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Original Research Article

To Study the Pre-Emptive Analgesic Efficacy of Single Low Dose Pregabalin for Postoperative Pain Relief in Patients Undergoing Inguinal Hernioplasty

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Abstract

Introduction: Postoperative pain is one of the most common concern for people undergoing surgery. Preventing and treating postoperative pain is crucial to the patient's early mobilisation and well-being. Pre-emptive analgesia prevents central sensitization caused by incisional and inflammatory damage during surgery and the early postoperative period and has the potential to be more effective than a similar analgesic treatment started after surgery, reducing immediate postoperative pain and preventing the development of chronic pain by reducing altered central sensory processing. Pregabalin, a GABA analogue, is effective in the treatment of neuropathic pain, incisional injury and inflammatory injury. Perioperative administration of pregabalin is reported to reduce perioperative anxiety, opioid consumption and opioid related side effects.

Materials and Methods: 60 patients of ASA 1 and 2 were randomized into two groups as Group A (placebo,n=30) and Group B (Pregabalin 75 mg,n=30). Patients received placebo or pregabalin 2 hours before surgery. Demographic data, postoperative pain score, sedation score, time since spinal anaesthesia to requirement of first rescue analgesic, total opioid consumption in 24 hours and side effects were recorded.

Results: Time for first rescue analgesic was longer in Group B as compared to Group A, although statistically insignificant. There was no significant reduction in mean VAS score between the two groups. The two groups were comparable in terms of total postoperative opioid consumption. Side effects were negligible.

Conclusion: Single preemptive oral pregabalin 75 mg is ineffective in reducing the severity of postoperative pain as compared to placebo in patients undergoing inguinal hernioplasty.

Keywords: pregabalin, pre-emptive, postoperative pain, hernioplasty.

Introduction

Every surgical procedure must have an effective means of managing postoperative pain. Ineffective pain management may increase mortality, delay healing, and lengthen hospital stays [3].

The most common cause of persistent postoperative pain is iatrogenic chronic neuropathic pain brought due to sensory nerve injury after open hernia surgery [4]. A strong predictor of chronic postoperative pain is the severity of acute postoperative pain. Therefore, managing perioperative pain and how it is done are crucial for promoting both short and long-term recovery following surgery.

The best way to achieve this goal is via multimodal and preventative analgesia.To produce postoperative analgesia, many medications including NSAIDS, opioids, ketamine, gabapentinoids, and antidepressants have been employed in multimodal approaches [5].

Pregabalin has been proven to reduce postoperative pain in a range of surgical populations. The release of excitatory neurotransmitters is decreased when pregabalin binds to the presynaptic alpha 2 delta subunit of voltage-gated calcium channels. This mechanism provides antihyperalgesic and antiallodynic characteristics by reducing the hyperexcitability of dorsal horn neurons impacted by tissue injury [5].

Materials and Methods

This was a prospective, randomized, double blinded, placebo controlled study conducted in patients undergoing elective inguinal hernioplasty surgeries.

Inclusion criteria

- ASA Physical Grade I and II
- 20 to 60 years
- Male and female.

Exclusion criteria

- Patient's refusal
- History of seizure disorder
- History of known psychiatric disorder
- History of chronic pain and chronic daily intake of analgesics
- History of allergy to pregabalin
- Pregnancy and breast feeding mothers
- Failed spinal anaesthesia.

After getting written informed consent from each participant, 60 patients satisfying the inclusion criteria were randomly allocated by lots method into two groups:

- Group A (Placebo group) and
- Group B (Pregabalin group).

All patients were visited the evening before surgery and were explained about the study methods, visual analogue scale chart and were provided with information sheet.

Patients in Group B received 75 mg pregabalin orally and Group A patients received a matching placebo capsule 2 hours prior to surgery. The drugs were prepared in prepacked boxes numbered randomly from 1 to 60 and was administered with sips of water two hours prior to the surgery by a staff nurse who was blinded to the study. No other drug was given to the patients.

