

Comparison of Preoperative Pregabalin Versus Dexamethasone for Postoperative Analgesia in Patients Undergoing Inguinal Hernia Repair

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ABSTRACT

Objective: To compare the efficacy of pregabalin versus dexamethasone for post-operative analgesia in patients undergoing inguinal hernia repair.

This randomized trial was carried out in the Department of Anaesthesia at Holy Family Hospital, Rawalpindi after the approval of the Ethical review board, from February 2019 to November 2019.

Methodology: A total of 120 patients were equally divided into two equal groups using lottery method. Group A received pregabalin and group B received dexamethasone. Patients were observed for 24 hours for post operative pain control. Visual Analogue Scale was used to grade pain at 6, 12 and 24 hours

Results: The mean age in Group-A was 43.38±15.80 and 42.85±14.52 years in Group-B, comparison of the effect of single dose preoperative Pregabalin and IV dexamethasone on mean post-operative pain in patients undergoing hernia surgery under spinal anesthesia shows that at 6 hrs 2.83±1.10 in Group-A and 3.98±1.41 in Group-B, p value 0.0001, at 12 hrs 2.22±1.28 in Group-A and 3.33±1.49 in Group-B, p value was 0.0001 and at 24 hrs it was calculated as 1.0±0.75 in Group-A and 1.6±1.0 in Group-B, p value was 0.0005.

Conclusion: Pregabalin is superior to dexamethasone for post-operative pain control in patients undergoing hernia repair under spinal anesthesia.

Keywords: Dexamethasone, pregabalin, Inguinal hernia, post-operative pain.

Authors' Contribution:

^{1,2}Conception; *Literature research; manuscript design and drafting;* ^{2,3} Critical analysis and manuscript review; ⁴Data analysis; *Manuscript Editing.*

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Introduction

Pain is defined as an unpleasant sensory or emotional experience associated with actual and potential damage, or described in terms of such damage.¹ Postoperative pain is a major cause of hospital stay following surgery and the main factor limiting patient mobilization and enhanced recovery.² Understanding of pathophysiology of pain has led to adoption of Multimodal analgesia as

the hallmark of enhanced recovery program and current approach to treat postsurgical pain. Currently Opioids and NSAIDs are cornerstone of surgical pain treatment. But opioids are associated with unwanted side effects, e.g., respiratory depression, nausea, vomiting, itching, hyperalgesia, increased duration of postoperative ileus and others.³ While NSAIDs have antiplatelet properties, increase risk of bleeding, gastritis and renal

impairment. Interventional techniques such as epidural analgesia require additional work and carry potential risk of serious complications.⁴ So there exists a need of alternate options for addition to multimodal pain management regimen for better postoperative analgesia.

Pregabalin is a structural analogue of GABA. It acts by presynaptic binding to alpha-2-delta subunit of voltage gated calcium channels that are widely distributed in spinal cord and brain. It leads to inhibitory modulation of overexcited neurons and returns them to a “normal” state. Centrally, pregabalin could reduce the hyper excitability of the dorsal horn neurons that is induced by tissue damage.⁵ Preoperative pregabalin use has shown reduced postoperative pain scores and decreased post-operative opioids consumption in patients undergoing various types of surgeries under general anaesthesia including cardiac surgery, laparoscopic cholecystectomy, percutaneous nephrolithotomy and thyroidectomies. Ghoghari *et al.*,⁶ concluded patients who received treatment with pregabalin 1 hour prior to surgery had significantly low pain score at 24 hours after surgery (1.80 ± 1.0) as compared to those with no treatment. These results were statistically significant with p value = <0.05 . The analgesic and anti-inflammatory effect of steroids (dexamethasone) is well known especially when there is tissue edema and tissue injury. Dexamethasone suppresses bradykinin and release of neuropeptides from nerve endings, hence reducing pain sensation in inflamed tissue. Dexamethasone also indirectly inhibits phospholipase A₂ (due to steroid mediated elevation of lipocortin) which blocks both arachidonic acid cascade and lipoxygenase pathway thus inhibiting prostaglandins production hence relieving pain.⁷ Dexamethasone interferes in mast cell degranulation resulting in decreased histamine release and decreases capillary permeability thus decreasing inflammation. Mohtadi *et al.*,⁸ reported concluded that patients who received treatment with dexamethasone had significantly low pain score

at 24 hours after surgery (2.95 ± 1.85) as compared to those with no treatment. These results were statistically significant with p value = <0.05 .

