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COMPARISON OF 150 MCG AND 200 MCG INTRATHECAL MORPHINE AS POST-OPERATIVE ANALGESIA FOR TOTAL KNEE REPLACEMENT SURGERIES - A PROSPECTIVE STUDY FROM THE WESTERN PART OF INDIA

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ABSTRACT

Background: Intrathecal morphine is used as post-operative analgesia for total knee replacement surgeries as it is simple to use, not associated with an increase in blood loss during surgery and has a longer duration of action.

Objective: To determine the clinical characteristics of intrathecal Morphine in different doses (150 mcg & 200 mcg) when administrated in patients after total knee replacement surgery.

Method: The prospective study was carried out at the Care Institute of Medical Science (CIIMS) from April 2022 to March 2023 based on the following inclusion Patients who underwent elective primary unilateral total knee replacement at CIIMS, age: 40-80 years, BMI <40 kg/m^2. Exclusion criteria as patients with severe renal or hepatic dysfunction, Contraindication to spinal anaesthesia (refusal, coagulopathy, sepsis, local infection, spinal defects, previous laminectomy), Contraindication to nonsteroidal anti-inflammatory drugs (NSAIDs), Patients with emotional or neurological conditions that would prevent their willingness to participate in the study and Creatinine clearance less than 50 ml/min.

Results: A total of 107 patients were included in the study. Further on randomisation 54 received 150 micrograms (group A) of morphine and the other 54 received 200 micrograms (group B) of morphine post-operative. With 200 micrograms the effect of analgesia was longer as compared to 150 micrograms of morphine with fewer side effects. The use of NSAIDs in group A was more as compared to group B (57.4%, 11.1%).

Conclusion: We conclude that 200 micrograms of intrathecal morphine is superior to 150 micrograms in total knee replacement surgery. Due to its potential benefits of long lasting analgesic effects and less requirement of other analgesic drugs and it has no major side effects.

Keywords: Intrathecal morphine, Knee Replacement Surgeries (TKR), nonsteroidal anti-inflammatory drugs (NSAIDs)

INTRODUCTION

Total knee replacement (TKR) is a frequent surgery, as obesity rates rise, more people are likely to get it. It is generally undertaken at end-stage knee osteoarthritis to gain functional recovery and pain relief **[1, 2]**. A market study found that India has an annual increase in the number of joint replacement procedures, with estimations for knee arthroplasty numbers around 200,000 in 2020 **[3]**. The success rate of TKR is around 90-95% in India **[4]**. However patient dissatisfaction following TKR in India is yet to be studied **[5]**. TKR is a procedure associated with significant acute and chronic postoperative pain **[6]**. Many methods have been applied to reduce pain following TKR, including local infiltration analgesia (LIA), oral analgesics, peripheral nerve block, and intrathecal morphine **[7-9]**. Hess *et al* also suggested that intrathecal morphine may not have a morphine-saving effect and may increase the occurrence of pruritus at doses over 0.3 mg **[10]**. Kaczocha *et al* indicated that intrathecal morphine reduces postoperative pain in TKR patients.

Morphine is the first opioid to be approved by the Food and Drug Administration for its use in neuraxial anaesthesia **[11]** Few of its benefits include being simple to use, not associated with an increase in blood loss during surgery and having a longer duration of action **[12]**. Additionally, it promotes early mobilisation and shortens hospital stays, it is cost-effective **[13]**. Associated side effects include pruritus, urinary retention, nausea and vomiting leading to delayed gastric emptying. The potentially life-threatening adverse effects include delayed respiratory depression. The hydrophilic nature of morphine increases the likelihood of late respiratory depression brought on by rostral diffusion as well as the duration of its analgesic effect **[14]**. Long duration of analgesia has made intrathecal morphine a suitable option for postoperative analgesia in patients with total knee with spinal anaesthesia **[12]**. There is evidence that shows that 100-200 mcg of intrathecal morphine maintains coordination between analgesic action and side effects **[15]**. We sought to assess the effect of two doses of intrathecal morphine and describe the intraoperative, and postoperative outcomes, and side effects at the Care Institute of Medical Sciences, Ahmedabad.

