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Research Article

A COMPARISON BETWEEN INTRA-ARTICULAR 0.2% ROPIVACAINE AND 0.25% BUPIVACAINE FOR POST-OPERATIVE ANALGESIA FOLLOWING DAY-CARE ARTHROSCOPIC KNEE SURGERIES

SAI KAUSHIK P H[1], SHAILA S KAMATH[1]*, SURENDRA U KAMINUATH[2]

[1]Department of Anaesthesiology, Kasturba Medical College, Mangalore, Manipal University, Manipal, Karnataka, India. [2]Department of Orthopaedics, Kasturba Medical College, Mangalore, Manipal University, Manipal, Karnataka, India. Email: shailakamath@ymail.com

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ABSTRACT

Objectives: The objective is to compare the effectiveness of intra-articular injection of ropivacaine and bupivacaine in providing pain relief after arthroscopic knee surgery.

Methods: A total of 60 patients of both genders aged 20–60 years, the American Society of Anesthesiologists physical Status I and II, undergoing day-care arthroscopic knee surgery under spinal anesthesia, were assigned into two groups randomly. Group 1 received 10 ml of 0.2% ropivacaine, while Group 2 received 10 ml of 0.25% bupivacaine intra-articularly at the end of the procedure. Pain was assessed for 24 h postoperatively using visual analog scale (VAS) and diclofenac sodium given as rescue analgesia when VAS >3. Time of first analgesic request and total rescue analgesic were noted and compared. Statistical analysis used: Students unpaired *t*-test and Chi-square test and Mann–Whitney test "Z" value wherever appropriate. A $p<0.05$ was considered statistically significant.

Results: Based on comparable demographic profiles, time for the requirement of first post-operative rescue analgesia (262.43±57.13 vs. 256.30±44.4) min and total mean rescue analgesic requirement was 152.50±57.367 vs. 142.50±41.07 mg in Groups 1 and 2, respectively. Group 1 showed slightly prolonged duration of analgesia, but total analgesic requirement was more than Group 2. However, comparing the duration of analgesia and total analgesic requirement showed no statistically significant difference between the groups ($p>0.05$).

Conclusion: Both ropivacaine and bupivacaine injected intra-articularly have similar efficacy statistically in relieving post-operative pain in day-care arthroscopic knee surgery.

Keywords: Surgical pain, Local anesthetic, Analgesia.

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INTRODUCTION

Arthroscopic knee surgery is a commonly performed minimally invasive surgical procedure on an outpatient basis. Its association with varying amounts of pain postoperatively, even in less complex procedures such as diagnostic arthroscopy or arthroscopic meniscectomies, is a concern though [1,2]. The hypothesized reason being irritation at the free nerve endings of synovial tissue and anterior pad of fat during surgical excision and resection [3]. Undoubtedly, post-operative pain which is poorly controlled often has an unfavorable impact on the patient's psychology causing discomfort, dissatisfaction, and hampering early ambulation and thus discharges from the hospital [1,4]. Using different analgesics and multimodal regimens also fail to achieve complete analgesia sometimes.

Multiple strategies for pain relief include systemic drug administration (nonsteroidal anti-inflammatory drugs, narcotics) [5]. Peripheral nerve blocks or central blocks [6,7], and not long ago, intra-articular injection of various local anesthetic agents has become popular in clinical practice [2]. Drugs such as ketorolac, α2-agonists [8], opioids [3,9], and local anesthetics [10,11] have been tried to interrupt the pain pathway. Usage of these drugs in combination, called as the multimodal approach, is usually sufficient for providing analgesia in the initial post-operative period [12].

Optimal pain relief in a day-care surgery perioperatively should be adequate and also safe, causing minimal side effect [3,13,14]. Intra-articular route of drug administration is an example for the management of pain after joint surgery utilizing the peripheral receptors [3]. Different authors in their previous studies with intra-articular ropivacaine [1,15], fentanyl [16], dexmedetomidine [11], levobupivacaine, and morphine [17] proved their efficacy in providing post-operative analgesia.

There are no direct comparative trials between these two agents with similar dosage, and concentration for arthroscopic knee surgeries is available, by intra-articular route at the end of knee arthroscopic surgery; however, these two agents with similar dosage are compared in pediatric supracondylar fractures for post-operative pain management [18]. Therefore, we undertook this study to compare the post-operative analgesic efficiency of ropivacaine (0.2%) and bupivacaine (0.25%) in intra-articular route following day-care arthroscopic knee surgery.

METHODS

This study was a randomized, prospective, comparative study conducted at our institution from November 2014 to July 2016, after obtaining the approval from the Institutional Scientific and Ethics Committee.

