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A Comparative Evaluation of Intra-Articular Bupivacaine v/s Intra-articular Bupivacaine and Diclofenac on Post-Operative Pain and Recovery Following Arthroscopic Knee Surgery

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Abstract | **Original Research Article**

Background: Despite the advances in surgical techniques and the improved safety of anesthetic practice, a large percentage of patients continue to experience inadequate postoperative pain relief. Several recent surveys have found that more than 60% of patients report moderate to severe pain after arthroscopic knee surgeries. ***Objective:*** The goal of this study was to compare the pain relief provided by an intra-articular injection of bupivacaine, and bupivacaine with intravenous formulation of diclofenac sodium, in patients undergoing arthroscopic knee surgeries. ***Materials and methods:*** A prospective, double-blinded, randomized placebo-controlled study was done in the department of Anaesthesiology, Maulana Azad Medical College and Lok Nayak Hospital, on patients undergoing elective arthroscopic knee surgery (like synovectomy, ligament reconstruction, and articular cartilage procedures) under spinal anaesthesia. A total of 50 patients with 25 patients in each group belonging ASA score of class I/II in the age group of 18-60 years were taken in to consideration in this study. ***Results:*** The time elapsed before the first analgesia request time was compared and it was found that the bupivacaine–diclofenac group patients remained pain free for a longer period of time than the plain bupivacaine group. Mean time elapsed in case was a mere 16.68 hrs for group A as against 27.28 hrs for group B, which was statistically highly significant (p = 0.000). VAS Score at the 24th post-operative hour was noted in each group and compared. All patients in group A had a VAS score of >4 at the 24th hour and 92% of the patient distribution (23 patients) had moderate pain i.e. VAS 4-6. In case of group B, only 8 patients had VAS 4-6 at the said time. As for severe pain, 2 patients from group A had VAS >7, whereas no patient in group B stated to have it, thus making the result of comparison highly significant (p = 0.000). ***Conclusion:*** Patients receiving intra-articular injection of 0.25% bupivacaine with 75mg diclofenac sodium, gives better postoperative pain relief, with increased time of first analgesic request and decreased need of total postoperative analgesia compared to patients receiving intra-articular injection of plain 0.25% bupivacaine.

Keywords: intra-articular injection, postoperative pain, arthroscopic knee surgery, bupivacaine, Diclofenac, VAS Score.

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INTRODUCTION

Total knee arthroplasty is a frequently performed procedure and the incidence is expected to increase 673% to 3.48 million procedures annually by 2030 [1]. It is associated with variable amount of postoperative pain, which is caused by irritation of free nerve endings of synovial tissue, anterior fat pad, and joint capsule during surgical excision and resection [2]. Total knee arthroplasty is a procedure that ensures improvement in quality of life, and is being performed in increasing numbers every year because of the increase in geriatric population due to improved medical care [3]. However, patients avoid this operation because of the associated variable post-operative pain, which undoubtedly, has a negative impact on patient's early mobilization, rehabilitation, psychology [4] and leads to prolonged hospital stay. Adequate pain relief reduces surgical stress response, so reduces patient's morbidity and improves postoperative recovery. Several analgesic strategies such as systemic medications (narcotic, NSAID) [5], central or peripheral nerve

blocks, and intra-articular drug administration (NSAIDs [6], α_2 –agonists [7-10], opioids [11-15], local anesthetics [16-19] have been used in conjugation to interrupt the pain pathway, and this combination therapy is known as multimodal approach. Periarticular injections have been reported to have good efficacy in controlling pain along with cost effectiveness, fewer side effects and ease of use, as this method can be used by every surgeon without further training, unlike the techniques like epidural anesthesia or nerve blocks, which require experience and further training [20-22]. However, none is free from limitations such as needs for special equipments, monitoring, and risks of complications. Utilizing the peripheral receptors for postoperative pain management is an important mode of such an approach and the intra-articular route of drug administration is an appropriate example. It provides analgesia locally utilizing the peripheral receptors with minimal systemic side effects.

The concept of intraoperative, intra-articular injection of narcotics and/or anesthetics, came after arthroscopic knee surgery, and significantly reduced the patients' subjective assessment of postoperative pain and the need for postoperative analgesia. The effective postoperative pain control that was accomplished with small doses of intra-articular drugs is postulated to occur secondary to local receptor activation rather than systemic analgesia [23, 24]. Though the recent studies have applied the concept of postoperative intra-articular analgesia to knee arthroplasty patients with mixed results, majority of these studies have been confounded by variability of patient perception to pain in the postoperative period [25-29].

