ORIGINAL ARTICLE

A prospective randomised double blind study comparing the efficacy of peri-articular injection with bupivacaine and levobupivacaine for postoperative pain control in total knee arthroplasty

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ABSTRACT

Objective: Adequate control of postoperative pain management after total knee arthroplasty (TKA) remains a big challenge for the clinicians, as if left unrelieved, it might cause a delayed recovery of the patient and a prolonged hospital stay. Not much literature is found regarding the peri-articular use of levobupivacaine in patients undergoing TKA. So, we aimed to compare the efficacy of peri-articular infiltration of bupivacaine and levobupivacaine for postoperative pain control in TKA.

Methodology: We organised a randomised, prospective, double blind study and enrolled sixty patients undergoing TKA by a single surgeon. Group L (Levobupivacaine) received peri-articular injections with 0.20% levobupivacaine before wound closure and Group B (Bupivacaine) patients received a 0.25% bupivacaine injection. All the cases were performed by a standardized anesthetic technique, postoperative pain control and rehabilitation protocol.

Results: Postoperative morphine consumption within first twelve hours was observed to be significantly reduced in Group L ($P < 0.05$). However, no significant difference was observed in the two groups on comparing postoperative morphine consumption between 12-96 hours. VAS scores were also found to be comparable between the groups.

Conclusion: Administration of peri-articular injection with levobupivacaine before the wound closure was shown to be an effective method for postoperative analgesia after TKA with minimal side effects.

Key words: Bupivacaine; Levobupivacaine; Peri-articular injection; Total knee arthroplasty

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INTRODUCTION

Postoperative pain (POP) is a real concern and an essential component of care in the postoperative patients of Total Knee Arthroplasty (TKA). Immediate postoperative pain after TKA delays the postoperative recovery and thereby increases the duration of the hospital stay. TKA being a major operation causes extensive tissue damage and leads to immediate changes in the neuro-endocrine systems and stimulate catabolic hormones (growth hormone, glucagon, cortisol, and catecholamine) thereby increasing the metabolic demands and imposing higher strain on cardiovascular system.[1]

Poor mobilization of the patients due to POP after TKA causes multi-system manifestations (ischaemic cardiac events, myocardial insufficiency, poor pulmonary reserve, gastro-intestinal ileus, decreased immunity, and decreased sleep).[2]

These multisystem manifestations together with the elderly-associated co-morbid conditions also persists increases the patients' suffering thereby prolongs the hospital stay and imposes a more financial burden on the patients.[2]

Peri-articular injections (bupivacaine, ropivacaine, opioids, steroids and epinephrine) had been used most widely for postoperative analgesia in patients of TKA.[3] These are used either alone or with combinations for peri-articular injections.[4] However, convincing data regarding the proper combinations of these drugs for postoperative analgesia in patients of TKA is still lacking.

According to the recent medline search, local anesthetics have been proved to be desirable agents for relieving POP after TKA. Next to local anesthetics, opioids (intravenous/epidural/ patient controlled) are suggested. Based on the literature and limited data regarding local anesthetics (levobupivacaine) we planned to undertake a prospective, randomized, double blind study to study the effectiveness of bupivacaine/ levobupivacaine for postoperative pain control in patients undergoing TKA.

METHODOLOGY

After approval from the Institutional Ethical Committee and obtaining due consent from 80 patients of either sex, aged between 55-80 years, Body-Mass Index (BMI) between 25-35 and ASA Grade I/II we designed a prospective, randomised study in Teerthankar Mahaveer Medical College and Research Centre in patients undergoing TKA under spinal anesthesia. Patients with history of allergy to local anesthetics, chronic renal/liver disease, in whom spinal anesthesia could not be administered and previous surgery on the knee undergoing total knee replacement were excluded from our study.

A sample size calculation was done using the standard deviation of 3.4 dose equivalent on mean morphine consumption. To achieve a significant difference between groups (1.5 dose equivalent on mean morphine consumption in early postoperative period) and two sided alpha of 5% and beta of 10%, 28 patients were required in each group. We decided to include 40 patients in each group to allow for possible dropouts.

All patients were divided into two groups by computer generated randomization before the incision, by the anesthesia nurse who prepared the drugs for periarticular injection and was not involved in any part of the study protocol. Group B (40 patients) received 20 ml of 0.25% bupivacaine and Group L (40 patients) received 20 ml of 0.25% levobupivacaine before wound closure. The volume of the drug was administered in periarticular tissues with a 23 G spinal needle at extensor mechanism (4 ml), capsule (5 ml), iliotibial band (2 ml), collateral ligament (2 ml), pes anserinus (2 ml) and subcutaneous tissues (5 ml).

