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Original Article

Anaesthesia Section

Comparison of Intra-Articular Injection and Femoral Nerve Block Using a Combination of Levobupivacaine with Clonidine for Postoperative Analgesia after Arthroscopic Anterior Cruciate Ligament Reconstruction- A Randomised Double-Blind Clinical Trial

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ABSTRACT

Introduction: Anterior Cruciate Ligament (ACL) is the most commonly injured ligament in the knee. Arthroscopic ACL reconstruction is the gold standard procedure for treating ACL tears. Good postoperative analgesia is the secret for immediate postoperative rehabilitation. Various techniques, such as Femoral Nerve Blocks (FNB), epidural blocks, adductor canal blocks, and Intra-Articular (IA) injections, are used to manage postoperative pain.

Aim: To compare the quality of postoperative analgesia using a combination of levobupivacaine with clonidine via IA and FNB in patients undergoing ACL reconstruction under spinal anaesthesia.

Materials and Methods: This randomised, double-blinded trial was conducted at Pondicherry Institute of Medical Sciences, Puducherry, India, from August 2016 to May 2018. Forty patients with American Society of Anaesthesiologists (ASA) physical status I and II, aged between 18-60 years, undergoing arthroscopic ACL repair under spinal anaesthesia were randomly assigned to two groups, with 20 patients in each group. After the surgery, patients in group 1 received FNB with 15 mL of 0.25% levobupivacaine and 30 mcg clonidine, while patients in group 2 received IA with 15 mL of 0.25% levobupivacaine and 30 mcg clonidine. Parameters such as the total duration of sensory block, the need for rescue analgesia, and total analgesic consumption within 24 hours were recorded postoperatively. The data were analysed using Student's unpaired t-test, Analysis of Variance (ANOVA), Chi-square test, and Fisher's-exact test. Statistical analysis was performed using Statistical package for the Social Science (SPSS) software (version 20.0 and info version 3.5.1) for Windows, with a p-value <0.05 considered significant.

Results: The quality of postoperative analgesia, including the total duration of block, the need for rescue analgesia, and total analgesic consumption within 24 hours, was similar in both groups. The total duration of block was 216±36.041 minutes for the FNB group and 224±47.395 minutes for the intra-articular group, with a p-value of 0.552. The time for rescue analgesia was 307±87.666 minutes for the FNB group and 305±82.00 minutes for the intra-articular group, with a p-value of 0.963. There were no significant differences between the groups in terms of sex, age, weight, or ASA physical status classification.

Conclusion: The present study showed that the postoperative analgesia following arthroscopic ACL reconstruction was equally effective in both groups. Both combinations reduced postoperative pain, expedited the return of postoperative function, maintained vital parameters, and had no apparent side-effects. However, IA may be considered as the preferred option since it is easier to perform than a femoral block.

Keywords: Knee surgeries, Ligament repair, Local anaesthetics, Rescue analgesia

INTRODUCTION

Reconstruction of the ACL and repair of a torn meniscus are commonly performed arthroscopic procedures. Arthroscopic ACL reconstruction is the gold standard for ACL tear [1]. It has been reported that ACL reconstruction is associated with moderate to severe pain, and more than 50% of patients may require opioid analgesics for postoperative pain [2]. Accelerated rehabilitation of the knee helps patients to regain early range of motion. Hence, it is important to provide good postoperative analgesia. Inadequate analgesia can hinder early mobilisation, postoperative rehabilitation, increase the risk of complications, and delay discharge. Various techniques, such as FNB, adductor canal block, epidural blocks, and Intra-Articular (IA) injections, are used for postoperative pain control. FNB has been shown to provide excellent analgesia but can lead to quadriceps weakness, delaying mobilisation and increasing the risk of falls [3-7]. IA injections have also demonstrated effective pain reduction and improved disability following knee surgery [8,9], but their efficacy is questioned [10]. An ideal postoperative analgesic therapy should anticipate and delay the onset of pain, reducing the need for additional drugs. The therapy should be long-lasting, with a rapid onset of action, easy administration, safety, and minimal side-effects [10]. The novelty of this study lies in comparing the quality of postoperative analgesia between intra-articular injections and femoral nerve blocks using a combination of levobupivacaine and clonidine for arthroscopic ACL reconstruction [7-9].