Sample size was calculated using the following formula:

$n = (2(Z\alpha+Z\beta)^2\sigma^2)/d^2$

Power of the study:

- $Z\alpha = 1.96$ at 95% confidence level.
- $Z\beta = 1.28$ at 90% power.
- σ = Combination of standard deviation.
- d = Mean difference between groups.

A total of 60 adult patients of either gender aged 20–60 years, the American Society of Anesthesiologists I and II, undergoing arthroscopic knee surgery under spinal anesthesia, were randomized into two groups after taking written informed consent. Each group had 30 patients and group "1" - 10 ml 0.2% ropivacaine was given and group "2" - 10 ml 0.25% bupivacaine was given. The patients were divided into 2 equal groups using block randomization.

Patients who refused for the study or with a known allergy, hypertensive, MAP <65 mmHg during intra-articular injection, pregnancy, lactating mothers, hepatic/renal/cardio-pulmonary abnormality, bleeding diathesis, or local skin infections were excluded from the study.

After a thorough pre-anesthetic evaluation and NPO status for a minimum of 6 h before surgery was ensured, a brief description was also given about the 10 cm visual analog scale (VAS) (0 - no pain to 10 - worst imaginable pain). Investigations such as hemoglobin %, total leukocyte count, differential count, platelet count, bleeding profile, and in few patients where indicated, random blood sugar, blood urea, serum creatinine, and also electrocardiogram and chest X-ray were asked. Patients were pre-medicated with tablet lorazepam 50 mcg/kg orally in the night before the surgery.

The anesthetic technique was standardized for all patients. Under all aseptic precautions, lumbar puncture was performed in the left lateral position at L3-L4 or L4-L5 intervertebral space with 25-gauge quincke babcock spinal (QBS) needle by an anesthesiologist with a minimum of 2 years experience. 3 ml (15 mg) of 0.5% hyperbaric bupivacaine injected into the subarachnoid space, and the patient was positioned supine. After 5 min of subarachnoid injection, arthroscopic procedure was allowed to start, after confirming the level of block. At the end of the surgery before skin closure, study drug was administered by the surgeon into the intra-articular space. Heart rate, non-invasive blood pressure, and pain VAS score were recorded at 1st, 2nd, 4th, 6th, 9th, 12th, 16th, and 20th post-operative hours. Injection diclofenac 75 mg IV was given as rescue analgesia if VAS ≥3. First post-operative analgesia request time and total diclofenac used in the first 24 h were recorded. All the data were gathered by an observer who was unaware of patients' group assignment.

Statistical analysis was carried out using the Students unpaired *t*-test and Chi-square test and Mann–Whitney test 'Z' value. A p<0.05 was considered statistically significant.

RESULTS

Demographic profile including age, sex, and weight of the patients was compared using students *t*-test and Chi-square test which showed no significant difference between the groups (Table 1). Heart rate and mean arterial pressure were analyzed using *t*-test and Mann–Whitney test for comparing change from baseline values.

The mean age of patients in Group 1 was 40.10 (±12.92) years and Group 2 was 39.57 (±12.67) years which were statistically non-significant. The male:female ratio in both groups was similar and statistically insignificant. The mean weight of the patients in Group 1 was 61.23 kg and Group 2 was 63.9 kg which was statistically not significant (Table 1).

Table 1: Demographic profile using students t-test and Chi-square *t*est

Patient variables	Group 1	Group 2	p
Mean age (SD)	40.10 years (±12.92)	39.57 years (±12.67)	0.872 (NS)
Mean weight (SD)	61.23 kg (±8.29)	63.9 kg (±8.38)	0.221 (NS)
Sex M/F	18/12	18/12	1.00 (NS)

SD: Standard deviation

Comparison of change in the heart rate from baseline in each group and between the groups. At 2nd h (p=0.038), 4th h (p=0.028), 12th h (p=0.033), and 20th h (p=0.014), the change from baseline was statistically significant implying the possibility of pain during that time. Looking at the mean values during these hours reveal that ropivacaine group produced lesser change in the heart rate post-operatively compared to bupivacaine group which may be attributed to better analgesia (Table 2).

Table 3 presents the comparison of mean arterial pressures with SD between both the groups which revealed no significant differences between both the groups.

While comparing the total mean duration of analgesia provided by the drugs, the mean duration in Group 1 was 262.43 min (±57.132) and median value being 242 min compared with Group 2 which was 256.300 min (±44.400) and median value being 242.50 min implying that ropivacaine provided slightly prolonged analgesia compared to bupivacaine but comparing the two groups showed no statistically significant difference (p=0.644) (Table 4).

