## **ORIGINAL ARTICLE**

# Role of Pregabalin in Reducing Postoperative Analgesic Requirement of Patients Undergoing Knee Arthroscopy Anterior Cruciate Ligament Repair

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### ABSTRACT

**Objective:** To assess the effect of pregabalin in reducing the postoperative requirement of analgesics of patient undergoing knee arthroscopic anterior cruciate ligament repair surgery.

Study Design: Prospective randomized control trial.

Place and Duration of Study: Department of Anesthesia, Ghurki Trust Teaching Hospital Lahore from 1<sup>st</sup> June 2021 to 31<sup>st</sup> December 2021.

**Methodology:** Eighty patients were randomly divided into two groups; group A and group B, each group comprised 40. Group A receive placebo and group B receive pregabalin 150mg once a day for two days after surgery. Pain assessment done with the help of Numeric Rating Scale and rescue analgesia was recorded.

**Results:** The mean age was 31±10.2 years of group A and 33±10.3 year of Group B. There were more males within both groups in comparison to females with a percentage of 77.5% and 85% respectively. The reduction was seen within Group B in comparison of Group A in terms of ASA class, VNRS, and maximum sensory block. Cumulative volume of PCA in mI was also less in group B than group A with a significant difference within 0-6 hours.

**Conclusions:** The use of pregabalin 150mg after surgery for two days significantly reduces the analgesic consumption **Keywords:** Pregabalin, Postoperative analgesic, Numeric rating scale

### INTRODUCTION

Arthroscopic anterior cruciate-ligament (ACL) renewal is a surgical procedure performed commonly. Femoral tunnels as well as tibial tunnel construction is required for passage formation during ACL grafting procedure. This cause moderate to severe pain during initial postoperative time.<sup>1</sup> Although the advancement in surgical techniques there has been a decrease in length of post-operative hospital stay but in conditions of patient's pain this period can get longer. Moreover, a inadequate management of pain can inversely effect rehabilitation and patient's recovery leading to adverse surgical outcomes.<sup>2</sup> Various analgesic combination is necessary for pain management.<sup>3</sup>

Pregabalin administration in multimode-analgesic prevents hyperalgesia as well as reduces post-operative pain and consumption of opioids in different surgical procedures.<sup>4-7</sup> It being an acid-analog can inhibit influx of calcium ions at the terminals of the nerves which consequently decreases the release of neurotransmitters involved in excitation and pain.<sup>8</sup>

Knee arthroplasty have proven the effect of pregabalin in controlling pain but the extent of this drug as well as frequency used has yet not been clearly documented.<sup>9,10</sup> Majority of the literature available focused on use of pregabalin in controlling post-operative pain until first twenty four hours<sup>11,12</sup> bringing a major gap in understanding the efficiency of this drug in presence of local anesthetics. Furthermore side effect related with the use of pregabalin also requires being explored.<sup>13</sup>

The present study was mean t to address all the above mentioned concerns in details and provide evidence base literature for facilitating health related outcomes in patients of ACL.

## MATERIALS AND METHODS

This randomized control trial conducted at Department of Anesthesia, Ghurki Trust Teaching Hospital Lahore from 1<sup>st</sup> June 2021 to 31<sup>st</sup> December 2021 and 80 patients were enrolled. The patients undergoing knee arthroscopy anterior cruciate ligament repair were included in the study. Those patients having previous history of knee arthroscopy, anxiety episodes, diabetes or any other correlated comorbidity were excluded. All patients were requested to provide informed written consent before being enrolled as study participants. The sample size of the study was 80 which was calculated sing WHO sample size calculator where 5% margin of error, 80% power of test and 95% Confidence interval

