ISSN 2515-8260 Volume 09, Issue 07, 2022

Original Research Article

Efficacy of pregabalin as premedication for postoperative analgesia in inguinal hernia surgery

[1]Dr. Navveen PM, [2]Dr. SK Srinivasan, [3]Dr. Sittaramane S

[1]Post Graduate, Department of Anaesthesiology, Government Medical College and Hospital, Cuddalore, Erstwhile Rajah Muthiah Medical College and Hospital, Chidambaram, Tamil Nadu, India

[2]Professor and Head, Department of Anaesthesiology, Government Medical College and Hospital, Cuddalore, Erstwhile Rajah Muthiah Medical College and Hospital, Chidambaram, Tamil Nadu, India

[3]Assistant Professor, Department of Anaesthesiology, Government Medical College and Hospital, Cuddalore, Erstwhile Rajah Muthiah Medical College and Hospital, Chidambaram, Tamil Nadu, India

Corresponding Author:

Dr. Navveen PM (dr.navveen@gmail.com)

Abstract

Aim: This study is aimed to determine the efficacy of preoperative administration of oral pregabalin 150mg against the administration of a placebo for postoperative analgesia in patients undergoing Inguinal Hernia Surgery under Spinal anesthesia.

Methodology: A Prospective Randomized Double Blinded Control Study was conducted among 60 patients posted for elective Inguinal hernia surgery and were divided into equal groups. Group C received placebo and Group P received Tab. Pregabalin 150mg which was administered 30 min before surgery. Visual Analogue Score was used to determine the pain at rest during postoperative period. The time of requirement of rescue analgesia during postoperative period was also assessed.

Result: VAS at rest was significantly reduced in Group P (p<0.05). Duration of analgesia was significantly prolonged in Group P when compared to Group C (p<0.05). Time of first rescue analgesic was administered in Group Panda in Group C was noted and the mean was found to be more in the pregabalin group than in the control group (p<0.05). Rescue analgesic consumption in 24hours during postoperative period was significantly decreased in Group P (p<0.05).

Conclusion: We observed that the postoperative analgesia was definitely of a longer duration with the Group Pwhen compared to Group C and decreased requirement of parenteral analgesics in Group P. It is concluded that Tab. Pregabalin 150mg has significant postoperative analgesia when compared to placebo.

Keywords: Pregabalin, post-operative analgesia, inguinal hernia surgery

Introduction

Postoperative pain is a form of pain occurring due to surgical trauma with an inflammatory reaction at the surgical site. Postoperative pain can be both acute and chronic pain: Acute pain is experienced immediately after surgery usually up to 7 days postoperatively and chronic pain which last for more than 3 months after the surgery. Postoperative pain begins with surgical trauma and usually terminates with tissue healing [1]. Poorly controlled acute postoperative pain is associated with increased morbidity, delayed mobilization, functional and quality-of-life impairment, delayed recovery time and prolonged use of opioids. Postoperative analgesia results in faster recovery and early mobilization. Conventional opioids remain the standard management for acute postoperative pain; however, the risk of opioid-related adverse events are high, hence limiting the optimal dosing for analgesia,

ISSN 2515-8260 Volume 09, Issue 07, 2022

leading to poorly controlled acute postoperative pain. The current approaches for multimodal postoperative analgesia are mostly based on a combination of opioids, non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, and perioperative administration of local anesthetics. Each of these approaches comes with its own set of complications like use of opioids can cause nausea, vomiting, excessive sedation, respiratory depression, pruritus, constipation and urinary retention [2, 3]. Since NSAIDs have adverse gastrointestinal effects such as gastritis and upper gastro intestinal ulceration, and interventional techniques such as epidural analgesia have potential risk of further complications such as hypotension and local anesthetic toxicity. Other modalities like use of Gabapentinoids, help in reducing postoperative pain with less adverse effects.

Gabapentinoids such as pregabalin and gabapentin can be used for postoperative pain and neuropathic pain management. The differences between gabapentin and pregabalin are mainly related to pharmacokinetic and pharmacodynamic characteristics and pregabalin has a faster onset time and a more predictable absorption profile than gabapentin [4]. Pregabalin, a structural analogue of gamma amino butyric acid (GABA), is shown to be effective in treatment of several types of neuropathic pain, surgical pain and inflammatory injury with less adverse effects. Alternatively, some evidence indicates that their antinociceptive mechanism may arise through activation of noradrenergic pain-inhibiting pathways in the spinal cord and brain [5]. Several studies have reported pregabalin as an effective postoperative analgesic with opioid sparing effects. Hence it was hypothesized that preoperative use of pregabalin may reduce the requirement of postoperative analgesics.

