Section: Anaesthesiology

Original Research Article

A PROSPECTIVE RANDOMIZED TRIAL TO COMPARE THE EFFECTS OF ORAL PREGABALIN AND GABAPENTIN ON POST-OPERATIVE PAIN AND ANALGESIC CONSUMPTION AFTER ABDOMINAL HYSTERECTOMY

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Abstract

Background: Preemptive analgesia involves the introduction of an analgesic regimen before the onset of noxious stimuli to avoid sensitization of the nervous system to succeeding stimuli that could intensify the pain. The study aims to compare the efficacy of Pregabalin and Gabapentin as preemptive analgesics in patients undergoing elective abdominal hysterectomy under spinal anaesthesia. **Materials and Methods:** Sixty patients scheduled for elective abdominal hysterectomy under spinal anaesthesia were randomly allocated into two groups. Group G (n=30) received a single dose of Gabapentin 600mg orally one hour before surgery, and Group P (n=30) received a single dose of Pregabalin 150mg one hour before surgery. Post-operative pain score, sedation score, time for first analgesic requirement, and 24-hour analgesic requirements were compared. **Result:** In the 24 hrs of the post-operative period, the mean VAS score at rest of Group P was significantly lower than Group G in the first 4 hours of the post-operative period (P <0.05). The mean Ramsay sedation score was significantly higher in Group P than in Group G in the first 4 hours of the post-operative period (P <0.05). The time for a first analgesic requirement in Group P (600±150.13 mins) is significantly lower than in Group G (519.67±155.55 min P-value is 0.046.24 Hrs). The total dose of Tramadol requirement was significantly lower in Group P (203.33±71.84) than those Group G (246.67±81.93). **Conclusion:** Pre-emptive use of Pregabalin 150mg is better than gabapentin 600mg in the first 4 hours of the post-operative period with a prolonged duration of post-operative analgesia.

INTRODUCTION

Adequate post-operative pain relief must be a vital part of administering anaesthesia. Reducing medicine dosage, decreasing adverse effects, and offering adequate pain relief are the main objectives of post-operative pain management. Anti-hyperalgesic medications can alleviate post-operative pain by avoiding the hypersensitive central nervous system since surgical stimulation is connected to peripheral and central sensitization. Pregabalin and gabapentin have been used extensively in trials to reduce post-operative pain based on our understanding of post-operative pain management.[1]

Gamma-aminobutyric acid (GABA), first made available as a medication for epilepsy, has a structural equivalent in gabapentin. It binds to the widely dispersed voltage-gated calcium channels' 2-protein subunit in the central and peripheral nervous systems. This prevents calcium influx and lessens the release of excitatory neurotransmitters in pain pathways.[2] Pregabalin has an amino acid substitution at position three that enhances lipid solubility and diffusion across the blood-brain barrier, improves pharmacokinetic profile, and reduces drug interactions because hepatic metabolism is absent.[3] It functions as a better ligand for the 2-protein subunit than gabapentin and is a more potent and effective counterpart of gabapentin.[4] In neuropathic pain models in rodents, it has demonstrated greater analgesic effectiveness than gabapentin.[5]

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At considerably lower doses than gabapentin, pregabalin is just as effective. Due to low intersubject variability and significantly increased bioavailability (90 percent vs. 33–66 percent).[6] Both the hepatic and plasma protein metabolism of pregabalin are absent.[7,8] It doesn't stimulate or suppress liver enzymes like the cytochrome P450 system. Therefore, pregabalin is unlikely to be the topic of pharmacokinetic drug-drug interaction research or cause such studies. Its elimination half-life ranges from 5.5 to 6.7 hours, and the kidneys nearly eliminate it unaltered (2% metabolism). This is not the case with gabapentin, as it has been discovered that plasma concentrations have a non-linear relationship to higher doses. Five to nine hours is the elimination half-life.[9]

So far, evidence of the analgesic properties of pregabalin and gabapentin in post-operative pain is limited to controlled randomized trials conducted in patients of dental pain, minor and day-case gynaecological surgery, laparoscopic hysterectomy, and hip arthroplasty.[10-14] Thus, the present study aims to compare the efficacy of pregabalin and gabapentin as preemptive analgesics in patients undergoing elective abdominal hysterectomy under spinal anaesthesia pain scores & time to first analgesic requirement.

MATERIALS AND METHODS

This Prospective Randomized Trial was conducted at K.A.P.V. Govt. Medical College, Trichy, involving 60 patients undergoing elective abdominal hysterectomy. After obtaining Institutional ethical committee clearance, informed consent was obtained from all patients.

Inclusion criteria: Those patients undergoing elective abdominal hysterectomy aged between 35-65 years of ASA physical status 1 & 2 were included.

