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Analgesic Efficacy of Levobupivacaine Injected Intraarticularly Following Knee Arthroscopy

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ABSTRACT

Background: One of the most popular surgeries is arthroscopic knee surgery. The majority of the knee's intraarticular structures include free nerve endings that may detect painful stimuli and cause excruciating pain. For the rehabilitation of the knee after surgery, effective pain treatment is crucial. Levobupivacaine is an example of an intraarticular local anaesthetic that may be used to treat pain because it produces a direct blocking of the nociceptive pain response at the site of injection with very little systemic absorption.

Objective: To evaluate the analgesic efficacy of levobupivacaine injected intraarticularly following knee arthroscopy.

Patient and method: Eighty patients (ASA I or II) of either sex, aged from 18-70 years undergoing elective arthroscopic knee surgery were randomly categorized into two groups 40 patients for each. **Group C** received 20 ml normal saline 0.9%. **Group L** received levobupivacaine 0.5% (Chirocaine® 5mg/ml from Abbott) intraarticularly at the end of the surgery and 10 min before tourniquet deflation. Patients were monitored postoperatively by using (VAS) score, (HR) and (MBP) at 1, 6, 12, 18, 24 hours.

Results: We found that intraarticular levobupivacaine injection after knee arthroscopy provides postoperative analgesia without causing hemodynamic instability with less postoperative supplemental analgesic requirements. Postoperative VAS score was statistically significant lower in group L when compared to group C. The time of the first request for analgesia was longer in group L than group C. However, there was no serious side effects detected in either groups.

Conclusion: Intraarticular levobupivacaine injection after knee arthroscopy provides efficient postoperative analgesia, less postoperative supplemental analgesic requirements with hemodynamic stability and insignificant complications.

Keywords: Levobupivacaine, Intraarticular, Postoperative pain, Arthroscopy.

INTRODUCTION

Knee arthroscopy has reduced morbidity compared to open operations and protected patients from having huge incisions, but it has not done away with discomfort [(1)]. The majority of the knee's intraarticular components, such as the synovial tissue, the anterior fat pad, and the joint capsule, have free nerve endings that may detect unpleasant stimuli and cause excruciating pain [(2)]. Due to their direct blockage of the nociceptive pain response at the site of injection and little systemic absorption, intraarticular local anaesthetics are frequently utilised for pain management following arthroscopic knee surgery [(3)].

An amino amide local anaesthetic is levobupivacaine. Levobupivacaine and bupivacaine share a chemical similarity, however research has demonstrated that levobupivacaine is less harmful to the heart and central nervous system [(4)]. Levobupivacaine appears to have a greater margin of safety than bupivacaine when it comes to adverse cardiovascular and central effects when taken at high doses [(5)].

The aim of this study was to evaluate the analgesic efficacy of levobupivacaine injected intraarticularly following knee arthroscopy. Post-operative complications and hemodynamic changes will be also evaluated.

PATIENTS AND METHODS

From March 2014 to April 2016, this randomised, double-blinded trial was conducted at the knee arthroscopic surgery department of Mansoura University Hospital. In this study, 80 arthroscopic knees surgery patients of either sex, 18–70 years old, with an American Society of Anesthesiologists (ASA) physical status I or II were included.

Exclusion criteria: Exclusion criteria included patients under chronic treatment with opioids or NSAIDs, patients with contraindication to spinal anesthesia (infection at site of administration, bleeding disorders), patients who are allergic to (levobupivacaine or diclofenac Na), patients who had hemorrhagic or clotting disorders, or who refused to take part in the trial.

Anesthetic Management:

Preoperative evaluations of all patients included obtaining their medical histories, doing physical exams, ordering electrocardiograms (ECGs), and reviewing their lab results (full blood counts, hepatic and renal function tests, and coagulation profiles). All patients received instruction on how to evaluate pain using a 10 cm visual analogue scale (VAS) the day before surgery. The scale is a horizontal 10 cm line that ranges from 0 ("no pain") to 10 ("worst imaginable pain") [(6)].

Patients were instructed to mark a vertical line at a position that corresponded to their point of discomfort. Using the closed-envelope approach, the patients were randomly split into two equal groups, 40 patients each. The administration of intraarticular medicines was concealed from the patients and the administrator. An anesthesiologist who was blind to the study created the study solutions.