Premedication was done with inj ondansetron (4 mg IV) and standard monitors were applied. Under strict aseptic precautions, spinal anesthesia was administered in the sitting position using 26 G Quincke needle at either L3-L4 or L4-L5 level. After observing the free flow of cerebrospinal fluid, 3 ml of 0.5% bupivacaine (heavy) with 25 μg of fentanyl was injected in subarachnoid space.

A solitary surgeon performed all the surgeries with a standard minimedial parapatellar approach and a drain was left in situ after the procedure. All of the operations were performed by a single surgeon. During the surgery, a tourniquet with a pressure of 300 mmHg was used. Posterior stabilized total knee prosthesis with a cementing technique was used in each operation.

Postoperative analgesia was provided by inj diclofenac (75 mg IM) thrice a day. Moreover, patient controlled analgesia (PCA) was used in all patients for 96 hours postoperatively. Morphine 1 mg IV was administered by PCA for break through pain with 15-minute lock-out interval. On the second postoperative day the Foleys catheter was removed, and physiotherapy exercises were started. Patients were encouraged to ambulate with a walker as endured.

The primary outcome of our study was postoperative morphine consumption via PCA that was evaluated by visual analog scale (VAS) and postoperative pain control every 3 hours in 0-24 hours and every 6 hours until 96 hours after operation.[5] Complications from morphine utilization, for example, nausea, pruritus, urinary retention, and constipation were recorded. Wound was assessed for any complication at two weeks postoperatively.

Statistical Analysis was performed using Statistical Package for Social Sciences (SPSS) for windows version 21.0 software, Chicago, SPSS Inc. Student's t-test was used for the analysis of parametric data while Fisher/Chi-square test for non-parametric

data. P<0.05 was considered as statistically significant.

RESULTS

All enrolled patients successfully completed the study. On comparing the demographic characteristics both the groups were found to be comparable between them (Table 1).

The postoperative PCA morphine consumption within first 6 hours in Group B and Group L was 1.95 ± 1.21 mg and 0.84 ± 0.71 mg respectively (p = 0.001). Similarly, statistical significance was observed between both the groups in morphine consumption between 6-12 hours (p = 0.001). The postoperative PCA morphine consumption between 12 to 18 hours was observed to be 1.13 ± 0.79 mg in Group B and 1.09 ± 0.72 mg in Group L (p = 0.81). Table 2 also reveals that there was comparable morphine consumption between 18 to 24 hours postoperatively (p = 0.36). We observed similar comparable results among both the study groups between 24 to 96 hours postoperatively also (Table 2).

Regarding VAS scores among the two groups within first 24 hours; Group B had a score of 0.78 ± 0.45 which was found to be comparable with Group L (0.67 ± 0.31) (p = 0.20). VAS scores of Group B (0.68 ± 0.51) was also statistically insignificant on comparing with Group L (0.51 ± 0.29) (p = 0.07). At 48-96 hours, we observed similar statistically comparable observations between both the groups on comparing the VAS scores (Table 3).

There was insignificant difference among the postoperative complications (nausea/vomiting, pruritus, urinary retention and constipation) (Table 4).

However, the patients' complaint of vomiting was successfully managed with inj ondansetron (4 mg IV). There was no other serious side effects.

Table 1: Demographic characteristics

Variables		Group B	Group L	P value
Age (years)		66.93 ± 7.89	65.25 ± 5.46	0.27
Weight (kgs)		62.79 ± 8.81	64.82 ± 10.16	0.34
Height (cm)		155.28 ± 6.73	156.45 ± 5.62	0.40
Side	Right	26	23	0.51
	Left	14	17	0.61
Sex	Male	6	4	0.74
	Female	34	36	0.68
Duration of Operation		91.56 ± 22.37	89.98 ± 20.63	0.74

Table 2: Postoperative PCA morphine consumption (Mean ± SD)

Postoperative time (hours)	Group B (mg)	Group L (mg)	P value
0-6	1.95 ± 1.21	0.84 ± 0.71	0.001*
6-12	1.72 ± 0.81	0.76 ± 0.62	0.001*
12-18	1.13 ± 0.79	1.09 ± 0.72	0.81
18-24	1.06 ± 0.59	0.89 ± 1.02	0.36
24-48	1.12 ± 0.91	1.05 ± 0.63	0.69
48-72	1.17 ± 0.85	0.94 ± 0.77	0.21
72-96	0.52 ± 0.42	0.60 ± 0.51	0.45

Table 3: Visual analogue scale score (Mean ± SD)

VAS	Group B	Group L	P value
0-24 hours	0.78 ± 0.45	0.67 ± 0.31	0.20
24-48 hours	0.68 ± 0.51	0.51 ± 0.29	0.07
48-72 hours	0.61 ± 0.73	0.58 ± 0.49	0.83
72-96 hours	0.57 ± 0.62	0.50 ± 0.41	0.55

