



Effects of pre-emptive oral pregabalin on post-operative pain in patients undergoing unilateral inguinal hernioplasty under spinal anaesthesia

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Abstract

Background: Studies have shown that pre-emptive pregabalin is effective in controlling post-operative pain and reducing the requirement of the post op analgesia. Our study is a randomised case control study to determine the efficacy and safety of pre-emptive pregabalin in undergoing unilateral inguinal hernioplasty under spinal anaesthesia.

Material and Methods: In this study a total of 90 patients aged 18-60yrs, belonging to ASA Grade I & II undergoing unilateral inguinal hernioplasty under spinal anaesthesia were included. Group I (n=45 study group) received oral Pregabalin 150mg 1hour prior to surgery and Group II (n=45 control group) received placebo 1hour prior to surgery. Post-operative assessment of pain was done using Visual analogue score (VAS) scale, sedation by Ramsay sedation score(RSS), time for requirement of first rescue analgesic and total number of analgesic doses given to the patients in 24 hours period were recorded. Incidence of side effects like dizziness, dry mouth, nausea, were also noted.

Result: During post-operative period Group I significantly lower pain scores and lower post-operative analgesic requirement as compared to Group II subject. Time for first rescue post analgesia was significantly higher in Group I subjects. RSS was significantly higher in Group I subjects immediately after surgery and at 2hrs. No significant difference in occurrence of side effects in-between two groups was seen.

Conclusion: Premedication with pregabalin 150 mg orally can be safely used to obtain better post-operative pain relief and pain control without any clinically significant side effects. It is an easily tolerated, effective, and inexpensive method with minimal side effects.

Keywords: Pregabalin, pre-emptive analgesia, post-operative pain

Introduction

All surgical procedures inflict pain during and after the procedure. It has been seen that 75% of patients in post-operative state reports pain and 80% of these patients have reported severe acute pain during their hospital stay ¹. Inadequately controlled post-operative pain has many undesirable acute and chronic effects such as increased postoperative morbidity, delay in recovery, a delayed return to normal daily living, and reduced patient satisfaction and puts extra burden upon the use of health care resources and inflates the health care costs ².

Development postoperative of pain is associated with tissue damage (such as preoperative pain, painful noxious intraoperative inputs such as retraction, as well as postoperative inflammatory processes) which results in prolonged modulation of the somatosensory system, with increased responsiveness of both peripheral and central pain pathways (central sensitization) ^{3, 4, 5}. Central sensitization due to tissue damage can be inhibited by the pre-surgical administration of an analgesic ⁶. This forms the concept of preemptive analgesia which was first described by Crile in 1913 ⁷. Pre-emptive analgesia is a treatment that is initiated before and is operational during the surgical procedure in order to reduce the physiological consequences of nociceptive transmission provoked by the procedure ⁸.

The post-operative pain control aids faster recovery of patient, helps in faster mobilizing, reduces post-operative morbidity, and reduces duration of hospital stay ⁹. Pregabalin (s-(+)-3-isobutylgaba) is a lipophilic GABA analogue substituted at the 3'-position to facilitate diffusion across the blood brain barrier. It is effective in several models of neuropathic pain, incisional injury, inflammatory injury, anxiety, anti-convulsant and is also a sleep-modulating drug ¹⁰.

Pre-emptive Pregabalin acts by attenuating central sensitization due to peripheral stimuli induced tissue damage during surgery, by decreasing the hyper-excitability in the dorsal horn neurons ¹¹. Pre-emptive pregabalin administration was associated with a significant reduction in pain scores and decreased opioid consumption post operatively in various types of surgeries as compared with placebo. Patients receiving pregabalin also reported lesser episodes of postoperative nausea and vomiting. Side effects such as sedation, dizziness, and visual disturbances were also reported with pregabalin. All doses of pregabalin tested (≤ 75 , 100-150, and 300 mg) resulted in opioid sparing at 24 h after surgery ¹².

Through our study we would like to see the effects of single oral dose of pre-emptive pregabalin on postoperative analgesia in patients undergoing unilateral inguinal hernioplasty under spinal anaesthesia.

Materials and Methods

After obtaining ethical committee approval and written informed consent from the patients the study was carried out in the Department of Anaesthesiology at Sri Ram Murthi Smarak Institute of Medical Sciences, Bareilly from September 2016-October 2018. For the purpose of study of 90 patients, aged 18-60 years, ASA grade I & II physical status, scheduled for elective hernioplasty were undertaken. Patients were randomly divided into two groups of 45 each.

Group I: Received oral pregabalin 150 mg 1 hour prior to surgery.

Group II: Received oral placebo 1 hour prior to surgery.

Inclusion criteria: Patients in age range of 18-60 years of either sex; Patients belonging to-ASA Grade I & II; Weight 50-70 kgs; Height 150-180 cms; BMI 20-30 kg/m²; Hemodynamically stable patients with normal laboratory investigations.

Exclusion criteria: Consent not giving; Infection at the site of injection; Bleeding disorder or patient on anticoagulant therapy; Known allergy to any of the medications to be used in the study; Patient with abnormal psychological profile, on drugs like antiepileptic and other drugs acting on CNS; Patients having chronic pain conditions; Patients who take analgesics last 48hours.