Different authors in their previous studies with intra-articular ropivacaine [30], fentanyl [31], dexmedetomidine [32], magnesium [33], levobupivacaine, ketorolac [34, 35] and morphine had proved their efficacy in providing post-operative analgesia in arthroscopic knee surgery. In our study we will compare the analgesic efficacy of plain bupivacaine (0.25%), and bupivacaine (0.25%) with diclofenac (75mg), in intra-articular route, following day care arthroscopic knee surgery. Bupivacaine is an amino-amide local anesthetic that blocks the peripheral afferents acting on voltage-dependent Na^+ channels. It is a long-acting local anesthetic. On the other hand, NSAIDs modulate pain pathway in multiple ways. Their principal effect is by reducing prostaglandin (PG) synthesis in the spinal cord, which therefore, causes decrease in inflammatory hyperalgesia and allodynia. I/V NSAIDs, in addition, act as an adjunct regional blockade, by causing PGE and cytokine inhibition, over and above the suppression of neural responses to noxious injury [36].

METHODS

The study was done after taking ethical clearance from the institutional ethics committee and written informed consent from all participating patients, in the department of Anaesthesiology, Maulana Azad Medical College and Lok Nayak Hospital, on patients undergoing elective arthroscopic knee surgery (like synovectomy, ligament reconstruction, and articular cartilage procedures) under spinal anaesthesia. The study has been designed as prospective, double-blinded, randomized placebo-controlled study with a sample size of 50, having 25 patients in each group. *"Inclusion criteria"* include men and women in the age group of 18-60 years, with a body mass index $\leq$30kg/m^2 and ASA score of class I/II. Patients shall were *"excluded"* if they refuse to give consent, have a history of known allergy to bupivacaine or diclofenac, are pregnant or lactating mothers, suffering any hepatic, renal or cardiopulmonary abnormality, have alcoholism, diabetes, long-term analgesic therapy, spinal cord deformities, bleeding diathesis or local skin site infections.

All patients were evaluated to undergo a detailed pre-anaesthetic check-up (PAC) along with investigations required as per the age, surgical condition and associated disease of patients. 50 patients was randomly allocated by computer generated random tables to one of the two groups comprising 25 patients each.

Group A – intra-arthroscopic injection of plain bupivacaine was administered.

Group B – intra-arthroscopic injection of bupivacaine with diclofenac was administered.

The anaesthetic technique was standardized for all the patients. Spinal anaesthesia was given according to the patient's height and weight. After 5 minutes of subarachnoid injection, arthroscopic procedure was allowed to start, once the level of block was confirmed. During the procedure if any patient needs further dose of analgesia, that patient was excluded from the statistical analysis. At the end of surgery before skin closure, the study drug was administered by the surgeon through the port site in the intra-articular space. For Group A; intra-articular injection of 10 ml of plain 0.25% bupivacaine along with 1ml of 0.9% isotonic saline was administered. For Group B; intra-articular injection of 10ml of 0.25% bupivacaine along with 75mg (1ml) of diclofenac sodium was administered. Tourniquet was not used. Drain put by the surgeon were clamped before administering the study drug and remain clamped for another 20 minutes. Postoperative pain and patient satisfaction related to knee was assessed via a Visual Analog Scale (VAS; range, 0 mm [no pain or completely satisfied] to 100 mm [extreme pain or completely dissatisfied] in 10-mm increments) at 24th post-operative hour. Injection diclofenac sodium (75 mg IM) was given as rescue analgesia if the pain VAS>4 complained at anytime post-operatively by the patient and then started 8 hourly thereafter. First postoperative analgesia request time was recorded. All

data was collected by an observer who was unaware of patients' group assignment.

RESULTS

There were no significant differences in the characteristics of patients receiving intra-articular injection of plain 0.25% bupivacaine or 0.25% bupivacaine with 75mg diclofenac sodium, except in terms of sex of the patients undergoing these types of surgeries Table-1. It was found that on comparing the two groups, the overall sex distribution was uneven amongst the groups. Group A had 72% male population involved in the study, whereas, group B composed of 96% male patients undergoing the study which was a statistically significant finding (p = 0.049). Apart from the sex distribution, there was no significant difference amongst the two groups studied, in terms of age group (p = 0.69) or ASA classification (p = 1.0).Table 1.

Table-1: Demographic data of patients

Variables	Group A N=25	GROUP B N=25	P VALUE
Age (years)	45.55±13.56	42.80±13.37	0.69
Sex (M/F)	18/7	24/1	0.049
Weight (kg)	61.50±8.87	62.50±10.99	0.158
Height (cm)	163.3±4.6	165.4±5.5	0.96
ASA class (I/II)	20/5	19/6	1.0

Comparison of sex and ASA distribution between the two groups was evaluated using Chi-square test. ASA: American Society of Anaesthesiologists

Patient distribution between the two groups was also analysed statistically to rule out any bias with respect to weight, height and body mass index (BMI) of the participants. No statistically significant difference was found so as to confirm an optimum choice of patients for the study [weight (p = 0.158), height (p = 0.96), BMI (p = 0.853)]. The type of surgeries which were performed in both the groups were also similar (p = 0.112) Table-1.