was taken into consideration. The age of the patients was between 20-69 years. The patients were divided into two major groups. Group A (n=40) were receiving placebo drug while Group B (n=40) received Pregabalin in 150mg OD dosage until two days postsurgery. Identical capsules production either with pregabalin or as placebo were made by the pharmaceutical company. They were administered with water sips orally through an independent nurse who was blinded to the information of the patients. Random permuted-block randomization-algorithm was used for generating randomized list which was not disclosed until analysis of data. There was no other drug administered except pregabalin in preoperative patients. Within the operating room standard condition of vital signs monitoring were opted. Spinal anesthesia using bupivacaine0.5% (14 mg in case of male and 12 mg in case of female combined with 10 µg of fentanyl) in the lateral-decubitus position (lumbar level 3/4) was delivered. Spinal blockage period was taken as maximum blockage till L2 segment block regression assessed through pin prick test, IV PCA administration in postoperative 24 hour was done with fentanyl in 1000ug with ramosetron in 0.3 mg (200 ml in saline) and administered in 4ml per hour as well as 2ml depending on demand of the patient with lockout of 20min. Surgical procedure involved preparation of graft. Quadruple-hamstring tendon-autograft was used. Standard knee arthroscopy anterior cruciate ligament repair procedure was opted.<sup>11</sup> The post operational pain within the primary 36 hours as well as at two weeks' time post-surgery was considered as the primary outcomes. The assessment of post operational pain was done by knee flexion passive movement (at 60°). Pain assessment was performed through eleven point verbal-numerical rating scale (VNRS) where 0 was none and 10 was worst pain. Post-operative pain was divided as 12, 24 and 36 hours. In case VNRS ≥ five, meperidine in 0.5mg/kg was given as rescue-analgesic (RE). The number/amount of RE was documented as 0 to 12, 12 to 24, and 24 to 36 hour. Clinical information, history, age, gender and results of pain assessment were documented. Data was analyzed while using SPSS-26. The Chi square test was applied and P<0.05 was considered as significant.

#### RESULTS

The mean age was  $31\pm10.2$  years of group A and  $33\pm10.3$  year of Group B. There were more males within both groups in comparison to females with a percentage of 77.5% and 85%

respectively. The reduction was seen within Group B in comparison of Group A in terms of ASA class, VNRS, and maximum sensory block. Duration of surgery and spinal block was also approximately similar within both groups (Table 1).

A smaller number of patients in group B receiving pregabalin were administered rescue analgesic when compared with control group A. The cumulative volume of PCA in ml was also less in group B than group A with a significant difference within 0-6 hours. The similar significant difference in cumulative bolus deliverance was also observed at 0-6 hours. It is also important to note that only 28 patients such as 70% required RE in group B while 38 such as 95% of group A requested RE (Table 2).

Variables	Group A (n=40)	Group B (n=40)	P-Value
Age (years)	31±10.2	33±10.3	0.379
Gender:	31/9	34/6 (85%/15%)	0.294
male/female	(77.5%/22.5%)		
Body mass index (kg/m <sup>2</sup> )	25.4±3.4	24.9±4.5	0.731
ASA class I/II	37/3(92.5%/7.5%)	36/4 (90%/10%)	0.329
Preoperative pain VNRS	4 (3–6)	4 (2–6)	0.492
Maximal sensory level of block	T8 (T5–10)	T8 (T6–10)	0.510
Duration of surgery (minute)	92±24	91±22	0.790
Duration of anesthesia (minute)	124±27	125±27	0.561
Duration of spinal blockade (minute)	147±33	147±25	0.974
Intraoperative crystalloid (mL)	547±180	542±177	0.900

Table 1: Comparison of Group A and B demographic, VNRS and intraoperative data

Table 2: Comparison of post-operative rescue analgesic in group A and	В
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Variables	Group A (n=40)	Group B (n=40)	P-Value		
Patient receiving rescue analgesics					
0–12 h	18 (45%)	11 (27.5%)	0.101		
12–24 h	12 (30%)	10 (25%)	0.524		
24–36 h	8 (20%)	7 (17.5%)	0.636		
IV-PCA use					
PCA cumulative volume in (mL)					
0–6 h	35.1±5.7	33.1±5.2	0.09		
7–12 h	70.2±12.3	67.1±11.6	0.151		
13–24 h	134.2±27.4	125.1±28.9	0.135		
Cumulative number of bolus administered					
0–6 h	5.6±2.9	4.6±2.7	0.080		
7–12 h	11.2±6.3	9.4±5.9	0.166		
13–24 h	19.3±14.1	16.3±11.2	0.275		