Exclusion criteria: Patients with contraindications for pregabalin and gabapentin, those with central nervous system disorders, and chronic pain were excluded.

The patients were randomized into two groups of 30 using a computer-generated table of random numbers. Patients in Group P received 150 mg of pregabalin, and Group G received Gabapentin 600mg one hour before surgery with sips of water.

All patients were familiarized with a 10cm linear Visual analogue scale (VAS) with 0= No pain and 10= Worst pain the evening before surgery (Figure 1). All patients received Inj. Ranitidine 50mg i.m. and Inj. Metoclopramide 10mg i.m. 45 minutes before surgery as premedication and preloaded with 10ml/kg of Ringer lactate. After connecting standard Monitors like ECG, NIBP, and Pulse oximetry, all patients were positioned in the right lateral decubitus position. Spinal anaesthesia was instituted with 17.5 mg of 0.5% hyperbaric bupivacaine in L3-L4 space using a 25G Quincke needle.

At the end of the surgery, patients were shifted to the ward. Post-operative pain & sedation was assessed with VAS score (Figure 1) and Ramsay sedation score (Table 1), respectively, in the interval of 0,1,2,3,4,6,9,12 and 24 hours.

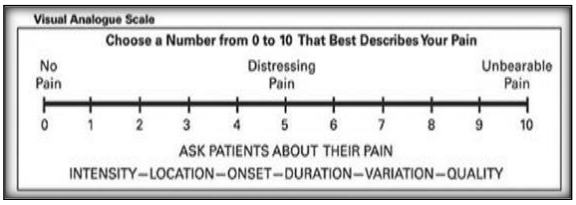

Figure 1: Visual Analogue Scale

Table 1: Ramsay Sedation Score

Awake levels	Asleep levels
1- Anxious, Agitated	4-Brisk response
2-Oriented, cooperative, Tranquil	5-Sluggish response
3-Responds to command	6-No response

The time required for the first analgesic (VAS >4) from the time of spinal anaesthesia and 24 hours analgesic requirement was noted. If the VAS Score is four or more, they were supplemented with 2mg/kg of Inj.Tramadol i.m. Side effects of the drugs, like nausea and vomiting, were noted and treated with Inj. Ondansetron 4mg i.v.

All data were analysed using the statistical software SPSS using Student's t-test and other appropriate tests. A p-value of <0.05 was considered statistically significant.

RESULTS

The demographic profile regarding age, height & weight were comparable between the two groups. [Table 2]

Table 2: Demographic Variable

Parameter	Mean ± S.D.		p-value
	Group p	Group G	
Age	49.67 ± 6.53	49.90 ± 5.59	0.882
Height	152.77 ± 7.14	152.30 ± 6.37	0.79
Weight	59.30 ± 7.48	62.43 ± 8.90	0.145

Table 3. Post-operative analgesia & analgesic consumption

Parameter	Mean ± S.D.		p-value
	Group P	Group G	
Time for first rescue analgesia (in minutes)	600.00 ± 150.13	519.67 ± 155.55	0.046
24-hour Tramadol used (in mg)	203.33 ± 71.84	246.67 ± 81.93	0.033

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All patients were monitored for VAS scores at rest in the immediate post-operative period (0 Hours), 1,2,3,4,6,9,12 and 24 hours postoperatively [Figure 2]. The mean VAS score for 4 hours in group P was less than group G ($p<0.05$). This shows a significant reduction in the mean VAS score in patients receiving Pregabalin premedication compared to the Gabapentin group in the first 4 hours after surgery.

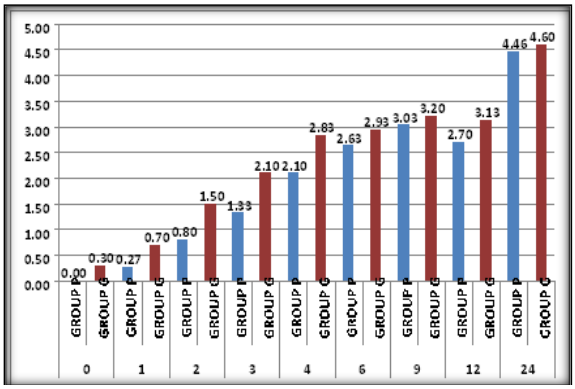

Figure 2. Comparison of VAS score

The mean sedation scores at 4 hours post-op were 1.63 and 1.17 in groups P & G, respectively, with $p<0.001$ [Figure 3]. This shows that level of sedation was significantly higher in Group P compared to Group G up to 4 hours.