MATERIALS AND METHODS

This randomised, double-blinded trial was conducted in the Department of Anaesthesiology and Critical Care Medicine at Pondicherry Institute of Medical Sciences, Puducherry, India, from

August 2016 to May 2018. The study obtained approval from the Institutional Ethical Committee (Ref no: IEC:RC/16/100) and the Clinical Trials Registry- India (CTRI/2018/04/012991).

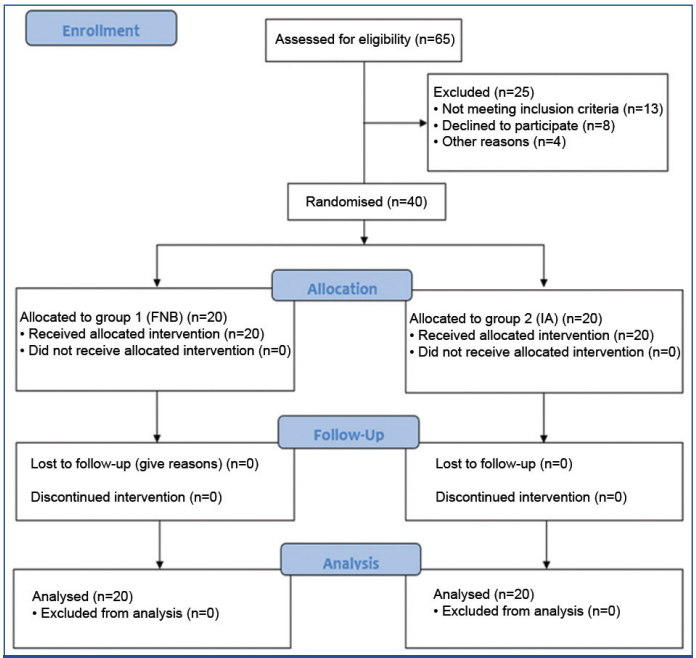
Inclusion and Exclusion criteria: The trial included patients aged 18-60 years, with ASA physical status I and II, of both genders, scheduled for ACL reconstruction under spinal anaesthesia. Patients with known allergies to local anaesthetic agents, local infection at the injection, site, those on oral anticoagulant drugs, and those with a BMI >35 kg/m^2 were excluded from the trial.

Sample size calculation: Based on the pilot study, authors assumed a mean difference of 60 minutes with a standard deviation of 55 minutes between the two groups. The calculated sample size was 40, with 20 participants in each group, aiming for 80% power and a significance level of 0.05.

The sample size was determined using the formula:

$n=2\ \{2\dot{\alpha}+2(1-\beta)\}\ 2\times SD^2/d^2$

The enrollment process is further detailed in the CONSORT flow diagram [Table/Fig-1].



[Table/Fig-1]: CONSORT flow diagram.

Procedure

After explaining the procedure an informed written consent was obtained from all patients a day before the surgery. Those patients willing to participate in the study were divided into two groups using computer generated randomisation. Group 1 received FNB with 15 mL of injection 0.25% levobupivacaine and 30 mcg clonidine and group 2 received IA of 15 mL 0.25% levobupivacaine and 30 mcg clonidine. All patients were premedicated with tab. iorazepam 1 mg and tab. rantidine 150 mg, given per orally night before surgery and also in the morning two hours prior to surgery. Preoperative routine investigations like haemoglobin, total blood count, differential blood count, urine routine were asked for and results were reviewed.

