Evaluation of role of preoperative oral pregabalin on postoperative pain in patients undergoing total abdominal hysterectomy

ABSTRACT

"Pain is a more terrible lord of mankind than even death itself" said noble laureate Albert Schweitzer. Pain is perhaps the most feared symptom of disease, which man is always trying to alleviate and conquer since ages. The relief of pain has been the fundamental aspect of the practice of anaesthesiology.

Wolf CJ & Max MB et al 3,4 in 1993, observed that hyper sensitisation contributing to post-operative pain can be controlled by blocking the initial nociceptive input to the spinal cord. This is the main rationale behind pre-emptive analgesia. 1 Pre-emptive analgesia is more effective than similar analgesia initiated after surgery. As pre-emptive analgesia, local anaesthetics, opioids, NSAIDS, gabapentin, pregabalin, clonidine and dexmedetomidine drugs are used.

Pregabalin, a precursor of gabapentin 3, is a structural analogue of inhibitory neurotransmitter alpha/gamma-aminobutyric acid. It binds to alpha-2-delta subunit of voltage gated calcium channels, reducing the release of several excitatory neurotransmitter & blocks the development of hyperalgesia & central sensitization. Pregabalin has anti-convulsant, anxiolytic, antiallodynic & anti-hyperalgesic properties.5,7,9,11,12 It is more potent than gabapentin with fewer side effects and better pharmacokinetics. The aim of this research was to study the effect of preoperative oral pregabalin on postoperative pain in patients undergoing elective total abdominal hysterectomy, as compared with a placebo.

Methodology: This study is a prospective, randomized, double blind placebo controlled study, approved by the Hospital Ethical Committee. The Aims and Objectives of study were to study the effect of preoperative oral pregabalin on postoperative pain in patients undergoing total abdominal hysterectomy & to study the side effects of preoperative oral pregabalin. The study included 74 ASA Grade I & II patients, posted for elective total abdominal hysterectomy under spinal anaesthesia, lasting up to 2 hrs.

Patients having any contraindication to spinal anaesthesia, not willing to participate in the study & those on analgesics, sedatives & psychiatric drugs were excluded. 74 patients were randomly divided into 2 groups:

Group G1 : Received Cap.Pregabalin 300mg
Group G2 : Received Cap.Placebo

A detailed pre-anaesthetic evaluation was done & a written informed consent obtained. An hour before surgery, in pre anaesthetic room, vitals were recorded & assigned drugs were given. Preoperative sedation was determined by Ramsay sedation score. Inside the OT, patients were preloaded with ringer lactate solution 10ml/kg. Spinal anaesthesia was administered with 3.5ml of 0.5% bupivacaine(Heavy). Intraoperatively heart rate, blood pressure, respiratory rate & SpO2 were recorded. The time of completion of surgery was noted & was considered as zero hour for studying post-operative pain. The following were recorded:

1) Sedation Score
2) VAS Score
3) Time for requirement of first analgesic.
4) Comparison of dose of analgesic required (in 24hrs)
5) Patient satisfaction score (On a scale of 1 to 5)
6) Quality of analgesia as experienced by patients (good, satisfactory or poor).
7) Postoperative side effects

Patient was shifted to PACU post-operatively & observed for 24hrs. When patient first complained of pain, time was noted along with VAS score. At a VAS score >4, injection diclofenac im 75mg was given & if VAS score remained >4, injection tramadol 1mg/kg was given. After this, VAS monitoring was done at 2 hourly intervals, and doses repeated when VAS>4 and tramadol was used for rescue analgesia, if needed. Total number & doses of diclofenac & tramadol boluses within 24 hours was noted.

Following parameters were noted postoperatively:
1) Quality of anesthesia intraoperatively
2) Quality of postoperative analgesia from VAS score at 0 hr, then hrly till first 8 hours, then 2 hrly till 12 hrs & 4 hrly thereafter till 24 hrs.
3) Time of first analgesic required.
4) Total number of inj.diclofenac doses & injection tramadol boluses within 24 hours
5) Patient satisfaction score at 2,4,8,12 & 24hrs
6) Incidence of side effects

Statistical analysis: Continuous variable between two groups were compared by unpaired t test. VAS score, amount of analgesia required and patient satisfaction score were compared by performing Mann-Whitney test. Categorical variables were compared by performing Chisquare test. Quality of anaesthesia was also better in Pregabalin group than the placebo group.