Methodology

After approval of Institutional Ethical committee, a Prospective Randomized Double Blinded Control Study was conducted on 60 patients undergoing elective Inguinal hernia surgery under spinal anesthesia, who were preoperatively assessed thoroughly regarding their physical status, general examination and systemic examination and preoperative investigations were assessed properly. They were categorised in to American society of Anesthesiology (ASA) I and II and were taken for this study. Written informed consent was obtained from all the patients. The visual analogue score was explained to the patients.

Inclusion criteria were as follows:

1. ASA grade 1 & 2.
2. Age 18-65 years.
3. Body Mass Index (BMI)-18-35 kg/cm2.

Exclusion criteria were the following:

1. BMI >35 kg/cm2.
2. Age >65 years.
3. History of drug/alcohol abuse.
4. History of headache.
5. Dizziness, or significant postoperative nausea or vomiting after any previous surgery.
6. History of chronic pain and daily intake of analgesic drugs.
7. History of Epilepsy.
8. Previous Failed Spinal anaesthesia and any contraindications to Spinal anaesthesia.

The study subjects were allocated into two groups of 30 patients each

Group P (Pregabalin 150mg): (n=30) All patients belonging to this group were administered Tab. Pregabalin 150mg 30minutes prior to surgery.

Group C (Control): (n=30) All patients belonging to this group were administered placebo 30 minutes prior to surgery.

The Preoperative baseline heart rate, blood pressure, respiratory rate and oxygen saturation were recorded. Group P received Tab. Pregabalin 150mg and Group C received placebo 30

ISSN 2515-8260 Volume 09, Issue 07, 2022

minutes prior to surgery. Spinal anesthesia was performed in all the patients with 0.5% Hyperbaric Bupivacaine in lateral position at L3-L4 level with 25G Quincke needle. All hemodynamic parameters were monitored intra-operatively.

Postoperative pain was assessed using Visual Analog scale (VAS) [Figure 1]

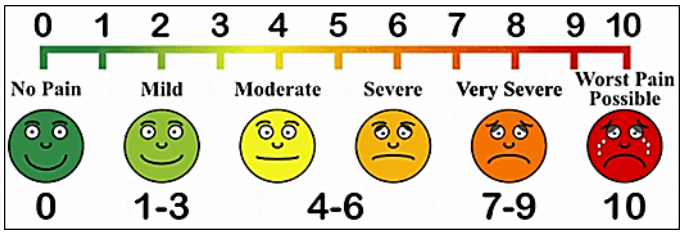

Fig 1: Visual Analogue Scale (VAS): 0-No Pain, 10-Very Severe Pain

The following parameters were assessed postoperatively:

1. Vitals-PR, BP, RR, SPO_2% were monitored.
2. VAS was assessed for pain at rest and on cough at 0, 30 minutes, 1, 3, 6, 12, 18 and 24 hours postoperatively.
3. The time of requirement of first rescue analgesic given was noted. Intravenous Inj. Tramadol 2mg/kg was given when VAS>4 and the total dosage of rescue analgesic required in 24 hours postoperatively was also documented.
4. Adverse events such as dizziness, nausea and vomiting were also noted

Data collection: Information on age, height and weight, co-morbidities were extracted from the case records and history sheets.

Statistical analysis: The data collected were entered into Microsoft excel 360 in order to create a master chart. The master chart was then loaded into statistical package for social sciences (SPSS) version 26 for further statistical analysis. Both quantitative and qualitative variables were present in the master chart. Both descriptive and inferential statistics were used for analysis.

For describing the qualitative variables-frequency and percentages were used. For describing the quantitative data-mean and standard deviation were used. In order to find out difference in distribution of qualitative variable between the experimental arms-chi-square test was applied. To find out the difference in mean between two groups, independent samples T test was applied. To find out the difference in change of mean between the groups for a repeatedly measured variables, Repeated measures analysis of variance (RM-ANOVA) was used. A 'P-value' of less than 0.05 was considered to be statistically significant.