Although some studies have been done which showed that these agents have had favourable effect on the post-operative pain management, no studies have yet been done to compare these two medicines with each other. Searching through both the national and international literature no study was found to compare these two medications. We decided to conduct this study to establish which amongst the two is superior and later should make it part of our multimodal regimen for pain management.

Methodology

We conducted a randomized trial at Holy Family Hospital, Rawalpindi between February to November 2019 after approval of the ethical review committee. A total of 120 patient who were admitted for elective inguinal hernia repair were included in the study. Consecutive non probability sampling was used. The patient was randomly divided in two groups ($n=60$) using the lottery method. Male patient ASA-1 or ASA-2 were included while obese patients ($BMI > 25$), patients with any chronic pain or having allergies to the medications under study were excluded from the study. Using the statistics from literature researches^{6,8} Openepi Sample size calculator was used for sample size calculations. With a confidence interval of 95% and level of significance of 5% sample size of 120 with 60 patients in each group was calculated. Data collection was done using a well-structured proforma while SPSS version 22 was used to analyse the data. Qualitative variables like ASA classification were measured in terms of frequency and percentage while the quantitative variables of age and pain scores were measured in terms of mean and standard deviation. Independent sample T-test was applied to compare mean pain scores in the two sets of patients keeping p value <0.05 as significant.

Effect modifiers like ASA, age and DM was controlled by stratification. Post stratification sample T test was applied with P value <0.05% considered as significant. Group A patients received Tab pregabalin 150 mg orally while group B patient received dexamethasone 8mg IV 2 hours prior to administration of anaesthesia. In the theater ASA standard monitors were applied the patient received Ringer Lactate 15ml/kg over 10 minutes as preload. Spinal anaesthesia was administered at L3-L4 using 25G Quinke needle and 0.75% hyperbaric bupivacaine was administered. Sensory level of block was assessed using the pin prick and alcohol evaporation while the motor block was assessed using the Bromage scale. Surgery was proceeded after adequate level of block was achieved. Patients were followed up for 24 hours and post operative pain was assessed using the Visual Analog scale at 06 hours, 12 hours and 24 hours. Rescue analgesia was provided using Ketorolac 30 mg intravenously in case of VAS of 3 or more. Data was collected by on call trainees and noted on the prescribed proforma.

Results

The two groups were similar in age. ASA standard and BMI. Age distribution of the patients was done, it shows that 26.67%(n=16) in Group-A and 21.675(n=13) in Group-B were between 18-30 years of age whereas 73.33%(n=44) in Group-A and 78.33%(n=47) in Group-B were between 31-50 years of age, mean±sd was calculated as 43.38±15.80 years in Group-A and 42.85±14.52 years in Group-B.

Table 1: Age distribution (n=120)

Age (in years)	Group-A (n=60)		Group-B (n=60)	
	No. of patients	%	No. of patients	%
18-30	16	26.67	13	21.67
31-50	44	73.33	47	78.33
Total	60	100	60	100
Mean±SD	43.38±15.80		42.85±14.52	

ASA status of the patients was done, it shows that 61.67%(n=37) in Group-A and 68.33%(n=41) in Group-B had ASA-I whereas 38.33%(n=23) in Group-A and 31.67%(n=19) in Group-B had ASA-II.

Table 2: ASA status of the patients (n=120)

ASA	Group-A (n=60)		Group-B (n=60)	
	No. of patients	%	No. of patients	%
I	37	61.67	41	68.33
II	23	38.33	19	31.67
Total	60	100	60	100

Mean BMI of the patients was calculated as 21.16±2.92 in Group-A and 21.08±2.89 in Group-B.

Table 3: Mean BMI of Patients

BMI	Group-A (n=60)		Group-B (n=60)	
	Mean	SD	Mean	SD
	21.16	2.92	21.08	2.89

Comparison of the pre-operative Pregabalin and dexmethsone is shown in the Table 4 which is clearly in favor of the pregabalin at all three assessment times.

Table 4: Comparison of Pregabalin and Dexamethsone Mean Pain Scores

Mean pain score	Pregabalin Group (n=60)		Dexamethasone Group (n=60)		P.value
	Mean	SD	Mean	SD	
At 6 hrs	2.83	1.10	3.98	1.41	0.0001
At 12 hrs	2.22	1.28	3.33	1.49	0.0001
At 24 hrs	1.0	0.75	1.6	1.0	0.0005