On the day of surgery after shifting to operation theatre, non invasive monitors like electrocardiogram, non invasive Blood Pressure, and pulse oximeter were connected and baseline blood pressure, Heart Rate (HR) and Oxygen Saturation (SpO_2) were recorded. Intravenous access was established with 18 gauge cannula and infusion of Ringer lactate at 10 mL/kg/hr was started. With strict aseptic precautions and using local anaesthetic infiltration, subarachnoid block was performed by the qualified Anaesthesiologists in L3-L4 space with 15 mg of 0.5% hyperbaric bupivacaine. A sensory level of T10 was achieved. Intraoperative HR, blood pressure, respiratory rate and oxygen saturation were noted. If there was a failure of spinal anaesthesia, general anaesthesia was given and patient was excluded from the trial. Study drugs were administered by an anaesthetist who was not involved in the study. In group 1 (FNB), after the surgery, a qualified and experienced Anaesthesiologist performed FNB with an 18 G Tuhoy's needle under ultrasound guidance. The linear transducer was placed on the axial (transverse plane) line near the inguinal ligament. A 15 mL of 0.25% levobupivacaine and 30 mcg clonidine were given and 15 mL of normal saline was injected intra-articularly by the surgeon before the closure of lateral port using a spinal needle to avoid bias. Ports were then closed and compression bandage was applied from the toes to the mid-thigh. The tourniquet was later released. In group 2 (IA), the surgeon administered intra-articular clonidine (30 mcg) with 15 mL of 0.25% levobupivacaine. A needle jab was given in the femoral region, and a plaster was applied to mimic the procedure. Patients were observed after the block administration. Sensation around the knee joint was monitored at 30-minute intervals in the postoperative period until rescue analgesia was provided.

Haemodynamic and respiratory parameters (heart rate, blood pressure, respiratory rate, and oxygen saturation) were measured at 30-minute intervals postoperatively until rescue analgesia was given. Subsequently, patients were monitored every two hours. The first rescue analgesia, diclofenac 75 mg injection, was administered intramuscularly by a service nurse when the Numeric Rating Scale (NRS) was above 4 or when the patient first complained of pain [11]. The follow-up team, blinded to the study and monitored the patients. The pain-free period was defined as the time interval between the administration of the test drugs and the requirement of the first rescue analgesia. The total duration of sensory analgesia, need for rescue analgesia, and total analgesic consumption in 24 hours were recorded for each group. Patients were shifted to the ward once they were haemodynamically stable and comfortable.

STATISTICAL ANALYSIS

Descriptive statistics were used for continuous variables, and frequencies were calculated for categorical variables. The data were analysed using SPSS software (version 20.0 and info version 3.5.1) for Windows, employing the Student unpaired t-test, ANOVA, Chi-square test, Fisher's-exact test. A p-value of less than 0.05 was considered significant.

RESULTS

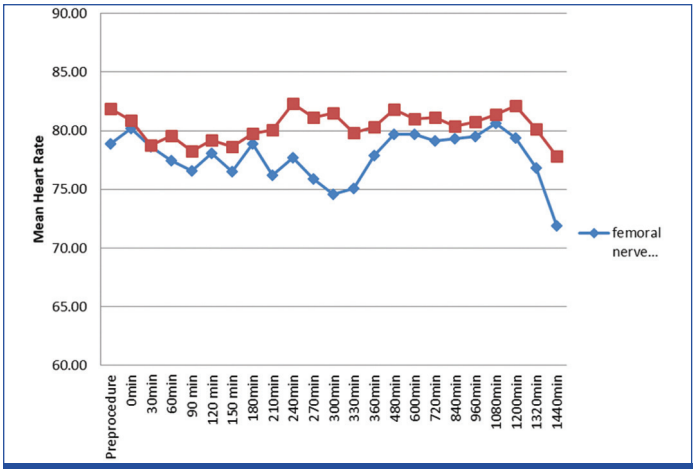
The demographic profile, including age, gender, weight, and ASA grade, was comparable between the groups and not statistically significant [Table/Fig-2].