While comparing the total mean analgesic requirement of diclofenac as rescue analgesia, Group 1 required 152.50 mg (±57.37), while Group 2 required 142.50 mg (±41.08) which was statistically not significant. (p=0.441) (Table 5).

Although ropivacaine group required more rescue analgesia than bupivacaine, it does not differ much indicating similar efficacy of both the drugs. When the VAS score of the patient was ≥3, rescue analgesia was given. The minimum and maximum scores in Group 1 were 4 and 6, respectively. In Group 2, minimum score was 3 and maximum score was 7. The mean scores being 4.90 (±0.76) in Group 1 and 4.67 (±0.96) in Group 2 did not differ much (p=0.300), and hence, not statistically significant, implying similar analgesia between both the groups (Table 6).

DISCUSSION

In our study, the noteworthy finding was that both intra-articular 10 ml bupivacaine 0.25% and 10 ml ropivacaine 0.2% reduce pain in the first few hours of post-operative period after knee arthroscopy. Ropivacaine and bupivacaine were almost equally efficient in providing analgesia at rest for at least 4–6 h postoperatively. Ropivacaine provided better pain relief in the immediate post-operative period for most patients although the total diclofenac requirement is more in this group. Bupivacaine being one of the most commonly used local anesthetics also provided a similar quality of analgesia comparable to ropivacaine.

Bupivacaine group required a lesser amount of diclofenac over 24-h period.

Factors influencing the post-operative analgesia are age and sex, experience of the surgeon, and activity levels postoperatively. The pharmacokinetics of bupivacaine after intra-articular administration has been well studied previously in few studies [4,9,19,20] when compared to ropivacaine. It is relatively safer than bupivacaine. Nevertheless, no side effects or symptoms of any toxicity were observed in either of the groups in the present study.

In 1989, Chirwa *et al.* [12] conducted a double-blinded randomized controlled trial (RCT) where intraarticular 0.5% bupivacaine (Marcaine) was compared with a saline placebo. Intra-articular bupivacaine was shown to be an effective and safe method of achieving analgesia after arthroscopic meniscectomy. Calmet *et al.* [21] performed a study using 10 cc bupivacaine 0.25% for patients with arthroscopic partial meniscectomies, and Dal *et al.* [22] conducted a study using 20 cc of bupivacaine 0.5% and concluded 0.5% to be more effective for 24 h in even smaller groups of 15 patients scheduled for arthroscopy.

There have been a few contradictory studies where intra-articular bupivacaine has not shown any superiority to other analgesics

Table 2: The comparison of change in the heart rate from baseline in each group and between the groups, using t-test and Mann–Whitney *t*est

Time	Groups	Change		Mann–Whitney test Z value	p	
		Mean±SD				
At 1st h	Group 1	14.900	5.803	1.346	0.184	
	Group 2	16.667	4.245			
At 2nd h	Group 1	12.067	6.136	2.123	0.038	Significant
	Group 2	15.067	4.719			
At 4th h	Group 1	8.400	6.044	2.249	0.028	Significant
	Group 2	11.533	4.659			
At 6th h	Group 1	6.200	6.713	1.775	0.081	
	Group 2	9.033	5.599			
At 9th h	Group 1	5.533	5.958	1.925	0.059	
	Group 2	8.100	4.221			
At 12th h	Group 1	5.800	6.110	2.182	0.033	Significant
	Group 2	8.667	3.800			
At 16th h	Group 1	4.467	6.230	1.418	0.161	
	Group 2	6.633	5.586			
At 20th h	Group 1	2.800	6.759	2.525	0.014	Significant
	Group 2	6.400	3.000			

SD: Standard deviation

Table 3: Comparison of mean arterial pressures using *t*-test and Mann–Whitney test

Time	n	Mean±SD	95% confidence interval for mean		t	p
			Lower bound	Upper bound		
Baseline						
Group 1	30	100.17±10.359	96.30	104.03	0.389	0.699
Group 2	30	99.23±8.089	96.21	102.25		
At 1st						
Group 1	30	82.17±9.976	78.44	85.89	0.407	0.685
Group 2	30	83.10±7.608	80.26	85.94		
At 2nd						
Group 1	30	83.09±10.257	79.26	86.92	0.842	0.403
Group 2	30	85.39±10.890	81.32	89.46		
At 4th						
Group 1	30	89.37±9.779	85.72	93.02	0.370	0.713
Group 2	30	88.50±8.320	85.39	91.61		
At 6th						
Group 1	30	91.50±9.081	88.11	94.89	0.016	0.987
Group 2	30	91.53±7.152	88.86	94.20		
At 9th						
Group 1	30	94.93±7.674	92.07	97.80	0.108	0.914
Group 2	30	94.73±6.622	92.26	97.21		
At 12th						
Group 1	30	94.80±8.323	91.69	97.91	0.636	0.527
Group 2	30	93.47±7.899	90.52	96.42		
At 16th						
Group 1	30	93.17±18.357	86.31	100.02	0.658	0.513
Group 2	30	95.67±9.799	92.01	99.33		
At 20th						
Group 1	30	97.27±7.153	94.60	99.94	0.147	0.884
Group 2	30	97.00±6.928	94.41	99.59		