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The two groups according to the intraarticularly injected solution were:

Levobupivacaine (L) group (n=40): They received 20 ml levobupivacaine (0.5%) (Chirocaine®, Abbott) 5 mg/ml intraarticularly at the end the surgery.

Control (C) group (n=40): They received 20 ml 0.9% normal saline intraarticularly at the end of surgery.

A 18 G IV line was placed in the operating room, and 500 ml of normal saline was given as a loading dose before 15 ml/kg/hr was administered as a maintenance dosage. All patients received 3 mg IV of midazolam as a premedication, and they were all subjected to the usual forms of monitoring (ECG, SPO_2 (pulse oxymetry), non-invasive blood pressure, etc.). Spinal anaesthesia was achieved in the sitting position using a 25 gauge spinal needle and aseptic method following local infiltration with 3 cc of 2% lidocaine at the L3-L4 intervertebral region.

Following local anaesthetic injection, the T12 dermatome level pin-prick test (needle prick) was used to measure the degree of sensory block. Patients who had unsuccessful or partial spinal anaesthesia were then removed from the research and given general anaesthesia. After administering spinal anaesthesia and determining the extent of the sensory block, tourniquets were placed around the whole patient population at a pressure of 250 to 300 mmHg. Anterolateral and anteromedial portals were used to execute a typical arthroscopy method after sterilising the operative area.

Rescue intravenous (IV) boluses of ephedrine 0.1 mg/kg were administered to treat hypotension, which is defined as a 20% fall in systolic blood pressure from the basal level. Atropine 0.01 mg/kg IV was used to treat bradycardia, which is defined as a heart rate below 50 beats per minute. The research was started after the conclusion of surgery, 10 minutes prior to the deflation of the tourniquet, and the study solutions were injected intraarticularly after the portals had been sewn to prevent extravasations [(3)]. The tourniquet was released, and a compression bandage was put on. Each patient was sent to the post-anesthesia care unit (PACU) and given 24 hours of observation.

After being moved to the PACU, the patient's pain score was measured and recorded using a (VAS) at 1, 6, 12, 18, and 24 hours. At the same time as measuring pain, (HR) and (MBP) were recorded. Patients were given 75 mg of diclofenac sodium (vulturine) intramuscularly if they were experiencing discomfort (VAS score > 4). The postoperative time in hours between the intraarticular injection of study solution and the patient's initial request for analgesia was noted. Each patient in both groups received a total of 24 hours of postoperative supplementary analgesia, which was noted. Throughout the 24-hour research period, any postoperative adverse effects such as nausea, vomiting, hypotension, bradycardia, and shivering were also noted.

Sample size calculation:

The G Power analysis programme version 3 was used to retroactively quantify the clinical trial's power. A total sample size of 80 patients resulted in a power of 0.97 using post-hoc power analysis with accuracy mode calculations with visual analogue scale score as the principal variation and assuming type-1 error protection of 0.05 and an effect size convention of 0.8.

Ethical approval

The study was approved by The Local Ethics Committee, Faculty of Medicine, Mansoura University. All participants gave their written informed consents. The entire process of conducting the study was adhered to the Helsinki Declaration.

Statistical analysis

SPSS 21 was used to examine the data. Initially, the data were checked for normality using the Kolmogorov-Smirnov test. Quantitative data were described using percentages and figures. Using the Chi-square test, associations between categorical variables were investigated. For non-parametric data and mean ± SD (standard deviation). For parametric data, continuous variables were reported. The Student t test (for parametric data) and the Mann-Whitney test (for non-parametric data) were used to compare the two groups. The Fischer exact test was applied when the anticipated cell count was fewer than 5. The accepted significance level for all of the aforementioned statistical tests is the 5% level (p-value). A difference or change was deemed statistically significant if its probability (P) was less than 0.05.

RESULTS

This research included a total of 80 participants who underwent elective knee arthroscopy. Age, sex, ASA physical status, and surgery data of the analysed groups' demographics revealed no statistically significant variations between the two groups (Table 1).

