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Original Research Article

Comparative Effects of Oral Pregabalin and Gabapentin on Postoperative Pain and Analgesic Consumption After Abdominal Hysterectomy- A Randomised Trial

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Abstract

Objectives: This study was designed to evaluate and compare the efficacy of a single preoperative doseb of pregabalin and gabapentin for attenuating postoperative pain and analgesic consumption after abdominal hysterectomy.

Methods: 60 patients of ASA grade I or II were randomly allocated to three groups, with 30 patients in each group. Patients in Group P were given Pregabalin 300mg, Group G were given Gabapentin 900mg 1 hour prior to surgery. Postoperative pain was assessed by a 100mm visual analogue scale.

Results: Postoperative pain and postoperative analgesic consumption was reduced in the pregabalin and gabapentin group compared ($P<0.05$).

Conclusion: A single preoperative oral dose of Pregabalin 300 mg and Gabapentin 900mg is an effective method for reducing postoperative pain and analgesic consumption in patients undergoing elective abdominal hysterectomy. Pregabalin is a better pre-emptive analgesic as compared to Gabapentin for decreasing post-operative analgesic consumption.

Keywords: postoperative pain, pregabalin and gabapentin, abdominal hysterectomy, preoperative dose.

1. INTRODUCTION

Galen described pain as "A complex multidimensional human perception. It is divine to allay pain". Postoperative pain, regardless of its site, can adversely affect nearly every organ function, and so affects the post operative morbidity and mortality. Postoperative pain also affects recovery from surgery and anaesthesia. Prevention and treatment of postoperative pain continues to be a major challenge in postoperative care and plays an important role in the early mobilization, shortened hospital stay, reduced hospital costs and wellbeing of the surgical patients.

Gabapentin is a structural analogueof gammaamino butyric acid, which was introduced in 1994 as an antiepileptic drug, particularly for partial seizures. Large placebo-controlled,doubleblind trials confirmed their effectiveness in neuropathic post-herpetic pain. Despite its name, gabapentin does not bind at the GABAA or GABAB receptor. However, it has a high binding affinity forthe α2 δ subunit of the presynaptic voltage-gated calcium

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channels which inhibits calcium influx and subsequent release of excitatoryneurotransmitters in the pain pathways.

Pregabalin is a structural analogue of gammaamino butyric acid, which shares some characteristics with its predecessor, gabapentin. Its mechanismof action is probably the same as gabapentin but it has a superiorpharmacokinetic profile. Its usefulness has already been established in the treatment of peripheral neuropathic pain. 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. The efficacy of pregabalin for treating symptoms of generalized anxiety disorder has been demonstrated in several clinical trials. There are initial studies showing some evidence thatit may have efficacy in acute pain similar to that of gabapentin.

Abdominal hysterectomy is one of the most common gynecologicsurgery that is associated with moderate to severe postoperative pain and requires multimodal analgesia.The analgesic effects of gabapentin and pregabalin have been investigated widely in surgical settings during the past few years.The findings of these trials suggest that gabapentin and pregabalin have analgesic effects in postoperative pain management. With this background in mind, we designed this study to compare pre-emptive Pregabalin with Gabapentin for post operative analgesia in abdominal hysterectomy.

2. METHODS

This prospective, randomized clinical study was designed to include 60 patients, ASA physical status I and II, undergoing elective abdominal hysterectomy. The study protocol was approved from the institutional ethical committee and written informed consent was obtained from all the patients. Patients having any known allergy to gabapentin or pregabalin, epilepsy, chronic pain syndrome, impaired renal function, any history of psychiatric disease and substance abuse were excluded from the study. In Pre-anaesthetic visit patients were familiarized with the use of a 100mm linear VAS for pain. Patients were randomly assigned into two study groups: Group G and P. Patients in group P received pregabalin 300 mg, Group G Patients received gabapentin 900 mg, 1 hour before surgery. All the medications were identical, and administered orally, 1 h before the induction of anaesthesia with sips of water. Rescue analgesia in PACU was given using IV tramadol 1mg/kg and time to first analgesic request was noted, this was the time from the end of the surgery to the first registration of VAS score (1- 10) $\geq$ 3. In the ward, postoperative pain was again assessed using VAS scores at 4, 8, 12 and 24 hours after surgery. Primary outcomes were severity of postoperative pain and postoperative analgesic requirement. Secondary outcomes were incidence of sideeffects such as (PONV), sedation, drowsiness and dizziness if any.