Parameters	Group 1 (FNB)	Group 2 (IA)	p-value
Mean age (years)	33.80	36.30	0.45
Gender (M:F)	17:3	20: 0	0.23
Mean weight (kg)	68.85	72.85	0.21
ASA grade (I:II)	19:1	19:1	1.00

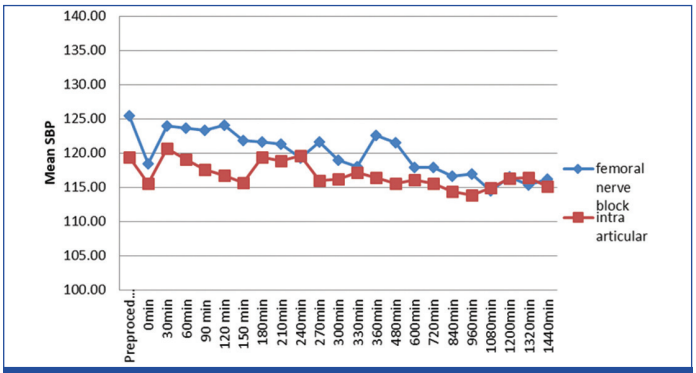
[Table/Fig-2]: Demographic data.
Student unpaired t-test was applied for age and weight
Fisher-exact test was applied for gender and ASA

Intraoperative parameters such as mean heart rate [Table/Fig-3], systolic blood pressure, and diastolic blood pressure, [Table/Fig-4,5] were comparable between the groups and not statistically significant.

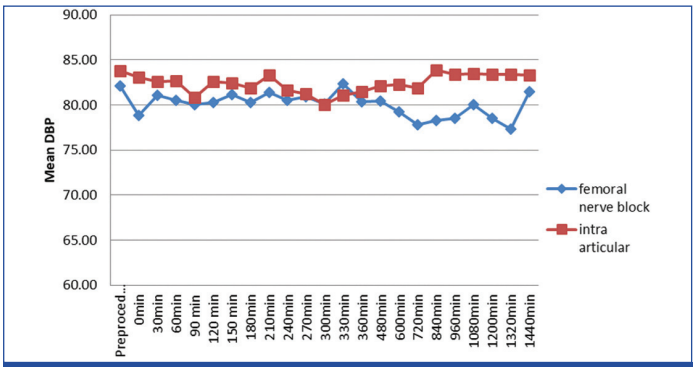
The duration of sensory analgesia [Table/Fig-6] and time for the first rescue analgesia [Table/Fig-7] were compared between the two groups. The duration of sensory analgesia was 216 minutes (SD: 36.041) for FNB and 224±47.395 for the intra-articular group, with a p-value of 0.552. The time for rescue analgesia was 307.00±87.66 for FNB (group 1) and 305±82.00 for the intra-articular group (group 2), with a p-value of 0.963. The total requirement of rescue analgesics [Table/Fig-8] in the first 24 hours postoperatively did not significantly differ between the two groups.



[Table/Fig-3]: Mean Heart Rate (HR) of study participants during pre procedure and during the first 24 hours postoperatively among the 2 group.
Repeated measures ANOVA for difference between two means
There was no statistical difference between the 2 groups



[Table/Fig-4]: Mean Systolic Blood Pressure (SBP) of study participants among 2 groups.
Repeated measures ANOVA for difference between 2 means
There was no statistical difference between the 2 groups



[Table/Fig-5]: Mean Diastolic blood pressure (DBP) of study participants among 2 groups.
Repeated measures Anova for difference between 2 means
There was no statistical difference between the 2 groups

	Group 1	Group 2	p-value
Mean duration sensory analgesia (mins)	216±36.041	224±47.39	0.552

[Table/Fig-6]: Mean duration of sensory analgesia between 2 groups.
Student unpaired t-test for difference between two means

	Group 1	Group 2	p-value
Mean time for first rescue analgesia (min)	307.00±87.66	305.75±82.00	0.96

[Table/Fig-7]: Mean time for first rescue analgesia among the 2 groups.
Student unpaired t-test for difference between two means

Time	Group 1	Group 2	p-value
6-12 hours	90±10	102±5	0.33
12-24 hours	240±10	250±5	0.14

[Table/Fig-8]: Total analgesic consumption (Diclofenac in mg).
Chi-square test was applied
p-value not significant. Values are expressed in mean±SD

DISCUSSION

Effective pain control after ACL repair is critical for recovery and rehabilitation. Early mobilisation after ACL reconstruction is important as it speeds up recovery, and reduces complications related to immobilisation, and facilitates early discharge from the hospital [12]. In order to mobilise the patients rapidly, good analgesia with minimum side-effects is essential [13]. Various techniques, such as epidural block, lumbar plexus block, FNB, adductor canal block, and intra-articular injections, have been used for postoperative pain relief with low opioid consumption.