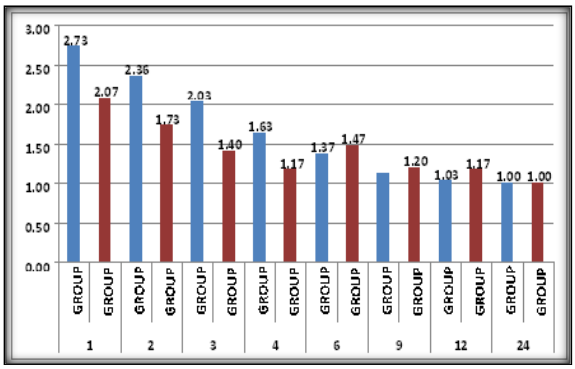

Figure 3: Results - Ramsay Sedation Score

The time interval between spinal anaesthesia and rescue analgesia in group P was 600.00 minutes compared to group G, which was 519.16 with a p-value of 0.046 [Table 3]. We observed that pregabalin gives more prolonged pain relief compared to gabapentin.

The total dose of tramadol requirement for 24 hours post-operative period was calculated. The total dose of tramadol requirement for 24 hours was 203.33 mg and 246.67mg in groups P & G, respectively, with a p-value of 0.033, reflecting the better analgesic effect of pregabalin over gabapentin.

Regarding the side effects, only two patients developed nausea and vomiting in group P in contrast to 5 in group G, but this was not statistically significant. The number of patients that experienced dizziness was 3 and 7 in groups P and G, respectively ($p>0.05$).

DISCUSSION

Post-operative pain is the main reason for many complications like delayed recovery, metabolic alterations, anxiety, and stress in the patients. Patient dissatisfaction also occurs due to post-operative pain. Hence several methods are used to provide post-operative pain relief, and many studies have been conducted to identify the effectiveness of these pain relief methods. The goal of multimodal analgesia is to reduce the dosage and side effects of opioids. Such preemptive analgesics like gabapentinoids are very effective in reducing the dose of opioids in patients who require post-operative pain relief for a prolonged duration.

Hence, this prospective, randomized, comparative clinical study compared the effects of preemptive analgesics Pregabalin and Gabapentin. This study selected 60 patients undergoing Abdominal hysterectomy under spinal anaesthesia. They were randomly allocated into two groups, Group P received Pregabalin 150 mg, and Group G received Gabapentin 600 mg 1 hour before surgery.

The dose of these drugs was chosen based on a similar study by Bafna et al.[15] Many other studies,[16-18] have tried various doses of pregabalin, from 150 to 300 mg, and observed that 150 mg is the correct dose with the least side effects. Similarly, different doses of gabapentin have been used (600 to 1200 mg), and the lowest effective dose of gabapentin is 600 mg.[18] This study followed the standard anaesthetic protocol for all the patients. The patients of the two groups were comparable in all demographic characteristics (age, sex, height, and weight). The two groups were also comparable with ASA physical status and comorbid conditions.

The mean VAS scores were significantly less in group P than in group G up to 4 hours. These results are in conjunction with other studies by Ghai A et al. [19] and Chaudhuri A et al. [20]. The sedation scores were higher in Group P than in Group G in our study, similar to those observed in Rajendran et al. [21]. In contrast, Pandey et al. [18] found that the gabapentin group had increased sedation. This difference may be due to the increased doses of the drugs used in their study.

The time interval for the first analgesic requirement in Group P was 600 minutes; in Group G, it was 519.67 minutes. Both drugs resulted in increased post-operative analgesia. Pregabalin gives pain relief significantly longer than gabapentin. This finding correlates with the study findings by Saraswat et al,[22] and Bafna et al.[15] The total dosage of rescue analgesic used in the Pregabalin group is less than that in the gabapentin group. This is in conjunction with Ghai A et al,[19] and

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Chaudhuri A et al.[20] Similar to studies by Rajendran et al,[21] and Pandey et al,[18] both groups had minimal nausea and vomiting.

According to Hill et al., 400 mg of ibuprofen and 50 mg of pregabalin were less efficient at reducing pain after dental extractions.[10] With a single preoperative dose of 100 mg pregabalin before minor gynaecological surgery involving the uterus and cervix, Paech et al. did not notice an improvement in analgesia.[11] Additionally, Jokela et al. reported that pregabalin 150 mg premedication in day-case laparoscopic gynaecological surgery did not decrease fentanyl usage.[12]

Limitations

Our study was limited because two different analgesics were being utilised simultaneously. It would have been far preferable to utilise a single drug in addition to a patient-controlled analgesia device, both of which were not accessible at the time.

CONCLUSION

To conclude, the preemptive use of 150 mg of pregabalin provided prolonged pain relief compared to 600mg of gabapentin in patients undergoing elective abdominal hysterectomy with minimal side effects. Future research should be focused on the investigation of a range of doses. Also, more controlled studies are essential to describe the benefits and outcomes of different dosages of these drugs.

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