Results

Table 1 denotes the distribution among participants based on the age, height, weight, BMI, Co-morbidities, ASA status, diagnosis, type of surgery and the duration of surgery. Both the groups were found to be similar with respect to the distribution of participants with P value of more than 0.05 and there was no statistical significant difference. All participants in both Groups were males. Postoperatively pain at rest and on cough assessed using VAS scale was noted and the time of first rescue analgesic (Intravenous Tramadol 2mg/kg) given was also noted.

Table 1: Distribution of subjects according to age, height, weight, BMI, Co-morbidities, ASA status, Diagnosis, Type of surgery and the Duration of surgery

Patient Details	Group P (n=30)	Group C (n=30)	P value
Age (years)	42.97±15.68	39.67±11.71	p>0.05
Height (cm)	164.97±5.66	166.10±6.61	p>0.05

ISSN 2515-8260 Volume 09, Issue 07, 2022

Weight (kg)	76.93±7.81	80.10±9.04	p>0.05
BMI (kg/m2)	28.31±3.08	29.02±2.52	p>0.05
Comorbidities S.HTN (%) T2DM (%) T2DM+S.HTN (%) NIL (%)	 16.7 20 23.3 40	 20 13.3 20 46.7	p>0.05
ASA 1:2	40:60	46.7:53.3	p>0.05
Diagnosis Left: Right inguinal hernia	56.7:43.3	46.7:53.3	p>0.05
Type of Surgery Left: Right hernioplasty	56.7:43.33	46.7:53.3	p>0.05
Duration of Surgery (minutes)	62.83±16.27	66.17±15.18	p>0.05

Table 2 denotes that in most of the observations, the mean VAS score of the control group was found to be higher than that of the pregabalin group. At baseline, 30 minutes, 1 hour 3 hours and in 18 hours the mean VAS score was higher in control group than in the pregabalin group. At 12 and 24 hours both the groups were found to have statistically similar P value. The VAS score was lower in Group P when compared to Group C which is Significantly low (p>0.05) at all times except at 12 and 24 hours.

Figure: 2 represents the mean VAS score was lower in Group P when compared to Group C which was statistically low (p<0.05) at all times except 12 and 24 hours.

Table 2: Change on mean VAS over timeline between the groups

Time line	Pregabalin		Control		P value (Within the groups)	P value (Between the groups)
	Mean	SD	Mean	SD		
0 minutes	1.40	0.49	2.13	0.68	0.001	0.001
30 minutes	1.53	0.51	3	0.58		
1 hour	2.30	0.46	4.17	0.37		
3 hours	3.57	0.50	4.83	0.37		
6 hours	4.50	0.50	3.97	0.71		
12 hours	4.23	1.10	4.60	0.62		
18 hours	3.80	0.76	4.43	0.85		
24 hours	4.33	0.47	4.60	0.67		

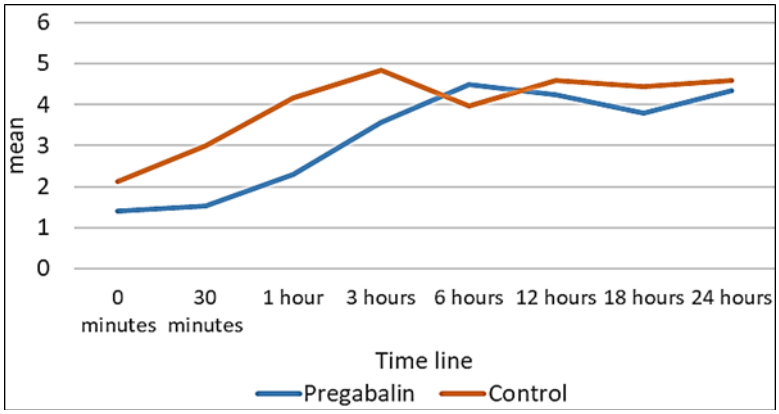

Fig 2: Line diagram showing change in mean VAS between the groups

Table 3 shows the mean duration after which tramadol was administered following surgery for the pregabalin group which was 394.67 ± 84.14 minutes and that of the control group was 111.67 ± 33.04 minutes. The mean was found to be more in the pregabalin group than in the

ISSN 2515-8260 Volume 09, Issue 07, 2022

control group, this revealed significant difference in time for the first rescue analgesic in Group P with P value of less than 0.05 which is statistically significant.

