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Analgesic effect of intraarticular ropivacaine-morphine combination in anterior cruciate ligament reconstruction patients on postoperative pain: A Randomized Control trial

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Abstract

Background: Arthroscopic ACL reconstruction surgery is commonly performed as an outpatient procedure and is often associated with postoperative pain.

Objectives: We aimed to find out the effects of intra-articular ropivacaine-morphine on postoperative pain in patients undergoing elective arthroscopic ACL reconstruction surgery.

Materials and Methods: A total of 46 patients undergoing elective arthroscopic ACL reconstruction under spinal anaesthesia were enrolled. The participants were allocated to two groups to receive the following intra-articular medications after completion of the surgery and before deflation of the tourniquet: Group I, 20 mL of saline, Group II, 0.25% Ropivacaine and 5 mg morphine 20 mL in volume. Visual analogue scale (VAS) values were recorded at 1, 3, 6, 12 and 24 hours postoperatively, duration of analgesia, total analgesic consumption, and number of rescue analgesia at 24 hours were evaluated.

Results: VAS was significantly higher in group I in comparison to other groups. Duration of analgesia was significantly longer in Group II than in Group I. Number of rescue analgesia and total analgesic consumption at postoperative hour 24 was significantly fewer in group II.

Conclusions: Intraarticular ropivacaine-morphine combination provides effective pain relief, longer analgesic duration, and less analgesic requirement when compared with intra-articular ropivacaine-clonidine combination and saline after arthroscopic ACL reconstruction surgery.

Keywords: Arthroscopic surgery, Knee, intra-articular analgesia, pain

1. Introduction

Arthroscopic knee surgery is one of the most common orthopaedic surgeries. These surgeries are usually day care procedures, hence effective pain relief is important after arthroscopic knee surgery to permit early discharge and improve patient comfort and mobility^[1]. Intra-articular analgesia is a mode of pain management after arthroscopic knee surgery. Local anesthetics, especially bupivacaine, are the most common drugs administered intra-articularly. Nonetheless, the analgesic effect does not last long. Moreover, the intra-articular use of bupivacaine has been shown to be toxic to chondrocytes^[2] and decreases the number of chondrocytes without causing tissue loss^[3].

Notable studies have been done to find the ideal regime for sufficient long-lasting postoperative analgesia such as using opioids, neostigmine, α 2-agonists, or nonsteroidal anti-inflammatory drugs (NSAIDs) separately, in combinations with each other, or with local anesthetics^[4-9].

In this study, we evaluated the efficacy of intra-articular administration of 0.25% Ropivacaine and 5 mg morphine 20 mL in volume for post-operative pain relief.

2. Material and Methods

After ethical committee clearance at Sant Parmanand Hospital, written informed consent was obtained from 46 patients aged between 20 to 45 years with ASA class I or II, undergoing elective arthroscopic anterior cruciate ligament (ACL) reconstruction, were enrolled in this prospective, randomized, double-blind study (Table 1).

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Table 1

	Group I	Group II	P Value
Age (yrs)	30.5±11.5	32.5±9.80	0.72
Gender	8 F, 13 M	10, 13 M	

Patients that received NSAIDs or narcotics in five days before operation, patients allergic to one of the study drugs, and those with alcohol or drug abuse were excluded. All patients were preoperatively instructed to use 10-cm visual analog scale (VAS) (0 = no pain; 10 = the worst imaginable pain). Preoperative baseline values of pain were evaluated at rest and at 90 degrees of flexion. None of the patients received premedication. Standard monitoring techniques were used including electrocardiography, non-invasive blood pressure monitoring, and end-tidal carbon dioxide and peripheral oxygen saturation. Regional unilateral plain spinal anaesthesia was given to all patients. A thigh pneumatic tourniquet at a pressure of 250 to 300 mmHg was applied on the same side of surgery. One surgeon performed surgical procedures using a standard surgical technique. When the surgery was completed, patients were randomly allocated to one of the two groups of 23 with the random selection of one of the envelopes in which assigned group was written. The drugs were prepared in a separate room and given to the surgical team at end of surgery. The drug solution was standardized as a total of 20-mL volume. Group I received 20 mL of isotonic saline; Group II received 0.25% Ropivacaine and 5 mg morphine 20 mL in volume. The study solutions were injected intrarticularly after closure of the surgical site at the end of surgery and ten minutes before tourniquet release. All surgery and injections were performed by the same surgeon who was blinded to the content of the syringe. After completion of the anaesthesia, patients were transferred to the postoperative care unit. Pain was assessed with VAS (it is in our clinical protocol to assess pain with VAS) by questioning the patients at hours 1, 3, 6, 12 and 24 postoperatively (Table 2).

Table 2: VAS SCORE

Follow up (hrs)	Group I			Group II			P Value
	SD	Range	Mean	SD	Range	Mean	
1	1.8	0-8	4.3	1.5	0-5	1.76	<0.001
3	1.6	2-8	3.96	1.4	0-5	1.90	<0.001
6	1.4	0-8	3.43	1.3	0-4	1.72	= 0.004
12	1.9	0-5	2.7	1.2	0-3	1.54	= 0.002
24	1.6	0-6	2.61	1	0-3	1	<0.001

When patients complained of pain (VAS score > 3), they were given 500 mg of paracetamol intravenously as rescue medication and total consumption was recorded over 24 hours. Patients' required rescue analgesia, number of rescue analgesia at 24 hours of operation, and duration of analgesia, which was considered as the time from intra-articular injection to first analgesic requirement, were recorded. Side effects such as vomiting, nausea, sedation, dry mouth, and any other adverse events were observed during the study period.

