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The effect of oral Paracetamol compared to oral Pregabalin for postoperative pain relief following Anterior cruciate ligament reconstruction surgeries under subarachnoid block - A prospective randomized trial

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Abstract

Introduction: Poor postoperative pain control after spinal anaesthesia impairs the functional recovery and increases the requirement of analgesics postoperatively. Good analgesia after the surgery is essential for early mobilization and rehabilitation following anterior cruciate ligament (ACL) reconstruction surgeries. Pregabalin and paracetamol are commonly used non-opioid analgesics in multimodal pain management perioperatively, but studies comparing their preoperative use in ACL reconstruction surgeries are very limited.

Objectives: To compare the analgesic efficacy of preoperative oral pregabalin and oral paracetamol in patients undergoing ACL reconstruction under subarachnoid block, and to study the associated hemodynamic changes and any adverse effects.

Methodology: In this prospective, randomized, double-blind study, 150 adult patients (ASA I-II) scheduled for ACL reconstruction under spinal anaesthesia were allocated to receive either oral pregabalin 75 mg or oral paracetamol 1 g two hours before surgery. Postoperative pain was assessed using the Visual Analogue Scale (VAS) for 24 hours. Duration of analgesia, need for rescue pain medications, hemodynamic parameters, and any adverse effects were recorded.

Results: Preoperative pregabalin resulted in significantly lower postoperative VAS scores and prolonged duration of analgesia compared to paracetamol. Rescue analgesic requirement was reduced in the pregabalin group. Hemodynamic parameters were comparable between groups and no significant adverse effects were observed in either group.

Conclusion: Preoperative oral pregabalin 75 mg provides superior postoperative analgesia with reduced rescue analgesic requirements compared to oral paracetamol 1 g in ACL reconstruction under spinal anaesthesia, supporting its role in multimodal perioperative pain management.

Keywords: Anterior cruciate ligament reconstruction; Pregabalin; Paracetamol; Spinal anaesthesia; Postoperative analgesia; Multimodal analgesia

Introduction

Postoperative pain remains the most common and distressing symptom in the postoperative period and is a major factor of patient satisfaction, hospital stay, and functional recovery. Inadequately controlled pain impairs respiratory function, and limits mobility, thereby increasing the risk of pulmonary complications, nausea, vomiting, and thromboembolic events and also activates the sympathetic nervous system, resulting in tachycardia and hypertension. Poorly managed acute postoperative pain is also associated with delayed recovery, increased hospital bills, and progression to chronic pain conditions with consequent impairment in quality of life.

In spite of recent advancement in field of pain and palliative medicine, significant deficits continue to persist and management of post-operative pain is quite challenging for anaesthesiologists. Different types of anaesthetic drugs used for post operative pain relief include opioids, nonopioids like NSAIDs, Paracetamol, Gabepentanoids, Ketamine etc.

Anterior cruciate ligament (ACL) reconstruction is a commonly performed arthroscopic procedure. It is associated with significant postoperative pain. Pain in the immediate postoperative period, apart from an unpleasant experience for the patient, can act as a barrier for static quadriceps contractions and for optimum execution of the initial rehabilitation protocol resulting in a slow recovery and a late return to the full function for a sports person. The success of anterior cruciate ligament reconstruction surgery depends up on the postoperative rigorous rehabilitation.

Pregabalin is a structural analogue of gamma amino butyric acid which shows analgesic, anticonvulsant and anxiolytic effects. In many countries it is approved for the treatment of neuropathic pain. Like its predecessor Gabapentin, it binds to the alpha 2 subunit of voltage gated calcium channel reducing the release of several excitatory neurotransmitter including glutamate, nor-epinephrine, substance P and calcitonin gene related peptide and blocking the development of hyperalgesia and central sensitization.