SD: Standard deviation

administered through the same route. For example, Marret *et al.* [15] could not prove 30 cc bupivacaine 0.5% to be more effective compared to saline in a power analysis based, small sample-sized randomized trial.

However, recently another study by Sun *et al.* [23] which was a systematic electronic literature search (through April 2014) conducted to identify those RCTs that addressed the safety and efficacy of a single administration of IA bupivacaine for pain management after arthroscopic knee surgery concluded that the use of single-dose of bupivacaine intra-articularly is effective for post-operative pain relief in patients undergoing arthroscopic surgery of the knee, with reliable short-term safety.

Convery *et al.* [4] documented lower pain scores by verbal rating when ropivacaine 150 mg was compared with bupivacaine 100 mg. Franceschi *et al.* [2] conducted a study which proved that 20 cc ropivacaine 0.75% to be superior to 20 cc saline as placebo for the first 4 h at least. They concluded that ropivacaine is a safe, site-specific, and long-lasting anesthetic drug with an earlier onset than morphine and almost the same duration as morphine, but these results were contradicted by Rautoma *et al.* [24] in a study performed under spinal anesthesia using 20 cc ropivacaine 0.75% compared to placebo after 8 h of post-operative period.

In a study by Samoladas *et al.* [1], comparing 10 ml and 20 ml of ropivacaine 0.75% showed that intra-articular use of ropivacaine is effective in reducing post-operative pain minimizing the use of systemic analgesia. These results were in concordance with the study conducted by Campo *et al.* [25], using 10 cc bupivacaine 0.5% and 10 cc ropivacaine 0.75% compared to saline.

Table 4: Duration of analgesia (min) using *t*-test and Mann–Whitney test

Group	n	Minimum	Maximum	Mean±SD	Median	t	p
Group 1	30	125.00	385.00	262.433±57.132	242.00	0.464	0.644
Group 2	30	130.00	310.00	256.300±44.400	242.50		NS

SD: Standard deviation

Table 5: The total mean analgesic requirement of diclofenac (mg) as rescue analgesia using *t*-test and Mann–Whitney test

Group	N	Minimum	Maximum	Mean±SD	Median	t	p
Group 1	30	75.00	300.00	152.50±57.37	150.00	0.776	0.441
Group 2	30	75	225	142.50±41.08	150.00		NS

SD: Standard deviation

Table 6: VAS score using *t*-test and Mann–Whitney test

Group	n	Minimum	Maximum	Mean±SD	Median	t	p
Group 1	30	4	6	4.90±0.76	5.00	1.045	0.300
Group 2	30	3	7	4.67±0.96	4.50		NS

VAS: Visual analog scale

Both bupivacaine and ropivacaine have proven to have systemic concentrations, below known toxic levels are safe to use intra-articularly [20,26,27]. There was no occurrence of any symptoms of toxicity in either of the groups. This may be attributed to the low volume and concentration of both the drugs used in our study.

However, a few study reports have shown chondrotoxic effects of bupivacaine *in vitro* as well as *in vivo* [28-30]. Ropivacaine 0.5% also has chondrotoxic effects, although to a less extent than bupivacaine 0.5% when tested *in vitro* [15,20,24,27,31,32]. Both substances appear to display a dose-dependent effect, making a low dose intra-articular injection strategy possibly the least harmful [31]. In a study, other modes of post-operative analgesia like epidural butorphanol have been discussed [33]. In a review article by Vidya and Felicita, it is stated that intra-articular local anesthetic was more effective when compared to piroxicam [34].

Thus, either bupivacaine or ropivacaine can be used intra-articularly for post-operative analgesia, but low concentration and lesser volumes can be used with considerable safety.

Limitation of our study includes the post-operative sensory blockade after spinal anesthesia. The analgesic effect of intra-articular local anesthetics might be confounded due to the difference in the variable time for emergence from the sensory blockade.

CONCLUSION

We conclude that despite the limitation in our study we encourage the usage of either ropivacaine or bupivacaine intra-articularly for post-operative analgesia as no adverse effects were noted. Both the drugs effectively provided post-operative analgesia and reduced the need for rescue analgesia.

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