gabapentin but it has a superior pharmacokinetic profile.11 Its usefulness has already been established in the treatment of peripheral neuropathic pain.12-14 It is claimed to be more effective in preventing neuropathic component of acute nociceptive pain of surgery, to produce more opioid sparing effect and for amelioration of perioperative anxiety. Some studies show some evidence that it may have efficacy in acute pain similar to that of gabapentin.15 Hence, these two drugs have been chosen to compare their efficacy for post-operative analgesia. The aim of present study was to evaluate post-operative analgesic benefit in patients administered gabapentin or pregabalin as premedication for surgery under spinal anaesthesia and to compare their postoperative efficacy with respect to duration of analgesia, total post-operative requirements of analgesics and study side effects and complications, if any attributable to these drugs.

MATERIAL AND METHOD

This study was conducted in Dhiraj hospital in department of Anaesthesiology. In a prospective randomized study 60 patients were scheduled for abdominal hysterectomy ranging from 20-60 years in grade I and II of American Society of Anaesthesiologist's (ASA) classification and allocated randomly into two equal groups and analysed the data statistically after clearance from the ethical committee. Patients were subjected to pre anaesthetic assessment and informed consent was obtained from all patients.

Patients in Group G were given single dose of the gabapentin 600 mg whereas in Group P single dose of pregabalin 150 mg per oral 1 hr. prior to administration of spinal anaesthesia in patients undergoing abdominal hysterectomy. Routine monitoring in the form of NIBP, Pulse oximetry and ECG were applied. All the patients were preloaded with Inj. RL 10ml/kg body weight. Spinal anaesthesia was instituted with 3.5 ml of 0.5% bupivacaine. No other premedication, analgesic or the sedative drugs were given during the surgery. Patients were monitored intra operatively for pulse rate, blood pressure, SpO2, ECG and any complications. Pain was assessed by visual analogue scale immediate postoperatively...
Preemptive gabapentin versus pregabalin for post operative analgesia after abdominal hysterectomy

and every 2 hrly thereafter. Any patient with the visual analogue scale more than 3 was given Inj. diclofenac 1mg/kg IM. Time since spinal anaesthesia to the first dose of analgesic and total dose of analgesic in first 24 hrs. was recorded. Any complications like dizziness, somnolence, vomiting, confusion, vertigo, visual disturbances and urinary retention were recorded in first 24 hrs.

RESULTS

Statistical methods

Data were collected and analysed using SPSS® computer software version 12.0. Numerical variables were presented as mean & standard deviation (SD) while categorical variables were presented as percent. As regard numerical variables; unpaired student – t test was done. P value <0.05 was considered statistically significant.

Sixty patients, thirty in each group were included in the study and analysed. The groups were comparable with respect to demographic characteristics like age, weight, physical status and duration of surgery [Table 1]. The intraoperative hemodynamic values i.e. mean blood pressure, heart rate and SpO2 were similar (p>0.05) in both groups at all measured times.

The total postoperative analgesic duration (time from spinal analgesia to first dose of analgesic) was 4.54h in Group G whereas 6.26h in Group P, which was highly significant (p<0.001) [Table 2].

Rescue analgesia was not required in 1 (3.3%) case in Gabapentin Group (G) whereas 4 (13.3%) cases in Pregabalin Group (P). Among those who required analgesia, maximum proportion of patients requiring one dose only was seen in Group P (n=19, 63.33%) while in Group G the proportion of patients requiring 2 doses was maximum (n=22; 73.33%). Statistically, the number of patients requiring 2 doses of rescue analgesia was significantly higher in Group G as compared to Group P (p=0.15). [Table 3]

Total number of analgesic doses given in first 24h was lower in Group P (mean 1.2 as against 1.77 in group G) statistically significant.

Mean dose of analgesic given in first 24 hrs was lower in group P (54.03mg as against 91 mg in group G) which was statistically significant.

Pain scores were similar, as patients were given analgesics immediately on reaching the VAS scale of three.

The incidence of side effects was significantly higher amongst Group gabapentin (G) as compared to Group pregabalin (P), however they were minor and easily controllable. Nausea was observed in both the study groups, with predominance in the gabapentin group (G) 33.3% vs. 16.67% in pregabalin group. Rigors were seen in 6.67% of patients in gabapentin group as compared to 0% in pregabalin group. Group G had more no. of cases of dizziness followed by Group P. Only a single patient in Group G complained of Visual disturbances (3.33%). Bradycardia, Headache, and Vomiting was noticed in 3.33% patients each in gabapentin group.

Hypotension was noticed in 3.33% of cases in each group while only 3.33% of cases experienced Somnolence in pregabalin group.