The incidence of side effects within group A and group B presented that dizziness was complained higher in group B patients at 0-12 hours while headache was higher at 0-12 hour in Group B but was subsided by 24-36 hour. At 24-36 hour the group A some patients developed headache. Vomiting and nausea sat 0-12 hour was significantly (p<0.05) higher in Group B than A. However it became equal at 12-24 hour and subsided in group A at 24-36 hour (Fig 1).

#### DISCUSSION

The present study was designed as a prospective randomized control double blinded research. The findings of the current research presented that post-operative pain was effectively reduced with the use of pregabalin without the requirement of supplemented opioid in post-operative conditions as well as IV-PCA. Pregabalin also reduced knee pain after twenty weeks of surgery in comparison with control group where only placebo was given. The results of the current research were in similarity with the previously reported literature however the present study provided detailed and more elaborated results.<sup>14-19</sup>

The patients who were given pregabalin were having higher dizziness episode as a side effect of this drug in comparison to the placebo control patients identifying it to be a side effect of pregabalin administration.<sup>18</sup>

Pain assessment between both groups showed a decreased in pregabalin group than placebo. Although the variance was insignificantly variant but was recordable. Studies have elaborated that in cases where pain managements done timely in surgical procedures the recovery time of the patients increase.<sup>19-21</sup> In the present study patients with pregabalin has an earlier postoperative knee movement and pain relief therefore assisting in their earlier recovery than placebo group.

The present study used 150 mg dosage of pregabalin. Previously reported research in its evaluation of two dosage of pregabalin as 75mg as well 150mg delivered an hour before spinal fusion and twelve hour later the spinal effusion showed a reduction in IV-PCA usage within a day and two with the use of 150mg dose.<sup>22</sup> The result of this study was in similarity with the present study findings proving 150 mg to be a reliable dosing.

#### CONCLUSION

The use of pregabalin 150mg after surgery for two days significantly reduces the analgesic consumption and facilitates early recovery in ACL patients.

#### REFERENCES

- Mardani-Kivi M, Mobarakeh MK, Keyhani S, Motlagh KH, Ekhtiari KS. Is gabapentin effective on pain management after arthroscopic anterior cruciate ligament reconstruction? A triple blinded randomized controlled trial. Arch Bone Joint Surg 2013; 1: 18-22.
- Abdallah FW, Brull R, Joshi GP. Pain management for ambulatory arthroscopic anterior cruciate ligament reconstruction: Evidencebased recommendations from the society for ambulatory anesthesia. Anesth Analg 2019; 128(4): 631-40.
- Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. Anesth Analg. 1993; 77: 1048-56.
- Zhang J, Ho KY, Wang Y. Efficacy of pregabalin in acute postoperative pain: a meta-analysis. Br J Anaesth 2011; 106: 454-62.
- Mishriky BM, Waldron NH, Habib AS. Impact of pregabalin on acute and persistent postoperative pain: a systematic review and metaanalysis. Br J Anaesth 2015: 114: 10-31.
- Lam DM, Choi SW, Wong SS, Irwin MG, Cheung CW. Efficacy of pregabalin in acute postoperative pain under different surgical categories: A meta-analysis. Medicine 2015; 94: e1944.
- Mathiesen O, Jacobsen LS, Holm HE, Randall S, Adamiec-Malmstroem L, Graungaard BK, et al. Pregabalin and dexamethasone for postoperative pain control: A randomized controlled study in hip arthroplasty. Br J Anaesth 2008; 101: 535-41.
- Engelman E, Cateloy F. Efficacy and safety of perioperative pregabalin for post-operative pain: a meta-analysis of randomizedcontrolled trials. Acta Anaesthesiol Scand 2011; 55: 927-43.
- Buvanendran A, Kroin JS, Della Valle CJ, Kari M, Moric M, Tuman KJ. Perioperative oral pregabalin reduces chronic pain after total

knee arthroplasty: a prospective, randomized, controlled trial. Anesth Analg 2010; 110: 199-207.