Single injection FNB has consistently shown superior analgesia compared to a placebo group for upto 24 hours in patients undergoing knee surgeries. However, its main drawback is the motor weakness of the quadriceps muscles observed in all dosages of FNB administered [14]. Similarly, many studies have demonstrated that intra-articular injection of bupivacaine with adjuvants provides adequate analgesia for upto 24 hours following arthroscopic knee surgeries [8,9].

In this trial, authors compared the quality of postoperative analgesia between ultrasound-guided FNB with a levobupivacaine/clonidine combination and intra-articular administration of a levobupivacaine/clonidine combination in patients undergoing ACL reconstruction under spinal anaesthesia. Authors observed that the duration of sensory analgesia was 216 minutes (3 hours 36 seconds) for FNB and 224 minutes (3 hours 44 seconds) for intra-articular administration, which is consistent with a study by Lamaroon A et al., The time for the first dose of analgesia was 307 minutes for FNB and 305 minutes for intra-articular administration, with no statistical significance [15]. Dauri M et al., also found similar results in terms of sensory analgesia and total amount of rescue analgesia consumption, despite using a higher concentration of bupivacaine compared to our trial [16].

Iskandar H et al., compared two groups receiving 1% ropivacaine and observed that FNB provided superior analgesia and a longer time to first rescue analgesia than intra-articular infiltration following ACL repair. The time for the first rescue analgesia in their study was 320 minutes, which was comparable to our study [2].

Levobupivacaine, an S-enantiomer of bupivacaine, is a safe and preferred drug for regional anaesthesia due to its stronger sensory block and minimal adverse effects on the cardiovascular and central nervous systems [17-20]. In the present study, authors used 37.5 mg of levobupivacaine with clonidine, and no patients experienced cardiac or neurological toxicity or any other adverse reactions. Therefore, we considered the volume and dosage of the drug administered during the trial to be safe. Studies by Frost S et al., and Toftdahl K et al., also reported no local anesthetic-related side-effects when using ropivacaine for postoperative analgesia in ACL reconstruction and intra-articular analgesia [21,22].

Minimising postprocedural side-effects like nausea, vomiting, sedation, and respiratory depression is an important goal of minimally invasive surgery [23]. NSAIDs, such as injection diclofenac, provide a safer alternative to opioids for breakthrough analgesia in ACL repairs. Injection tramadol was supplemented for patients who underwent surgery only under spinal anaesthesia, without femoral nerve block or intra-articular injection. Studies by Priyanka S and Shalini P; and Guirro UB et al., concluded in their study that FNB reduces postoperative opioid/NSAID consumption after ACL repair [24,25]. Wang YL et al., in their meta-analysis, concluded that a single dose of bupivacaine significantly reduced postoperative analgesia and opioid consumption compared to the placebo group, which is consistent with our study [26]. Similarly, in our study, authors found that a single rescue analgesia (injection diclofenac) was sufficient to keep the Numerical Rating Scale (NRS) below four for the first 24 hours.

Limitation(s)

The present trial had some limitations. Firstly, motor function was not assessed postoperatively. Secondly, the motor sparing effect

of FNB or IA was less relevant by virtue of institutional protocol of not allowing ambulation on the same day. Therefore, the results are restricted to inpatient arthroscopic surgeries only. Further studies with larger and more diverse patient groups are required to assess the efficacy of these techniques.

CONCLUSION(S)

The combination of FNB and intra-articular analgesia using levobupivacaine with clonidine was found to be equally effective for analgesia after arthroscopic ACL reconstruction. Both combinations reduced postoperative pain, hastened the return of postoperative function, and maintained vital parameters without any observed side-effects. However, intra-articular analgesia may be considered the preferred option since it is easier to perform than femoral nerve block.

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