Table (1): Demographic and surgical data in the studied groups

	L group (n:40)	C group (n:40)	P-value
Age (years)	34.47±11.68	37.77±12.41	0.224
Sex (M:F)	30:10(75.0%:25.0%)	32:8(80.0%:20.0%)	0.592
ASA (I:II)	35:5(87.5%: 12.5%)	31:9(77.5%: 22.5%)	0.239
Diagnosis **Torn ACL** **Torn medial meniscus** **Torn lateral meniscus**	 9(22.5%) 30(75.0%) 1 (2.5%)	 4(10%) 34(85.0%) 2(5.0%)	0.286
Operation **Reconstruction** **Meniscectomy**	 9(22.5%) 31(77.5%)	 4(10.0%) 36(90.0%)	0.130

L= Levobupivacaine, C= Control, n =number, M=Male, F=Female, ACL=Anterior Cruciate Ligament

No statistically significant differences were found between the two groups regarding postoperative hemodynamic alterations in terms of heart rate (HR) and mean blood pressure (MBP) (Table 2).

Table (2): Heart rate after surgery (bpm) and average blood pressure (mmHg) among the groups under study

	Postoperative hours				
	1	**6**	**12**	**18**	**24**
Heart rate (bpm)					
L group (n: 40)	76.55±7.61	77.82±7.84	77.82±6.89	78.20±7.12	80.02±7.64
C group (n: 40)	76.15±8.68	78.25±8.64	78.93±7.49	79.80±8.24	81.00±8.41
P – value	0.827	0.818	0.497	0.356	0.589
Mean blood pressure (MBP)					
L group (n: 40)	83.50±7.35	81.72±6.35	83.05±6.48	82.90±5.52	85.72±4.96
C group (n: 40)	85.07±12.88	85.42±13.79	85.55±14.03	85.90±11.58	88.70±12.04
P – value	0.504	0.127	0.310	0.143	0.153

L= Levobupivacaine, C= Control, n =number

At 6, 12, 18, and 24 hours postoperatively, regarding VAS score was statistically lower in the levobupivacaine group as compared to the control group (p value >0.001) (Table 3).

Table (3): Postoperative VAS scores (0–10) for evaluating pain in the groups under study

Time	L group (n:40)	C group (n:40)	P-Value
1hr	0.00 (0.00-0.00)	0.00 (0.00-0.00)	1
6hrs	2.00 (1.00-4.00)*	5.00 (4.00-8.00)	<0.001
12hrs	4.00 (1.00-6.00)*	5.00 (4.00-7.00)	<0.001
18hrs	4.00 (1.00-6.00)*	6.00 (5.00-8.00)	<0.001
24hrs	4.00 (2.00-6.00)*	6.00 (5.00-7.00)	<0.001

L= Levobupivacaine, C= Control, n =number *statistically significant in comparison to control group ($p < 0.05$)

Levobupivacaine group's time to initial request for analgesia was statistically significantly longer than control group (p value < 0.001). Levobupivacaine group intake of diclofenac Na in its whole was statistically significantly lower than that of the control group (p value < 0.001) (Table 4).

Table (4): Time to first seek analgesia (hr) and total post-operative diclofenac Na consumption (mg) in the groups under study

Variables	L group (n:40)	C group (n:40)	P-Value
Time to first request for analgesia(hr)	9.55±2.62*	4.35±0.86	<0.001
Total analgesic consumption(mg)	56.25±44.12*	150±0.0	<0.001

L= Levobupivacaine, C= Control, n =number

Regarding postoperative complications, there were no statistically significant differences between the two groups (Table 5).

Table (5): Complications following surgery in the groups under study

Variables	L group (n:40)	C group (n:40)	P-Value
Nausea	2(5%)	1(2.5%)	1
Vomiting	1(2.5%)	1(2.5%)	1
Bradycardia	2(5%)	2(5%)	1
Hypotension	3(7.5%)	1(2.5%)	0.615
Shivering	2(5.0)	4(10.0%)	0.396

L= Levobupivacaine, C= Control, n =number

DISCUSSION

This study was designed to evaluate if intraarticular levobupivacaine injection provides postoperative analgesia or not. An earlier research described how several medications were injected intraarticularly during arthroscopic knee procedures to increase analgesia [(7)], but few studies used levobupivacaine for intraarticular injection. In the current study, levobupivacaine group and control group were compared regarding (HR), (MBP) and postoperative pain. The initial 24-hour postoperative research period's first analgesia request time, total analgesic needs, and any negative effects were also noted and compared.