2.1 Statistical Analysis

Number, percentage, mean and standard deviation were used for data description. To compare the data in the two groups, the t-test and Mann-Whitney test were used for the normal and non-normal (and ranked) distribution of the data, respectively. We used SPSS software version 11.5 (SPSS Inc., Chicago, IL) for data analysis and a P-value less than 0.05 was considered as statistically significant.

3. Results

There were no statistically significant differences among the groups with respect to age, sex and duration of surgery. The mean of post-operation pain severity in 1, 3, 6, 12, and 24 h was significantly lower in the intervention group (II) in comparison with the control group (I). In the control group, 18 of 23 patients (78.2%) needed intravenous analgesic for postoperative analgesia; however, for the intervention group, it was only 4 of 23 (17.3%) and the difference between the groups was statistically significant ($P<0.001$) (Table 3).

Table 3

Post op analgesia	Group I		Group II	
	Percent	Number	Percent	Number
Required	78.2	18	17.3	4
Not Required	21.8	5	82.7	19

The mean duration of analgesic effect in the patients and the total dose of paracetamol consumption in the two groups was calculated; the mean of the total dose of paracetamol consumption was significantly lower in the intervention group in comparison with the control group ($P<0.001$) (Table 4).

Table 4

Variables	Group I	Group II	P Value
No. of rescue analg	2.88± 0.55	0.42± 0.28	<0.001
Duration, min	142± 65	335± 120	<0.001

During the first 24 h after surgery, no side effects such as nausea, vomiting, pruritus, hypotension, and reduced heart rate were observed.

4. Discussion

We evaluated the efficacy of intra-articular administration of ropivacaine-morphine combination on reducing postoperative pain after knee arthroscopies. Effective pain management shortens hospital stay, improves recovery from knee surgery, and contributes to early rehabilitation. Many intra-articular drugs such as local anesthetics, opioids, NSAIDs, clonidine, and neostigmine have been used for postoperative pain relief after arthroscopic knee surgery [6-11]; however, none of them have yet been identified to be the ideal method. Although local anesthetics, mostly bupivacaine, have been found to be effective for postoperative pain, they are short lived and patients usually require supplementary analgesia [11]. On the other hand, bupivacaine can produce toxic effects on chondrocytes [2, 3].

There is no study regarding ropivacaine toxicity in intra-articular administration. In a study by Kazak Bengisun *et al.* [16], intra-articular levobupivacaine and bupivacaine were compared with saline (control); both local anesthetics decreased pain scores at rest and after movement and consumption of postoperative tramadol compared saline. Moreover, bupivacaine and levobupivacaine produced similar effects on pain and analgesic consumption when administered intra-articularly.

We preferred to use ropivacaine in our study after the studies showing bupivacaine's toxic effects on chondrocytes; moreover, there are only a few studies in the literature using ropivacaine.

Talu *et al.* [21] demonstrated that administration of bupivacaine plus tenoxicam provides good analgesia at rest and during active-passive motion in the postoperative period. Opiates such as morphine and tramadol have peripheral and central analgesic effects, and there is evidence opiate receptors

presence at the terminals of afferent peripheral nerves; therefore, administration of opiates peripherally might provide a significant analgesic effect [22, 23]. Stein *et al.* showed that low doses of intra-articular morphine, injected on the completion of arthroscopic knee surgery, can produce postoperative analgesia via activation of local opioid receptors in the knee joint [24]. This peripheral effect of narcotic-like analgesics could explain why the intra-articular administration of morphine and tramadol could provide a satisfactory pain relief state as well as fewer systemic adverse effects [25].

Morphine, as an opioid, and bupivacaine, as a local anaesthetic, alone or compound form, are frequently injected into the IA space of the knee joint after arthroscopic surgery [26, 27]. Gurkan *et al.* [28] used 2 mg of morphine and 0.25% bupivacaine combination and Joshi *et al.* [29] used 5 mg of morphine and 0.25% bupivacaine combination versus saline alone. In both studies, VAS scores were significantly lower in IA morphine and bupivacaine combination than was in IA saline. Similar to the combination of these two studies, we used ropivacaine and morphine combination and found significantly lower VAS scores in comparison to saline alone. Senthilkumaran *et al.* [30] demonstrated that IA combination of 10 mg of morphine and 20 mL of 0.5% bupivacaine reduces requirement for systemic opiate analgesia after arthroscopic ACL reconstruction than morphine alone does.

Boden *et al.* [26] and McSwiney *et al.* [31] used IA morphine-bupivacaine combination versus saline as control group and reported significantly lower supplementary analgesia and lower analgesic requirements, respectively. In our study, total analgesic consumption was significantly lower in our local anesthetic with tenoxicam and morphine group compared to saline group, which was in accordance with the mentioned studies.

Hosseini *et al.* compared administration of morphine-bupivacaine and tramadol-bupivacaine combinations in patients undergoing knee surgery [4]. In their study, VAS scores were significantly less in morphine-bupivacaine and tramadol-bupivacaine groups in comparison with the control group. Moreover, analgesic duration was longer and analgesic consumption was substantially less in the morphine-bupivacaine group than were in tramadol-bupivacaine and control groups. Similar to this study, our study group had lower VAS scores than control group had.

Combining tramadol or morphine with other drugs can decrease the high postoperative dosages of administered opiates and thus, can lead to less drug adverse effects [4, 36]. Several studies have suggested ways to manage postoperative pain after arthroscopy, some of which are intra-articular injection of different drugs combination. However, no study had used combination of ropivacaine-morphine in patients undergoing arthroscopic knee surgery.

We concluded that intra-articular ropivacaine-morphine provides effective pain relief, longer analgesic duration, and less analgesic requirement when compared with normal saline after knee arthroscopic surgery.

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