Table 3: Comparison of mean duration after which tramadol have been administered following surgery between the groups

Variable	Pregabalin		Control		T value	P value
	Mean	SD	Mean	SD		
Duration (In minutes)	394.67	84.14	111.67	33.04	17.14	0.001

Table 4 shows the mean dose of tramadol in the pregabalin group which was 160 ± 49.82 mgs and that of the control group was 280 ± 40.68 mgs. The mean dosage was more in the control group than in the pregabalin group with statistically significant P value of less than 0.05.

Table 4: Comparison of mean dosage of tramadol between the groups

Variable	Pregabalin		Control		T value	P value
	Mean	SD	Mean	SD		
Dosage of tramadol (in mg)	160	49.82	280	40.68	10.21	0.001

Table 5 shows the average incidence of complications like Giddiness, nausea and vomiting between Group P and Group C. 6.7% from pregabalin group reported nausea and 26.7% from the control group reported the same. The difference was found to be significant with P value of less than 0.05.13.3% from the control group reported vomiting and none from the pregabalin group did. The difference was significant with P value of less than 0.05.16.7% from the pregabalin group reported giddiness while none from the control group did. The difference was found to be significant with P value of less than 0.05.

Table 5: Comparison of nausea, vomiting and giddiness between the groups

Variable	Pregabalin		Control		P value
	N	%	N	%	
Nausea	2	6.7	8	26.7	0.038
Vomiting	0	0	4	13.3	0.038
Giddiness	5	16.7	0	0	0.020

There was no neurological deficit or post dural puncture headache noted in any patients.

Discussion

Pregabalin is used as an adjunct to other modalities for managing postoperative pain. Pre-emptive analgesia given before surgical incision focuses on managing postoperative pain including decreasing the consumption of analgesics as well as conferring neuroprotective characteristics [6]. Perioperative pregabalin administration reduces opioid consumption and opioid-related adverse effects after surgery [7]. Multimodal treatment of postoperative pain using adjuncts such as pregabalin is becoming more common. Pregabalin has anti-hyperalgesic properties similar to gabapentin [7]. Also the potent binding of pregabalin at alpha-2-delta site has been shown to reduce the depolarization-induced calcium influx at nerve terminals with a consequential reduction in the release of several excitatory neurotransmitters, including glutamate, norepinephrine, substance P and CGRP [8-10]. Pregabalin appears to be absorbed throughout the small intestines and demonstrates linear uptake without transporter saturation at therapeutic concentrations [11, 12]. Given the evidence suggesting that it takes 8 h for pregabalin to reach peak cerebrospinal fluid levels [13]. The optimal dose or frequency of administration of pregabalin is unclear. Pregabalin has an

ISSN 2515-8260 Volume 09, Issue 07, 2022

elimination half-life estimated to range from 5.5 to 6.7 h which is independent of the dose and frequency of administration [14]. Experimental models of neuropathic pain and inflammatory hyperalgesia have shown that g-aminobutyric acid analogues such as gabapentin and pregabalin have antinociceptive and anti-hyperalgesic properties [15]. In addition, pregabalin has no effect on arterial pressure or heart rate [16].

Observations were made that preoperative administration of single-dose pregabalin (150 mg) was effective in reducing both the static and the dynamic components of postoperative pain which was measured using VAS score and was statistically significant when compared with the control group. Although many meta-analyses have investigated the analgesic efficacy of perioperative PGB or GBP administration so far, the role of PGB or GBP in acute postoperative pain management still remains elusive. Moreover, few studies compared different doses of abovementioned drugs for preventing acute postoperative pain [17]. The more numerous positive studies suggesting the effect size of gabapentinoids for preventing chronic pain may be quite substantial and clinically relevant [18].

Reporting on postoperative nausea and vomiting (PONV) indicated a reduction in the pregabalin group compared with the control, whereas there might be an increase in incidence of dizziness in the pregabalin groups compared with control group. The side-effect profile of pregabalin is also very promising with the most common adverse events being dizziness and somnolence [19, 20].

Conclusion

In conclusion, oral pregabalin 150 mg administered preoperatively was effective in reducing postoperative pain when compared to the control group. The side effect such as PONV was less and few patients experienced dizziness when compared to control group. It should now be generally accepted that the Pregabalin is effective in reducing immediate postoperative pain and may reduce the requirement of postoperative opioids and other analgesics. We therefore suggest that oral preoperative single dose of pregabalin 150 mg is an effective method for reducing postoperative pain in patients undergoing Inguinal hernia surgery under spinal anesthesia.