Table: 1 Comparison of patient’s characteristics

<table>
<thead>
<tr>
<th>Demographic Data</th>
<th>Mean ± SD</th>
<th>P value</th>
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<tbody>
<tr>
<td></td>
<td>Group G</td>
<td>Group P</td>
</tr>
<tr>
<td>Mean Age (years)</td>
<td>41.73 ± 7.72</td>
<td>40.46 ± 6.03</td>
</tr>
<tr>
<td>ASA II</td>
<td>23.7 ± 25.5</td>
<td>25.5 ± 30.16</td>
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<tr>
<td>Mean Wt. (kg)</td>
<td>50.63 ± 8.45</td>
<td>52.63 ± 10.15</td>
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</tbody>
</table>

Table: 2 Time from Spinal to Rescue Analgesia (in hours)

<table>
<thead>
<tr>
<th>Duration of Analgesia</th>
<th>Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group G</td>
<td>Group P</td>
</tr>
<tr>
<td>Total time from Spinal</td>
<td>4.54 ± 0.485</td>
<td>6.26 ± 0.382</td>
</tr>
</tbody>
</table>

Table: 3 Comparison of post operative analgesia in both groups

<table>
<thead>
<tr>
<th></th>
<th>Group G</th>
<th>Group P</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.O. Surgery(min)</td>
<td>88.83 ± 30.61</td>
<td>97.83 ± 38.34</td>
<td>0.319</td>
</tr>
<tr>
<td>D.O. Analgesia (hrs)</td>
<td>4.54 ± 0.485</td>
<td>6.26 ± 0.382</td>
<td>0.000</td>
</tr>
<tr>
<td>No of doses in 24 hrs</td>
<td>1.77 ± 0.68</td>
<td>1.20 ± 0.847</td>
<td>0.004</td>
</tr>
<tr>
<td>D.O. Total dose of Analgesic (mg)</td>
<td>91.00 ± 31.13</td>
<td>54.03 ± 28.65</td>
<td>0.000</td>
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</tbody>
</table>
DISCUSSION

Preemptive 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. 17,18,19,20

Recent studies 19,21 suggest that gabapentinoids may be useful in the perioperative setting, as an adjuvant to parenteral opioids. This study shows a different mechanism, using gabapentinoids as adjuvants to regional analgesia. 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. 21,22

Anand 23 in a study concluded that pregabalin in doses of 150mg and 225mg used preemptively offers good postoperative pain control and decreases the requirement of analgesics in the first 24 hrs after spinal anaesthesia. Higher doses of pregabalin 225mg was associated with increased incidence of adverse effects.

Hence single highest safe dose of pregabalin (150mg) was selected for this study, which is same as used in most of the studies 17,25,26,27 the antihyperalgesic effects of pregabalin have been observed at dosages twofold to fourfold lower than that of gabapentin in rodent models of neuropathic pain 28,29. Our purpose of choosing gabapentin 600 mg was also to find whether a dose below the already tested dose of 1200 mg could be equally efficacious at the cost of less side effects as the absorption of gabapentin is limited by saturable, active, dose-dependent transport in the gastrointestinal tract 30. So the doses for two drugs was selected that is 150mg for pregabalin and 600mg for gabapentin. All these trials justified the equipotent doses of pregabalin and gabapentin used in the present study.

Our study shows that, in infraumbilical surgery, in absence of opioid or nonopioid analgesics, gabapentin and pregabalin, when given preoperatively, prolong the analgesic effects of spinal analgesia, which far exceeds the normal duration of spinal analgesia. The analgesic effect is longer lasting following pregabalin as compared to gabapentin (4.5 h in Gabapentin group Vs 6.26h in Pregabalin group). The difference in two groups was highly significant.

Total number of analgesic doses and total dose of analgesic in first 24h were lower in Pregabalin group, the difference was statistically significant. The limitation of the current study design is that single dose of gabapentin and pregabalin has been used. The half-life of these drugs is 5-7 hours and conclusions about the optimal dose and duration of the treatment cannot be made. Although pregabalin has been more effective than gabapentin in the present study, further studies are needed to determine the long-term benefits, if any, of perioperative gabapentin and pregabalin comprehensively. The real challenge in the clinical setting is not simply to minimize the dose of analgesic drug, but to minimize long-term complications and occurrence of chronic pain syndromes within weeks or months after surgery.

This study shows that, in infraumbilical surgery, Gabapentin and Pregabalin, when given preoperatively, prolong the analgesic effects of spinal analgesia, decrease rescue analgesic requirements study groups. The analgesic effect is longer lasting following Pregabalin as compared to Gabapentin (4.54 hrs in Group G, 6.26hrs in Group P), which was highly significant (p<0.001), with minimum side effects.

To conclude, gabapentin and pregabalin, both can be an effective tool in the armamentarium of anaesthesiologist in treatment of perioperative pain. It can be
used as part of multimodal therapy if not as sole analgesic.

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