The time elapsed before the first analgesia request time was compared and it was concluded that the bupivacaine–diclofenac group patients remained pain free for a longer period of time than the plain bupivacaine group. Mean time elapsed in case was a mere 16.68 hrs for group A as against 27.28 hrs for group B, which is statistically highly significant (p = 0.000). VAS Score at the 24th post-operative hour was noted in each group and compared. All patients in group A had a VAS score of >4 at the 24th hour and 92% of the patient distribution (23 patients) had moderate pain i.e VAS 4-6. In case of group B, only 8 patients had VAS 4-6 at the said time. As for severe pain, 2 patients from group A had VAS >7, whereas no patient in group B stated to have it, thus making the result of our comparison highly significant (p = 0.000) Fig-1.

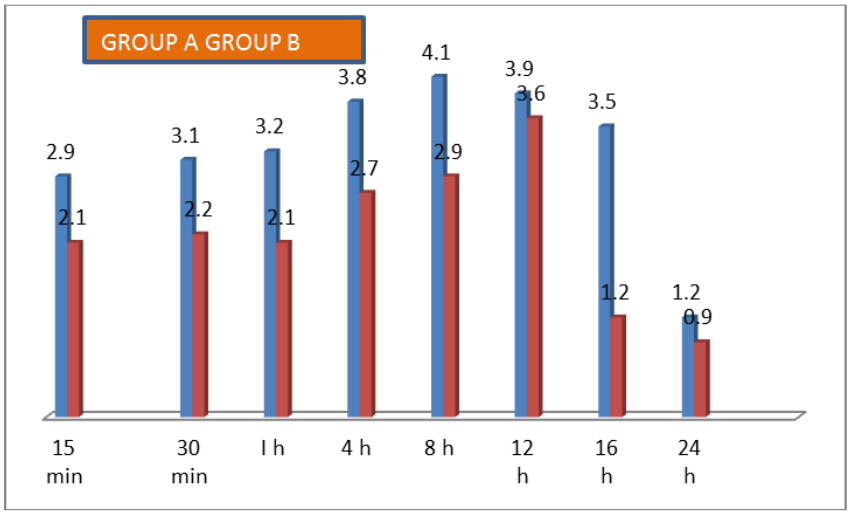

Fig-1

The two groups were also evaluated with reference to the number of rescue analgesia shots a patient demanded in either of the groups. Intramuscular Diclofenac sodium 75mg was given to the patients as and when demanded by them during the first 24hrs. 20 patients in group A demanded for a single shot of rescue analgesia and 5 patients needed even a second shot. This was compared with just 2 patients from group B who demanded rescue analgesia once, while none wanted it twice and the results were found to be statistically highly significant (p = 0.001) Table-2.

Table-2: Comaprsion of rescue analgesia (Intramuscular Diclofenac sodium 75mg) among the study population

Rescue analgesia	No. of patients Group A	No. of patients Group B	P VALUE	Remarks
Zero dose	0	0	0.001	significant
Single dose	20	2		
Two doses	5	23		

DISCUSSION

Postoperative arthroscopic knee surgery is the one of the most common minimally invasive surgical procedures in modern orthopedic setup. An insufficient pain control after knee arthroplasty surgeries may lead to insomnia, antalgic ambulation and difficulty in rehabilitation. Current strategies, like the use of femoral nerve catheters, may control pain but due to the associated motor blockade and quadriceps inhibition, might lead to falls. Whereas, intra-articular infiltration with the appropriate technique and proper knowledge of knee anatomy may increase pain control and maximize rehabilitation.

In our study, we assessed the post-operative analgesia property of intra-articular diclofenac sodium in terms of: 1) VAS Score at 24th post-operative hour, 2) Time elapsed until first analgesia request time, and 3) Evaluation of Range of Motion on post-operative day 2, by comparing two groups, A & B, given intra-articular injection of plain bupivacaine (0.25%), and bupivacaine (0.25%) with diclofenac (75mg) respectively. We found that patients who received intra-articular diclofenac sodium after arthroscopic knee surgery conducted under spinal anesthesia experienced less post-operative pain and seldom required rescue analgesia.