Paracetamol has both analgesic and antipyretic properties. The analgesic effect may be spinally mediated involving N-methyl-D-aspartate receptor (NMDA receptors) and substance P. The mode of action of Paracetamol suggests that the metabolite of Paracetamol acts on Transient receptor potential ankyrin 1 (TRPA1) receptor in the spinal cord to suppress signal transduction from superficial layers of dorsal horn thus alleviating the pain.

This study compares the analgesic efficacy of oral pregabalin (75 mg) and oral paracetamol (1 g) administered preoperatively in patients undergoing ACL reconstruction under subarachnoid block.

Methods

After Institutional Ethics Committee approval and written informed consent from the patient, this prospective, randomized, double-blind study was conducted in the Department of Anaesthesiology, Baby Memorial Hospital, Calicut, Kerala.

A total of 150 adult patients (18-65 years), ASA physical status I-II, weighing 60-85 kg, scheduled for elective anterior cruciate ligament (ACL) reconstruction under subarachnoid block were included. The exclusion criteria were allergy to pregabalin or paracetamol, intake of analgesics within 24 hours, posterior cruciate ligament involvement, and surgery lasting more than two hours.

Patients were randomly allocated by block randomisation into two groups (n = 75 each). Group 1 received oral pregabalin 75 mg and Group 2 received oral paracetamol 1 g, administered two hours

before surgery. Drug administration was performed by a nurse not involved in the study. Both patients and outcome assessors were blinded to group allocation.

With standard monitoring, the baseline hemodynamic parameters were recorded. Intravenous access was secured, and all patients received intravenous midazolam 1 mg and ondansetron 4 mg as premedications. Subarachnoid block was performed under aseptic precautions at the L3-L4 intervertebral space using a 25-gauge Quincke needle with 4 mL of 0.5% hyperbaric bupivacaine. Hemodynamic variables such as blood pressure, heart rate, SPO₂ were monitored intraoperatively. Intravenous paracetamol 1 g was administered at the end of surgery to all patients.

Postoperative pain was assessed using the Visual Analogue Scale (VAS) at 30-minute intervals for 24 hours. Intravenous paracetamol 1 g was repeated after six hours. Intravenous diclofenac 75 mg was used as rescue analgesia when VAS 4 or more, with intravenous tramadol 25 mg administered if required. Duration of analgesia, rescue analgesic consumption, hemodynamic changes, and adverse effects were recorded.

Results

A total of 150 patients undergoing anterior cruciate ligament (ACL) reconstruction under subarachnoid block were enrolled and randomly allocated into two groups of 75 each. The majority of patients were male population. There was no statistically significant difference in ASA grading between the two groups. A reduction in heart rate and blood pressure was observed intraoperatively during the first 30 minutes in both groups; however, these changes were comparable and attributed to the subarachnoid block. There were no statistically significant hemodynamic differences between the two groups.

Postoperative pain was assessed using the Visual Analogue Scale (VAS) at 30 minutes, 1, 2, 4, 6, 8, 12 and 24 hours. Patients in the Pregabalin group (Group 1) demonstrated significantly lower VAS scores compared to the Paracetamol group (Group 2) at the assessed postoperative intervals. The reduction in pain scores in the Group 1 was statistically significant.

Table: Comparison of VAS score at various intervals using Independent T test.

VAS	P value	Independent T test
VAS at 30 min.	P<0.05	There is significant difference between the two groups at all intervals except at 24 hours. It is lower among pregabalin group.
VAS at 1 hr.	P<0.05	
VAS at 2 hr.	P<0.05	
VAS at 4 hr.	P<0.05	
VAS at 6 hr.	P<0.05	
VAS at 8 hr.	P<0.05	
VAS at 12 hr.	P<0.05	
VAS at 24 hr.	P>0.05	

The total consumption of rescue analgesic was significantly higher in group 2 than group 1. But in

the immediate postoperative period it was statistically insignificant as p value is >0.05 . This may be due to the residual effect of spinal anaesthesia. At 4 hours postoperatively, the requirement for rescue analgesia was significantly higher in Group 2 compared to Group 1 ($p < 0.05$). Thirteen percent of patients in Group 2 required the rescue analgesic dose. At 6 hours postoperatively, rescue analgesic requirement remained higher in Group 2, with 21% of patients requiring the maximum dose. At 8 hours postoperatively, a greater proportion of patients in Group 1 required rescue analgesia, with 17% receiving the maximum dose.