Anaesthesia protocol

Inside the operating room, monitors (ECG, NIBP, Pulse oximeter) were connected. Intravenous access established with 18G cannula. Bladder was catheterized to monitor urine output. All patients were preloaded with 10ml/kg of Ringer's lactate solution.

Under all strict aseptic precautions, spinal anaesthesia was instituted at L3-L4 interspace using 25G Quincke needle with 3ml of Inj.Bupivacaine heavy (15mg). At the end of surgery, patients were shifted to ward. Pain quantification was done by Visual Analog Scale Score and Sedation score was done using Ramsay Sedation Scale.

VAS scores were assessed in the immediate postoperative period (0hr) and at 2, 4, 6, 12 and 24 hours post operatively by previously trained observer blinded to the study. Patients were given Inj. Tramadol 2 mg/kg intravenously when the VAS score was 4 or greater. The dosage of tramadol did not exceed 250 mg at one time and 600 mg per day.

Time since spinal anaesthesia to first requirement of analgesic (T1), Total analgesic requirement in first 24 hours, VAS scores,

Ramsay sedation score, side effects of the drug like dizziness, confusion, nausea, vomiting were recorded in first 24 hours postoperatively.

During all phases of the study, the patients, staffs, data collectors, data analysts were kept blinded to all study groups.

Statistical analysis

The observations recorded in the two groups were tabulated and statistical analysis was carried out by using statistical software SPSS 2.0. $p<0.05$ was considered as statistically significant.

Results

Table 1: Demographic profile and duration of surgery among two groups

Parameters (Mean±SD)	Group A	Group B	p value
Age (yrs)	45.9±12.5	46±12.9	>0.05
Sex (M:F ratio)	29:1	29:1	>0.05
Height (cms)	164.1±2	164.2±2.3	>0.05
Weight (Kgs)	65.9±3.3	65.2±5.6	>0.05
Duration of surgery (mins)	53.4±1.8	53.2±2.2	>0.05

The two groups were comparable with respect to demographic data (age, sex, height,weight) and duration of surgery (mins) as shown in table 1

Table 2: Time for rescue analgesia (T1) among two groups

Parameter (Mean±SD)	Group A	Group B	p value
T1 (mins)	287.2 ±41.2	307.2± 58.5	>0.05

Table 2 shows the time since spinal anaesthesia to the requirement of first rescue analgesic (T1) which was prolonged in Pregabalin group (307.2± 58.56 mins) as compared to placebo (287.2 ±41.2 mins) group, although it was statistically insignifican.

Table 3: Mean VAS score between group A and group B

VAS (Mean±SD)	Group A	Group B	p value
0 hr	1.2±0.4	1.2±0.4	0.7
2 hrs	2.8±0.6	2.6±0.6	0.3
4 hrs	4±0.9	3.8±0.9	0.4
6 hrs	2.3±0.5	2.4±0.7	0.5
12 hrs	4.3±1.2	4±1.1	0.3
24 hrs	3±0.9	3.1±1	0.6

The mean VAS score at all time intervals except 6 hours and 24 hours post surgery was comparatively lower with pregabalin group than placebo group but statistically insignificant (p value >0.05) as shown in table 3.

Table 4: Ramsay sedation score between group A and group B

RSS (Mean±SD)	Group A	Group B	p value
0 hr	2.0±0.3	2.0±0.4	0.7
2 hrs	2.0±0.3	1.9±0.3	0.4
4 hrs	2.0±0.5	1.9±0.4	0.8
6 hrs	2.0±0.3	2.0±0.2	0.6
12 hrs	1.9±0.4	2.0±0.3	0.5
24 hrs	1.9±0.3	1.9±0.3	0.4

Table 4 shows the mean sedation score between the two groups. At all time intervals the mean sedation score was statistically insignificant (p value>0.05)

Table 5: Total dose of tramadol in 24 hours among two groups

Parameter (Mean±SD)	Group A	Group B	p value
Total tramadol in 24 hours (mg)	210±30.5	210±30.5	>0.05

The total dose of tramadol given in 24 hours as rescue analgesic was comparable between the two groups as shown in table 5.