Discussion

Post-operative pain experienced by patients mandates precise measurement and active management. Rational use of the pain medications requires continuous research and development of SOPs as new medications become available. For good pain management the medications for pain may be administered according to a standardized plan. This plan should include preemptive analgesia, i.e. establishing the effect of the medicines prior to surgical incision. The neuro endocrine response is mediated via the cascade of local and systemic inflammatory substances. There is a surge of catecholamines and stress hormones that results in salt and water retention.⁸ The blood levels of the glucose, free fatty acids, ketone bodies and lactate jump. Impaired sugar control shall inevitably lead to poor wound healing and immune compromised state. Stress response produced in this way is directly proportional to the degree of the surgical injury. Amongst the physiological processes this stress will lead to break up of fibrin, increased tendency of clotting leading to deep vein thrombosis, vascular grafts failing and myocardial ischemia. Furthermore, as part of this phenomenon there is decreased gut motility, atelectasis in the alveoli which leads to fall in pulmonary gas exchange as well as pulmonary infections. The phenomenon of pain transmission and its severity can be explained in terms of Transduction, Modulation, Perception and Transmission.⁹ Keeping in view of this mechanism the concept of multimodal analgesia was born.¹⁰ This concept advocates the use of different medications working as different levels of pain modulation and transmission. Instead of using larger dose of a medication using a single mechanism of action for pain control, smaller doses of multiple medicines belonging to different classes are used. Thus, a targeted approach is taken for pain management. This leads to a smaller dose requirement of each class of medicine and so the rate of complications is reduced.

In our study we investigated the efficacy of a pre-operative dose of pregabalin and dexamethasone for the management of post-operative pain in patients undergoing inguinal hernia repair. We chose inguinal hernia repairs because this was a common procedure and is done as part of the day care surgery. Delay in discharge resulting from inadequate pain control would result in failure to discharge on time and hence a failure of the day care concept.

In our study we used a VAS of 3 or more as a threshold for rescue analgesia. Ketorolac 30 mg IV was used for the rescue. Although considered a safe medication for post-operative pain control, since it is NSAID it leads to platelet dysfunction and could potentially lead to a compromise in the renal function. Thus, keeping its dosage to a minimum would be a rational plan.

Both dexamethasone and pregabalin have been tried and tested as part of the multimodal regimen and both have proven their worth for the purpose. Mathiesen et al administered 300 mg pregabalin in combination with 8 mg of dexamethasone in adult patients undergoing tonsillectomy and reported a statically significant fall in opioid requirement.¹¹ Considering that dexamethasone has a good antiemetic effect there was no increase in the incidence of nausea and vomiting.¹² However, the authors did observe an increased incidence of dizziness in their patients. This was not one of the parameters under study in our study so we cannot comment on it. On the contrary to the above another study¹³ did not demonstrate any additional benefit of dexamethasone in combination with pregabalin in terms of pain relief after hip surgery. This was judged by a decrease in the morphine requirement of these patients. De Souse Santos et al¹⁴ stated that the combination of tramadol and dexamethasone was beneficial in-patient undergoing surgery for their third molar. Dursteler *et al.*,¹⁵ used a similar combination and demonstrated a synergistic effect of these two medicines. However, looking at the literature we did

not come across a single study that would compare these two medicines in patients undergoing day care surgeries of inguinal hernia. Our team wanted to establish via research which of the two medicines was superior for the purpose and hence could then be made part of our SOPs for pain management. In our study it was apparent based upon the results that pregabalin was superior in the management of the post operative pain at all the three times, i.e. 6, 12 and 24 hours.

Our patients did not have any significant side effects. This was probably due to the low dose of pregabalin that we were using. When used in higher doses Pregabalin has led to side effects like dizziness and blurring of vision. These side effects were directly proportional to the dose of pregabalin used. In one study pregabalin dose of 600mg and 300 mg were compared. The side effects of dizziness and blurring were observed as 70% vs 60% and 63% vs 50% respectively.

The meta-analysis by Zhang *et al.*,¹⁶ demonstrated that the use of pregabalin in the pre operative period showed a statistically significant reduction in the opioid requirements. One of the findings was that in the early and late period there was no statistically different pain scores. This was in contrast to our finding as there was a reduction in VAS scores at the initial as well as the late post-operative period.

The authors were of the view that this difference between the two findings was due to the heterogeneity of the groups under study. They also demonstrated an increased incidence of visual disturbances as demonstrated in the studies included in the meta-analysis however, we did not study this parameter.

The strength and the peculiarity of our study was that we compared these two medications which was not done in the past. Both dexamethasone and pregabalin are effective as part of the pre emptive analgesia plan. However, if we have to choose one, pregabalin would be the appropriate medicine.

Conclusion

Single dose pregabalin is superior to dexamethasone for post-operative pain control in patients undergoing hernia repair under spinal anesthesia.

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