KEYWORDS

"It is easier to find men who will volunteer to die, than to find those who are willing to endure pain." This quote by Julius Caesar precisely sums up the importance of relieving pain. This prospective, randomized, double blind placebo controlled study aims to study the effect of preoperative oral pregabalin on postoperative pain in patients undergoing total abdominal hysterectomy. 74 patients, posted for total abdominal hysterectomy under spinal anaesthesia, were divided into two groups, receiving Pregabalin 300mg or placebo one hour prior to surgery. Pregabalin group & placebo group had VAS score 4 until 7hrs & VAS score 4 after 3hrs postoperatively, required first rescue dose of Diclofenac at 450 mins & 129.71mins respectively. Quality of anaesthesia was better in Pregabalin group than the placebo group.
Preoperative sedation score was significantly (p<0.05) more in patients receiving 300 mg pregabalin than placebo. (Table 1)

<table>
<thead>
<tr>
<th>Post-operative time/hrs</th>
<th>VAS Score (mean±SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>0</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>1</td>
<td>1.06±0.00</td>
<td>1.43±0.55</td>
</tr>
<tr>
<td>2</td>
<td>3.11±0.92</td>
<td>4.30±0.79</td>
</tr>
<tr>
<td>3</td>
<td>4.30±0.92</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5.00±0.89</td>
<td></td>
</tr>
</tbody>
</table>

Group 2 required first analgesic at mean time of 129.71 mins compared to Group 1 who required at 450 mins; the difference being statistically significant. (Table 2)

<table>
<thead>
<tr>
<th>No of analgesia doses</th>
<th>Number of patients (%)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Group 1</td>
</tr>
<tr>
<td>1</td>
<td>29 (82.85%)</td>
</tr>
<tr>
<td>2</td>
<td>06 (17.14%)</td>
</tr>
<tr>
<td>3</td>
<td>00 (0.00%)</td>
</tr>
</tbody>
</table>

Patients postoperative satisfaction score which was >1 but <2 in Group 2 up to 24 hrs postoperatively. The score was >3 in Group 1 up to 4 hours but <3 till 24 hrs

Initially 74 patients were included in study, but in 4 patients quality of anaesthesia was poor & had to be converted to general anaesthesia. Hence, only 70 patients were considered. When compared with quality of anaesthesia it was good in maximum number of patients, in Group 1, whereas quality was satisfactory in maximum number of patient in Group 2. (Table 4)

<table>
<thead>
<tr>
<th>Quality of anaesthesia</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>20</td>
<td>06</td>
</tr>
<tr>
<td>Satisfactory</td>
<td>15</td>
<td>29</td>
</tr>
<tr>
<td>Poor</td>
<td>00</td>
<td>04</td>
</tr>
</tbody>
</table>

The side effects like somnolence and dizziness was not observed in any group. 85.7% and 11.42% of patients amongst the control group had vomiting and nausea respectively.

Discussion: Most of the drugs, used for the treatment of postoperative pain have side effects, which limits there use in clinical practice; demanding a new drug which significantly prevents central sensitization, improves the quality of opioid analgesia, reduces opioids requirement, prevents or reduces opioids tolerance, relieves anxiety, does not depress respiration & has no effect on the gastric mucosa, platelets and renal function.
In our study, in G2 & G1, the minimum amount of analgesic hours required postoperatively was 150mg & 75mg, with mean of 218.57mg & 87.85mg, respectively, the difference being statistically significant. E Engelman et al,201110 found that the total requirement of analgesics postoperatively was much less in pregabalin group than when they used oral pregabalin for preemptive analgesia for various surgeries. Pradeep Jain et al,201146, A Agarwal et al,200847 while studying the role of oral pregabalin in reducing postoperative pain also had comparable observations.

In our study, patient satisfaction score was > 1 but <2 upto 24hrs postoperatively in G2. However, the patient satisfaction score in G1 was >2 throughout postoperative period upto 24 hours, showing that the patients receiving oral pregabalin were more satisfied. Monica Kohli et al,201145 support our findings, who also found patient satisfaction was better in pregabalin 300 mg group.

It was observed that quality of anaesthesia was significantly better in G1 than G2. No studies in literature have commented about quality of anaesthesia intraoperatively.

The side effects like somnolence and dizziness were not observed in any of the patients in the study.

In our study, 8.57% and 11.42% of patients in G2 had vomiting & nausea respectively. Engelman E et al,201110 found that pregabalin 300mg when given preoperatively had a role in reducing the incidence of postoperative nausea and vomiting. This finding in our study supports the finding of our study. Godrat Akhavanakbari et al,201348 also had similar observations.

**Conclusion.** To conclude, the present study suggests that 300mg preoperative oral Pregabalin can be used effectively for reducing postoperative pain with minimal side effects in patients undergoing total abdominal hysterectomy.

**References:**