Statistical Methods

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Statistical software SPSS (version 20.0) and Microsoft Excel were used to carry out the statistical analysis of data. Continuous variables were summarized in the form of means and standard deviations and categorical variables were summarized as percentages. Analysis of variance (ANOVA) was employed for inter group analysis of data and for multiple comparisons, least significant difference (LSD) test was applied. Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables. A P-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

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3. RESULTS

Sixty patients, thirty in each group, were included in the study and analyzed. 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

Table 1 Patient variables [Values are mean (SD), number]

	Group G	Group P	P value
Age (Yr)	50.7±6.17	53.4±5.13	P>0.05 (NS)
Weight(Kg)	67.5 (9.90)	61.67 (9.27)	P>0.05 (NS)
Physical status ASA I/II	23/7	22/8	P>0.05 (NS)
Duration of surgery (Min)	51.17(23.66)	48.17(27.68)	P>0.05 (NS)

(P>0.05) in the two groups at all measured intervals
The total postoperative analgesic duration (time to first dose of analgesic) was 8.98h in Group G whereas 14.17h in Group P, which was highly significant (P < 0.001) (Table 2) .

Table 2 - Comparision of post operative analgesia and side effects[values are mean(SD), number(%)]

	Group G	Group P	P value
Time to rescue analgesia (h)(HS)	8.96 (5.38)	14.15 (6.67)	P < 0.001
Mean no. of doses	1	0.9	P>0.05
Total dose of Analgesic (mg)	72.4 (23.99)	62.4 (28.43)	P<0.01
Side effects			
Nausea/Vomiting	2(6.7%)	2 (6.7%)	0.308
Dizziness	4 (17%)	3 (14%)	P>0.05 (NS)

Table 3: Comparison of pain scores using VAS among the study groups.

Time Interval	Group P	Group G	P value
I hr	2.77±1.194	3.63±1.732	<0.001*
4 hrs	1.83±1.117	2.67±1.470	<0.001*
8 hrs	1.03±0.615	1.57±0.774	<0.001*
12 hrs	0.57±0.568	0.70±0.702	<0.001*
24 hrs	0.40±0.498	0.53±0.507	<0.001*

Postoperative pain scores using VAS showed statistically significant difference among the two groups (P<0.05] with Pregabalin group having the least VAS scores for pain (Mean±SD).

4. DISCUSSION

Pre-emptive analgesia prevents the establishment of altered central processing of afferent input which amplifies postoperative pain.18 It consequently decreases the incidence of hyperalgesia and allodynia after surgery. In our study we compared pre-emptive pregabalin

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with gabapentin for post operative analgesia in patients undergoing abdominal hysterectomy. The quality of analgesia was assessed using VAS at 1hr, 4hrs, 8hrs, 12hrs, and 24hrs postoperatively and our results showed that there was statistically significant difference in mean VAS scores among the three groups ($P < 0.05$).The quality of analgesia was better in Pregabalin group, followed by Gabapentin group. Our results are in concordance with the results of Pandey CK et al.

Agarwal et al. in their study found that a single preoperative oral dose of pregabalin 150 mg is an effective method for reducing postoperative pain in patients undergoing laparoscopic cholecystectomy. 19 In our study the mean time to first rescue analgesia (minutes) was compared among the two groups and found to be statistically significant (p value <0.05)

In our study the percentage of patients who received tramadol as rescue analgesia was compared and this difference was statistically significant (p value< 0.01). Our results showed that Pregabalin group had the least requirement of rescue analgesia in PACU, followed by Gabapentin group. Anju Ghai et al. in their study found that the difference in the consumption of diclofenac and tramadol between study groups (pregabalin and gabapentin group) and control groups was statistically significant (p>0.001).20 Similarly, Induja Rajendran et al.21 in their study found that consumption of tramadol as rescue analgesia was less in pregabalin and gabapentin groups compared to control and this difference was statistically significant ($P < 0.001$).22

We compared the mean consumption of paracetamol (mg) and found that Pregabalin group had the least mean paracetamol (mg) consumption, followed by Gabapentin group. Our results are in accordance with the results of Michael G.F. Rorarius et al. who in their study found that preemptive Gabapentin reduced the need for additional postoperative pain treatment (PCA boluses of 50 mg of fentanyl) by 40% during the first twenty postoperative hours. 23 Dirks et al. who in their study concluded that a single dose of 200 mg oral Gabapentin administered preoperatively result in a 50% reduction in postoperative morphine consumption 2 and 4 hour after radical mastectomy. 24

Our results are in accordance with the results of A. Agarwal et al who in their study found that the incidence and severity of PONV and number of patients requiring antiemetics was similar among the study and control groups ($P<0.05$). 25 We observed that both pregabalin and gabapentin were associated with significant drowsiness and dizziness. Our study is in accordance with the findings of Saraswat V et al. who in their study compared the efficacy of Gabapentin and Pregabalin and found that dizziness and somnolence were the only side effects noticed in both groups. 26

5. CONCLUSION

A single preoperative oral dose of Pregabalin 300 mg and Gabapentin 900mg is an effective method for reducing postoperative pain and analgesic consumption in patients undergoing elective abdominal hysterectomy. Pregabalin is a better pre-emptive analgesic as compared to Gabapentin for decreasing post-operative analgesic consumption.

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