- Buvanendran A, Kroin JS, Della Valle CJ, Moric M, Tuman KJ. Cerebrospinal fluid neurotransmitter changes during the perioperative period in patients undergoing total knee replacement: a randomized trial. Anesth Analg 2012; 114: 434-41.
- Yadeau JT, Paroli L, Kahn RL, Jules-Elysee KM, Lasala VR, Liu SS, et al. Addition of pregabalin to multimodal analgesic therapy following ankle surgery: a randomized double-blind, placebo-controlled trial. Reg Anesth Pain Med 2012; 37: 302-7.
  Gray A, Kehlet H, Bonnet F, Rawal N. Predicting postoperative
- Gray A, Kehlet H, Bonnet F, Rawal N. Predicting postoperative analgesia outcomes: Nnt league tables or procedure-specific evidence? Br J Anaesth 2005; 94: 710-14.
- 13. White PF, Kehlet H. Improving postoperative pain management: what are the unresolved issues? Anesthesiology 2010; 112: 220-25.
- Nimmaanrat S, Tangtrakulwanish B, Klabklay P, Boonriong T. Perioperative administration of pregabalin in patients undergoing arthroscopic anterior cruciate inligament reconstruction: does it help to relieve postoperative pain? J Med Assoc Thail Chotmaihet Thangphaet 2012; 95: 1297-1301.
- Myles PS, Weitkamp B, Jones K, Melick J, Hensen S. Validity and reliability of a postoperative quality of recovery score: The qor-40. Br J Anaesth 2000; 84: 11-5.
- Gupta R, Kapoor D, Kapoor L, Malhotra A, Masih GD, Kapoor A, Joshi S. Immediate post-operative pain in anterior cruciate ligament

reconstruction surgery with bone patellar tendon bone graft versus hamstring graft. J Orthop Surg Res 2016; 11: 67.

- Kim SY, Song JW, Park B, Park S, An YJ, Shim YH. Pregabalin reduces post-operative pain after mastectomy: a double-blind, randomized, placebo-controlled study. Acta Anaesthesiol Scand 2011; 55: 290-96.
- Pesonen A, Suojaranta-Ylinen R, Hammaren E, Kontinen VK, Raivio P, Tarkkila P, Rosenberg PH. Pregabalin has an opioid-sparing effect in elderly patients after cardiac surgery: a randomized placebocontrolled trial. Br J Anaesth 2011; 106: 873-81.
- Luo ZD, Chaplan SR, Higuera ES, Sorkin LS, Stauderman KA, Williams ME, et al. Upregulation of dorsal root ganglion (alpha)2 (delta) calcium channel subunit and its correlation with allodynia in spinal nerve-injured rats. J Neurosci 2001; 21: 1868-75.
- 20. Gajraj NM. Pregabalin: its pharmacology and use in pain management. Anesth Analg 2007; 105: 1805-15.
- Agarwal A, Gautam S, Gupta D, Agarwal S, Singh PK, Singh U. Evaluation of a single preoperative dose of pregabalin for attenuation of postoperative pain after laparoscopic cholecystectomy. Br J Anaesth 2008; 101: 700-4.
- Kim JC, Choi YS, Kim KN, Shim JK, Lee JY, Kwak YL. Effective dose of peri-operative oral pregabalin as an adjunct to multimodal analgesic regimen in lumbar spinal fusion surgery. Spine 2011; 36: 428-33.