Over the years, many modes of postoperative analgesia have been tried and tested with success for patients undergoing knee arthroscopy [37]. Opioid drugs, via varying routes, have been administered to deal with postoperative pain efficiently but have had their share of side effects, like nausea, vomiting, respiratory depression, drowsiness, pruritus, reduced gut motility, and urinary retention [38]. Providing analgesia locally has thus been an attractive option with minimal systemic side effects, and possible earlier discharge from the hospital. One of the simplest of these techniques to provide local anesthesia is Intraarticular drug administration. An added advantage being no need of any specialised equipment [39].

Various drugs including local anesthetics, opioids and NSAIDs have already been studied in this regard over years now. It has been proven that peripheral inflamed tissues have opioid receptors, responsible for afferent sensory input to the central nervous system, expressed within hours after surgical trauma [40-42]. Local anesthetics like bupivacine, block both the generation and the conduction of nerve impulses, thus inhibiting afferent nociceptive activity [43, 44]. Non steroidal anti-inflammatory drugs like ketorolac, on the other hand, act by inhibiting cyclo-oxygenase and lipo-oxygenase enzymes thereby preventing the synthesis of both prostanglandins and leukotrienes, and might also release endogenous opioids [45, 46]. It has been demonstrated to be effective in patients after knee arthroscopy [47]. In our study, we combined the use of bupivacaine with diclofenac sodium in one of the groups, against bupivacaine alone.

The demographic profile of the patients included in our study, mainly age, weight, height, BMI, type of surgeries and ASA classification, is comparable among the groups. However, the sex distribution amongst the two groups was significantly uneven. Many studies reveal that sports knee injuries are more common among women as they are a physically more vulnerable group [48]. Rick P Csintalan *et al.*, in their study concluded that the incidence of ACL reconstruction among females has risen significantly over the period from 2001-2005, with most dramatic change in the age group of 14-17 years, which we did not include in our study [49]. No study supporting our data could be found, which leads us to assume that, though the sports related and other knee injuries might be common amongst the females, but as for seeking medical help, the male gender is still the prominent one.

In 1993, Allen GC *et al*., did a study with 120 ASA Physical Status 1-2 outpatients, age 18-60 yrs, undergoing knee arthroscopy, by randomizing into four treatment groups wherein all patients received general anesthesia with intravenous fentanyl, propofol, N_2O, O_2, and isoflurane [50]. At the end of surgery before tourniquet release, the following were injected intraarticularly through the arthroscope: group I, 0.25% bupivacaine; group II, 1mg morphine in saline; group III, 2mg morphine in saline; and group IV, 1mg morphine in 0.25% bupivacaine. Total volume injected was 30ml and all solutions contained 1:200,000 epinephrine. Visual analog pain scale (VAPS) scores and the McGill Pain Questionnaire (MPQ) were performed hourly from 1-6 h, and at 24 h postoperatively to conclude that 1mg intraarticular morphine in 30ml 0.25% bupivacaine with 1:200,000 epinephrine, provides superior postoperative analgesia for up to 24hrs versus bupivacaine or morphine alone.

A few years later, Convery PN *et al.*, compared the postoperative analgesic effect of ketorolac 10mg given intravenously with 5mg given intra-articularly in 60 patients undergoing arthroscopy of the knee joint under general anaesthesia and concluded that a reduced amount of locally applied ketorolac (5mg) provides similar analgesia to a higher systemic dose (10 mg) following knee arthroscopy [51]. Around the same time,

Gurkan Y *et al*., studied the effects of diclofenac and intra-articular morphine/bupivacaine on postarthroscopic pain control in 40 patients divided into 4 groups receiving 25 ml of 0.25% bupivacaine and 2 mg of morphine intraarticularly in group I, 75 mg of diclofenac I/M in group III, the combination of 75 mg of diclofenac I/M and 25 ml of 0.25% bupivacaine and 2 mg of morphine intraarticularly in group II, and placebo in group IV to state that combination of diclofenac I/M and intra-articular morphine/bupivacaine appears to be the most beneficial analgesic combination due to its lower VAS scores and supplemental analgesic requirements in the postoperative period [52]. These studies helped us put together or study sample. In our study, we concluded that combining 0.25% bupivacaine with 75mg diclofenac sodium proved to be highly beneficial, not only in terms of prolonged time interval before first analgesia request by the patient, but also due to an evidently reduced VAS score at the 24th post-operative hour.

Our conclusion about longer time elapse before first analgesia request time in case of group B, was further supported by the data regarding total number of intramuscular diclofenac shots demanded by the patients in either group as a rescue analgesia during the first 24hours. Highly significant difference was found between these groups with only 2 patients demanding rescue analgesia in group B as against all the patients in case of group A, thus confirming the superiority intra-articular injection of bupivacaine-diclofenac combination.

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