Table 4: Postoperative complications

Postoperative complications	Group B	Group L	P value
Nausea/Vomiting	4	3	0.99
Pruritus	0	0	-
Urinary Retention	0	0	-
Constipation	2	3	0.99

DISCUSSION

TKA causes trauma to the soft tissues and bone, thus

leading to postoperative pain and discomfort. Peri-articular injections given intra-operatively allow direct visualization and precise placement of the drug solution over the affected area.[6,7] This localized injection of the drug causes the entrapment of the medication and thereby prolongs the analgesic effect.[8] In addition to this direct effect, local anesthesic agents provide pain relief by inhibiting the neuro-endocrine stress response to surgery.[8]

In our study, we observed a significant difference between groups in the postoperative PCA morphine consumption within first 6 hours (p = 0.001). Yuenyongviwat et al performed a comparative study using periarticular injections of bupivacaine and normal saline.[9] They observed significant difference between the groups and the patients given periarticular bupivacaine received less doses of PCA morphine as compared to normal saline group. However, Browne et al compared intra-articular bupivacaine with normal saline observed insignificant reduction in pain intensity and opioids consumption for the first 24 postoperative hours.[10] Mauerhan et al compared intra-articular morphine and bupivacaine with placebo and observed significantly reduced pain scores in the first 4 hours.[11]

Between 6-12 hours significantly better analgesia was observed in patients given peri-articular levobupivacaine (p = 0.001). However, the postoperative requirement of PCA morphine was comparable in the study performed by Yuenyongviwat et al.[9] Busch et al also compared the peri-articular injection of ropivacaine, epimorphine, epinephrine, ketorolac, and normal saline and observed a decreased consumption of PCA at 12 hours after the operation and a better analgesia in the patients of TKA who did not receive any peri-articular injection.[12] The addition of epinephrine to the local anesthetic causes localized vasoconstriction which leads to decreased reabsorption of the local anesthetic agent and hence prolongs its duration of action. Lombardi et al[13] and Karaoglu et al[14] used epinephrine in their study drug solution and therefore, were able to demonstrate a decrease in the blood loss after the release of the tourniquet.

However, some researchers did not observe a significant difference in postoperative pain scores and PCA opioids consumption when compared with intra-articular saline injection with local anesthetic solution for the first 24 hours.[10,15,16]

Based on the above findings a broad spectrum of studies was observed comparing peri-articular local anesthetics (commonly bupivacaine) with normal saline/placebo but convincing results are still lacking. The better results of levobupivacaine, used in our study could be attributed from the fact that, it has a more prolonged duration of action as compared to bupivacaine.[17]

The postoperative PCA morphine consumption between 12 to 96 hours was observed to be statistically insignificant in our study. Kao et al compared intra-articular local anesthetic injection with femoral nerve block and observed similar efficacy for controlling postoperative analgesia between them.[18] However, the comparable efficacy of intra-articular local anesthetic could be because of the fact that they had used two-six fold higher doses of local anesthetic (60 ml of 0.5% bupivacaine) in their study.

In our study, the VAS scores were comparable between the two groups from 0-96 hours. Our findings were supported by Ritter et al, who formulated a study comparing the intra-articular administration of normal saline and morphine/bupivacaine and no significant change in pain intensity was observed.[16] However, Tanaka et al observed a decrease in pain intensity for the first 24 hours in patients receiving morphine with bupivacaine.[19] Rosen et al conducted a study comparing 0.2% ropivacaine with normal saline and no significant difference was observed for the first 24 hours.[20] The finding of comparable VAS scores in our study between the groups suggests that the patients were well explained the use PCA system. Moreover, the patients had injected morphine to themselves as soon as they felt the first instance of pain.

We did not encounter any significant complications/side effects of peri-articular injection in our study which is consistent with other previous studies. Few patients complained of nausea/vomiting which was managed successfully with ondansetron. TKA carries a greater risk of postoperative infection and wound complications and our study advocates the safe use of periarticular injections when used in knee replacement procedures.

LIMITATIONS

One of the limitation in our study was that we had not adopted a control group for our study protocol, thinking of the fact that it would be inhumane

and unethical of not giving an analgesic agent to a certain group of postoperative patients for TKA.

CONCLUSION

Our study demonstrates that intraoperative periarticular injection with 0.2% levobupivacaine alone is more effective than 0.25% bupivacaine for better pain relief and decreased postoperative morphine consumption with minimal complications and can be used for postoperative pain in patients of TKA.

Conflict of interest: None declared by the authors. The study was carried out on departmental resources and no outside funding was involved.

Authors' contribution: RKV - Manuscript writing, case monitoring and interventions and manuscript editing, language check and literature search; NH - Manuscript writing, case monitoring, interventions and manuscript editing

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