References

1. Rajappa Geetha, Vig Saurabh, Bevinaguddaiah Yatish, Anandaswamy Tejesh. 2016/05/14. Efficacy of Pregabalin as Premedication for Post-Operative Analgesia in Vaginal Hysterectomy. 10.5812/aapm.34591. Anesthesiology and Pain Medicine.
2. Cashman JN, Dolin SJ. Respiratory and haemodynamic effects of acute postoperative pain management: evidence from published data. Br J Anaesth. 2004;93(2):212-23. Doi: 10.1093/bja/aeh180. [PubMed: 15169738].
3. Dolin SJ, Cashman JN. Tolerability of acute postoperative pain management: nausea, vomiting, sedation, pruritus and urinary retention. Evidence from published data. Br J Anaesth. 2005;95(5):584-91. Doi: 10.1093/bja/aei227. [PubMed: 16169893].
4. Ben-Menachem E Pregabalin pharmacology and its relevance to clinical practice. Epilepsia. 2004;45(6):13-8.
5. Hayashida K, De Goes S, Curry R, Eisenach JC. Gabapentin activates spinal noradrenergic activity in rats and humans and reduces hypersensitivity after surgery. Anesthesiology. 2007;106:557-62.
6. Gottschalk A. Update on preemptive analgesia. Tech Reg. Anesth Pain Manag. 2003;7(3):116-121.
7. Zhang J, Ho KY, Wang Y. Efficacy of pregabalin in acute postoperative pain: a meta-analysis. Br J Anaesth. 2011 Apr;106(4):454-62. Doi: 10.1093/bja/aer027. Epub 2011 Feb 26. PMID: 21357616.
8. Ben-Menachem E. Pregabalin pharmacology and its relevance to clinical practice. Epilepsia. 2004;45:13-8.

ISSN 2515-8260 Volume 09, Issue 07, 2022

9. Dooley DJ, Donovan CM, Pugsley TA. Stimulus-dependent modulation of [(3)H] norepinephrine release from rat neocortical slices by gabapentin and pregabalin. J Pharmacol. Exp. Ther. 2000;295:1086-93.
10. Fink K, Dooley DJ, Meder WP, *et al*. Inhibition of neuronal Ca(2þ) influx by gabapentin and pregabalin in the human neocortex. Neuropharmacology. 2002;42:229-36.
11. Piyapolrungroj N, Li C, Bockbrader H, Liu G, Fleisher D. Mucosal uptake of gabapentin (Neurontin) vs. pregabalin in the small intestine. Pharm Res. 2001;18:1126-30.
12. Schulze-Bonhage A. Pharmacokinetic and pharmacodynamic profile of pregabalin and its role in the treatment of epilepsy. Expert Opin. Drug Metab. Toxicol. 2013;9:105-15.
13. Buvanendran A, Kroin JS, Kari M, Tuman KJ. Can a single dose of 300mg of pregabalin reach acute antihyperalgesic levels in the central nervous system? Reg. Anesth. Pain Med. 2010;35:535-8.
14. Gajraj NM. Pregabalin: its pharmacology and use in pain management. Anesth Analg. 2007;105:1805-1815.
15. Wolf CJ, Chong MS. Pre-emptive analgesia treating postoperative pain by preventing the establishment of central sensitization. Anesth Analg. 1993;77:362-79.
16. Reuben SS, Buvanendran A, Kroin JS, Raghunathan K. The analgesic efficacy of celecoxib, pregabalin and their combination for spinal fusion surgery. Anesth Analg. 2006;103:1271-7.
17. Hu J, Huang D, Li M, Wu C, Zhang J. Effects of a single dose of preoperative pregabalin and gabapentin for acute postoperative pain: a network meta-analysis of randomized controlled trials. J Pain Res. 2018;11:2633-2643.
18. Clarke H, Bonin RP, Orser BA, Englesakis M, Wijeysundera DN, Katz J. The prevention of chronic postsurgical pain using gabapentin and pregabalin: A combined systematic review and meta-analysis. Anesth Analg. 2012;115:428-42.
19. Kavoussi R. Pregabalin: from molecule to medicine. Eur Neuropsychopharmacol. 2006;16:S128-33.
20. Bockbrader HN, Wesche D, Miller R, Chapel S, Janiczek N, Burger P. A comparison of the pharmacokinetics and pharmacodynamics of pregabalin and gabapentin. Clin Pharmacokinetics. 2010;49:661-9.