This study demonstrated that intraarticular injection of levobupivacaine provided postoperative analgesia following knee arthroscopy as the VAS score was statistically significant lower in levobupivacaine group when compared to control group during the first postoperative 24 hrs. Also, the time to the first request for analgesia was statistically significant longer in levobupivacaine group when compared to control group. The result of the current study is supported by **Karaman *et al.*** [(8)], who found that intraarticular administration of effective analgesia equivalent to that offered by 20 ml 0.5% bupivacaine is delivered by 20 ml 0.5% levobupivacaine. Similar result is reported by **Ozdemir *et al.*** [(9)] comparing the effects of intraarticular injection of 0.5% levobupivacaine and 0.5% bupivacaine with 2 mg morphine and 100 mg adrenaline. They discovered that intraarticular levobupivacaine mixed with morphine and adrenaline reduces the need for analgesics, shortens the time spent using them after surgery, and expedites mobilisation just as well as bupivacaine. **Bengisun *et al.*** [(10)] proved that administering intraarticular levobupivacaine improves recovery following total knee arthroplasty and lowers pain ratings. Also, **Jacobson *et al.*** [(11)] stated that arthroscopy of the knee with levobupivacaine 5 mg/ml was shown to be more successful than using lidocaine with adrenaline for local anaesthesia and to offer better postoperative analgesia.

In the current study, the total 24 hrs postoperative diclofenac Na consumption was statistically significantly lower in levobupivacaine group when compared to control group. This is in accordance with **Nagpure *et al.*** [(12)] who claimed that as compared to ropivacaine, intraarticular levobupivacaine provides superior postoperative pain relief, lengthens the period until the first analgesic request, and reduces the requirement for complete postoperative analgesia. **Sahin *et al.*** [(13)] studied the adjuvant effect of intraarticular levobupivacaine used with IV dexketoprofenon on postoperative pain relief following knee arthroscopy. They found that in comparison with IV dexketoprofenon alone or intraarticular levobupivacaine alone, they discovered that intraarticular levobupivacaine with adjuvant IV dexketoprofenon administration provided superior pain relief and less of a need for analgesics following arthroscopic knee surgery within the first 24 hours. **Isik *et al.*** [(14)], reported that after an outpatient arthroscopic meniscectomy, the pain is better relieved when intraarticular levobupivacaine is added to ketamine. **Bhattacharjee *et al.*** [(15)], studied the efficacy of intraarticular dexamethasone as adjuvant to levobupivacaine for postoperative analgesia after arthroscopic knee surgery. They discovered that adding dexamethasone to levo-bupivacaine in patients having arthroscopic knee surgery enhances the quality and lengthens the time that postoperative analgesia lasts.

In a study done by **Totoz *et al.*** [(16)], who studied 4 groups of patients scheduled for elective knee arthroscopy, they came to the conclusion that fentanyl or tramadol combination with levobupivacaine lessens the need for rescue analgesics when compared to levobupivacaine alone.

The current study showed that there were no statistically significant difference as regards postoperative HR and MBP in both groups. This result is in accordance with a study done by **Heppolette *et al.*** [(17)] who found that intraarticular levobupivacaine administration provides good analgesia after total knee arthroplasty (TKA) without effect on hemodynamic stability when compared to intraarticular bupivacaine following intrathecal levo-bupivacaine**.**

In the current study, no serious side effects were detected in either groups. This result passes in agreement with previous studies, this probably due to less systemic absorption of intraarticular levobupivacaine, which is safer on CNS and CVS [(8)]**.**

STUDY LIMITATIONS

We did not check on the patients to see if the study treatment had caused any intraarticular tissue damage locally. To determine the ideal dosage range to reduce pain, it would be more beneficial if we could investigate various levobupivacaine concentrations, but this would need larger patient populations and more extensive research.

CONCLUSION

This study concluded that intraarticular levobupivacaine injection after knee arthroscopy provides efficient postoperative analgesia, less postoperative supplemental analgesic requirements with hemodynamic stability and insignificant complications.

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Competing interests: Nil.

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