Table 6: Incidence of adverse effects among two groups

Adverse effects	Group A	Group B	p value
Nausea	4 (13%)	1 (3%)	>0.05
Vomiting	2 (7%)	0	
Dizziness	0	0	

Table 6 shows the incidence of adverse effects among the groups. In Group A, 4 patients had nausea and 2 patients had vomiting while 1 patient had nausea in Group B. There was no dizziness in both group

Discussion

Pregabalin is safe when used to treat acute pain, however two recent meta analyses conducted by Engelman E *et al* [6] and Mishriky BM *et al* [7] reports that using large doses (100–300 mg/day) during the perioperative phase resulted in unwanted side effects like sedation, dizziness, and visual disturbances. To prevent the frequent dosage-dependent unpleasant effects, it is essential to determine the lowest effective dose. However, there is limited and inconclusive evidence to support the use of a single low dose of pregabalin [8]. Hence, single preoperative dose of 75 mg pregabalin was chosen for this study.

The patients in each group received the drugs 2 hours prior to surgery. This is based on the pharmacokinetic profile of pregabalin . Elinor Ben Menachem [9] reported that the time of maximal plasma concentration of pregabalin was approximately 1 hour. In our study, there was no significant reduction in mean VAS score at all time intervals between the two groups. This shows that the analgesic property of single preoperative pregabalin 75 mg is comparable to placebo.

These findings also correlated with previous study done by Fujita N *et al* [10] in patients undergoing posterior lumbar interbody fusion surgery where there was no significant difference in the mean VAS score between pregabalin 75mg and placebo. Pratibha S *et al* [11] observed that there was no significant difference in static and dynamic pain in patients undergoing laparoscopic cholecystectomy at all time intervals between the pregabalin 75mg and placebo group. Paech *et al* [12] reported that a single preoperative dose of 100 mg pregabalin was ineffective in reducing acute postoperative pain or improving recovery after minor surgery involving only the uterus.

On contrary, the results of few previous studies (Sagit M *et al* [13], Aydogan H *et al* [14], Rajappa GC *et al* [5], Pourfakhr P *et al* [15], Mohammadi A *et al* [16], Kheirabadi D *et al* [17]) were in favour of a single low dose pregabalin 75mg in decreasing postoperative pain at rest in different clinical settings such as septoplasty, percutaneous nephrolithotomy, vaginal hysterectomy and lower extremity orthopaedic surgery.

In our study, the level of sedation were comparable in two groups. This may be due to single preoperative low dose of pregabalin. White PF *et al* [18]evaluted the dose ranging effects of pregabalin on preoperative anxiety and sedation levels. They observed that anxiety levels remained unchanged and was comparable between the study groups and perioperative sedation increased in dose related fashion. Similarly the results of few previous studies (Jokela R *et al* [19], Fujita N *et al* [10], Martins MJ *et al* [20], Pratibha S *et al* [11]) shows that total analgesic requirement is comparable between pregabalin 75mg and placebo. However, few studies (Sagit M *et al* [13],Aydogan H *et al* [14],Rajappa GC [5], Pourfakhr P *et al* [15], Kheirabadi D *et al* [17]) suggests that there was significant reduction in rescue analgesic consumption and the time of administration of first rescue analgesic was prolonged with 75mg pregabalin.

In our study, side effects were negligible in both groups.This finding is similar to few studies (Jokela R *et al* [19],Mohammadi A *et al* [16], Pratibha S *et al* [11]) which showed no significant side effects in patients receiving pregabalin.

There are few limitations to our study. Firstly, we studied only the patients undergoing inguinal hernioplasty surgery and therefore, cannot generalize our findings to patients undergoing different surgical procedures. The study lacks any information about opioid sparing effects of pregabalin. Lastly, the study period was for 24 hours postoperatively and long term clinical follow up was not done to evaluate possible effect on chronic postsurgical pain.

Conclusion

In our study, patients receiving pregabalin 75 mg had a prolonged duration of first rescue analgesia and lower pain scores although it did not differ significantly compared to placebo and did not reduce the amount of postoperative opioid requirement. Thus we conclude that single preoperative pregabalin 75mg is ineffective in reducing postoperative pain and is comparable to placebo.

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