Outcome measures: Post-operative assessment of pain was done by visual analogue score (VAS) scale. Post-operative analgesia was achieved by I/V Inj. Diclofenac sodium 75mg slow i.v. when patient complain of pain or VAS score >4. The time for first rescue post-operative analgesia requirement was noted. The total number of analgesic doses given to the patient in 24hours period post operatively were recorded. Level of sedation was assessed by modified Ramsay Sedation Score (RSS). Incidence of side effects like dizziness, nausea, vomiting visual disturbances was noted.

Data analysis: Data was analysed using unpaired-t-test, chi-square test. SPSS software version 20 for windows was used for data analysis .Power of the study was kept at 90%. P-value < 0.05 was considered significant.

Observations and Result

The mean age of the patients in group I was 38.49 ±11.41 years and group II was 38.49 ±11.41 years.

It was observed that during post-operative period pain scores were significantly lower in Group I as compared to Group II subject at 2hrs and 12hrs after surgery. Table-1

Table 1: VAS Scores

VAS Score	Group I Mean ± SD	Group II Mean ± SD	P-Value
Immediate	1.02 ± 0.78	0.98 ± 0.87	0.80
2HRS	2.22 ± 0.67	3.31 ± 1.16	<0.001
6HRS	3.29 ± 0.69	3.47 ± 1.18	0.39

12HRS	3.09 ± 0.73	3.42 ± 0.66	0.026
24HRS	3.00 ± 0.56	3.02 ± 0.69	0.868

The time for first rescue post analgesia was significantly higher in Group I subjects as compared to the Group II subjects. The number of analgesic doses required during the post-operative first 24hrs was significantly less in Group I as compared to the Group II subjects. Table no. 2.

Table 2

	Group I Mean ± SD	Group II Mean ± SD	P-Value
Duration of Postop Analgesia (MINS)	372.67 ± 36.71	214.44 ± 26.59	<0.001
Post op Analgesic Requirement (No. of Doses)	2.40 ± 0.58	4.44 ± .50	<0.001

Ramsay Sedation score was significantly higher in Group I subjects immediately after surgery and at 2hrs as compared to Group II subjects.

Table 3

Ramsay Sedation Score	Group I Mean ± SD	Group II Mean ± SD	P-Value
Immediate	2.36 ± 0.48	2.09 ± 0.47	0.09
2 Hrs.	2.60 ± 0.49	2.36 ± 0.48	0.20
6 Hrs.	2.56 ± 0.50	2.49 ± 0.51	0.53
12 Hrs.	2.69 ± 0.47	2.62 ± 0.49	0.51
24 Hrs.	2.40 ± 0.49	2.38 ± 0.49	0.83

In our study some patients complained of episodes of dizziness, nausea and vomiting during the post-operative period. However, there was no significant difference in the occurrence of side effects in the two groups as analysed using Chi-square test.

Table 4: Post-operative side effects

	Group I (n=45)		Group II (n=45)		p-value
	No. of patients	%	No. of patients	%	
Dizziness	8	17.78	6	13.33	0.56
Nausea	5	11.11	7	15.56	0.53
Vomiting	4	8.89	5	11.11	0.72

Discussion

In this study we found pain scores were reduced during post-operative period in GROUP I patients as compared to the GROUP II patients. The requirement of post-operative analgesia was delayed in GROUP I patients. The number of analgesic doses required during the post-operative first 24hrs were significantly less in GROUP I as compared to the GROUP II. Studies conducted by Peng *et al.*, Eidy *et al.*, and Li *et*

al., showed that pre-emptive pregabalin in doses of 50mg, 75 mg, 150 mg, and 300mg produced significant pain relief post operatively^{13, 14, 15}. Greater pain relief and comfort post-operatively is observed in patients receiving higher doses of pregabalin^{16, 17}.

Some authors also observed preoperative administration of pregabalin is associated with a significant reduction of post-operative analgesic consumption and reduced occurrence of morphine-related side effects such as nausea and vomiting^{17, 18}.

Post-operative pain relief by pregabalin might be due to the inhibition of the trafficking of voltage gated calcium channels rather than directly inhibiting calcium currents, thereby decreasing the hyper-excitability in the dorsal horn neurons. This mechanism attenuates the process central sensitization due to peripheral stimuli induced tissue damage during surgery^{11, 19}.

Some authors also found that addition of NSAIDS such as ibuprofen and other analgesics to pre-emptive pregabalin leads to better pain control and reduced opioid consumption post operatively than pre-emptive pregabalin alone^{20, 21}.

In our study we found that Mean RSS was significantly higher in GROUP I patients immediately after surgery and at 2hrs post-operatively, suggesting increased sedation in GROUP I patients as compared to GROUP II patients post-operatively. Studies done by various researchers supports our finding, that sedation is a common side effect of pregabalin²². White *et al.* found in his study that preoperative administration increased perioperative sedation in a dose-related fashion as compared to placebo, higher the dose higher the severity of sedation²³.

Side effect profile was not statistically significant in between the two groups. Patients in both groups experienced side effects like nausea, vomiting and dizziness. Some authors also reported increased incidence of trouble of vision with pregabalin premedication, but in our study there was no reporting of such incidents. Higher doses of pregabalin are associated with more occurrence of side effects¹⁶.

Conclusion

From our study we can conclude that premedication with pregabalin 150 mg orally can be safely used to obtain better post-operative pain relief and pain control without any clinically significant side effects. It is an easily tolerated, effective, and inexpensive method with minimal side effects.

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