At 12 hours postoperatively, rescue analgesic requirement was higher in Group 1, with 6% of patients receiving the maximum dose. There was no statistically significant difference in the incidence of nausea, vomiting, sedation, or other complications between the Pregabalin and Paracetamol groups.

Discussion

Relief of surgical pain with minimal side effects is the major goal during post operative care. Inadequate postoperative analgesia is a major source of fear and dissatisfaction for surgical patients. Also, adequate postoperative pain relief is important for better surgical outcome including early mobilisation, optimal participation in rehabilitation protocols and improved functional outcomes. The actual degree of postoperative pain will be difficult to establish.

The present study compared the analgesic efficacy and safety of preoperative oral Pregabalin 75 mg with oral Paracetamol 1 g in patients undergoing ACL reconstruction under subarachnoid block. The major finding of our study was that oral Pregabalin provided greater postoperative analgesia compared to oral Paracetamol, as shown by the significantly lower VAS scores at multiple postoperative time intervals.

Moreover, the requirement for rescue analgesia was significantly lower and the time to first rescue analgesic was prolonged in the Pregabalin group. These findings indicate that Pregabalin provides more sustained postoperative analgesia.

The analgesic efficacy of Pregabalin may be due to its mechanism of action. Pregabalin binds to the alpha 2 delta subunit of voltage-gated calcium channels, and thus reducing the excitatory neurotransmitter release and attenuating central sensitisation. Since central sensitisation contributes significantly to postoperative hyperalgesia, preoperative administration of Pregabalin may exert a preventive analgesic effect.

In a comparative study conducted by Ibrahim M Esmat and Hanan M Farag pain score was lower in Pregabalin group than Paracetamol group which is similar to our observations. Similarly, In a study conducted by Agarwal there was significantly lower requirement of rescue analgesic in Pregabalin group (P value < 0.001), which is similar to our observations. Rajappa et al. in their study also observed delayed rescue analgesic requirement and reduced pain scores with Pregabalin administration in patients undergoing hysterectomy under spinal anaesthesia.

In the present study, although initially a fall in heart rate and blood pressure was observed intraoperatively in both groups, these changes were comparable and attributed to the effect of subarachnoid block rather than the study drugs. No statistically significant hemodynamic differences were noted between the groups.

This suggests that both oral Pregabalin and Paracetamol are hemodynamically stable when administered preoperatively in patients undergoing spinal anaesthesia. With regard to safety, no significant adverse effects were observed in either group. The absence of significant sedation, nausea, vomiting or other complications suggests that low-dose Pregabalin (75 mg) is well tolerated in this clinical setting.

Although Paracetamol is widely used as part of multimodal analgesia and acts via central prostaglandin inhibition and serotonergic pathways, its analgesic efficacy in isolation appears to be inferior to that of Pregabalin in the context of ACL reconstruction. The strengths of our study were randomized selection, and blinded outcome assessment. However, certain limitations must be acknowledged. First, the study was conducted at a single centre. Second, long-term pain outcomes were not assessed. Third, serum drug concentrations of pain medications were not measured to correlate pharmacokinetic properties with analgesic efficacy. Future studies comparing Pregabalin as part of multimodal analgesic regimens and evaluating its impact on long-term functional recovery following ACL reconstruction would be valuable.

Conclusion

Preoperative oral Pregabalin 75 mg provides superior postoperative analgesia, delays rescue analgesic requirement and reduces overall analgesic consumption compared to oral Paracetamol 1 g in patients undergoing ACL reconstruction under subarachnoid block, without significant hemodynamic instability or any adverse effects.

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