Objectives

To determine the clinical characteristics of intrathecal Morphine in different doses (150 mcg & 200 mcg) when administrated in patients after total knee replacement surgery

Method

The prospective study was carried out at the Care Institute of Medical Science (CIIMS) from April 2022 to March 2023 based on the following inclusion and exclusion criteria

Inclusion criteria

- Patients who underwent elective primary unilateral total knee replacement at CIIMS
- Age: 40-80 years
- BMI <40 kg/m^2

Exclusion criteria

- Patients with severe renal or hepatic dysfunction
- Contraindication to spinal anaesthesia (refusal, coagulopathy, sepsis, local infection, spinal defects, previous laminectomy)
- Contraindication to nonsteroidal anti-inflammatory drugs (NSAIDs)
- Patients with emotional or neurological conditions that would prevent their willingness to participate in the study.
- Creatinine clearance less than 50 ml/min
- Participation already enrolled for any other Total knee replacement clinical trials

The physical status classification system was used for each patient before surgery. American System of Anaesthesiologists (ASA) was used for this purpose. ASA classification uses a grading system. ASA grade I to V. Grade I identifies a person in good health, grade II indicates a mild but well-managed condition, grade III indicates, a serious condition that has an impact on a person's overall health, grade IV indicates life-threatening serious condition and V indicates a severe, life-threatening condition that required immediate surgery, the VI status identifies deceased organ donors.

All patients underwent an operative procedure. Injection of ropivacaine 0.2% 40 ml, with Normal Saline 20 ml, Injection of cefoperazone sulbactam 1500 mg, injection of Kenacort (Triamcinolone acetonide) 80 mg, injection of Tramadol 100 mg total 60 ml into the collateral ligament and posterior capsule was given.

Further, subjects were randomized into two groups.

Group A received an injection of morphine 150 mcg with Injection Sensorcaine 0.5% (4 ml) (20 mg) was given intrathecal for intraoperative anaesthesia.

Group B received an injection of morphine 200 mcg with Injection sensorcaine 0.5% (4 ml) (20 mg) was given intrathecal for intraoperative anaesthesia.

Data collection was done using a case report form (CRF). Information on demographic,

vital signs, comorbidities, total time of surgery and concomitant medication was collected. Intraoperative blood pressure values and pulse pressure values were collected at specific intervals (At the beginning of the surgery, at 5, 10, 15,30,60,120,180 minutes). Postoperative blood pressure values were collected at 1, 2,6,12, 18 and 24 hours respectively. Postoperative adverse events were noted. Information on anaesthesia was collected. The assistant doctor/nurse at the hospital filled in CRF, and data was transferred to an Excel sheet. Descriptive statistics were done for both groups in Excel. Informed consent was taken from the patient or his/her legal guardian and/or impartial witness after explaining the rationale for and the details, aims and objectives of the study, the risks and benefits and the extent of the patient's involvement.

The Institutional Ethics Committee of Care Institute of Medical Science Hospital approved the study protocol.

RESULTS

Baseline characteristics (Table 1)

A total of 107 patients were enrolled in the study, 54 in each in both groups. There were more females than males in both groups. The mean age of patients in groups A and B was 65.07 years and 75 years respectively. The mean weight and BMI were 70.6 kilograms, 25.1 kg/m2 and 75.02 kilograms, 31.1 kg/m2. As per ASA classification, 19 patients were healthy, 51 had mild but manageable conditions and 19 had saviour health issues that impact the overall health of a person.

The majority of patients had hypertension and diabetes mellitus (n=37,31) (n=16,15) and few had a history of myocardial infarction (n= 1) and cardiogenic shock (n=3) All of them (107) were on cox-2 selective inhibitors, 5 patients were on NSAIDs, and only 1 patient was on gabapentinoids.

The blood pressure values were high in both groups (Group A 31, Group B 10) and rest vitals were well controlled within the normal range. Group B showed more analgesic effects as compared to Group A. The need for NSAIDS was greater in Group A compared to Group B.

Post-operative

Number of patients who have incidence of hypertension and bradycardia

Post-operative, at 6 hours 7 patients had hypertension and at the end of 24 hours, there were 9 patients with hypertension in group A.

Post-operative, at 6 hours 3 patients had hypertension and at the end of 24 hours, there were 4 patients with hypertension.

Postoperative bradycardia was evident in 2 patients from both groups at 24 hours.

Side effects

In both groups, itching was the more prevalent post-operative at 6 hours and

continued for 24 hours. Other common side effects observed in both groups were nausea/vomiting and constipation. No sedation was observed in group A and 2 participants in group B had a sedative effect for 12 hours **(Figure 2, Figure 2A)**.

Visual Analogue Scale (VAS) score

Patients in both groups experienced mild to moderate pain. None of the groups had a history of severe pain. Group B has less pain as compared to group A after 12 hours **(Table 3, Table 4)**.

Table 1: Baseline characteristic of patients administrated with 150 mcg and 200 mcg of intrathecal morphine as post-operative analgesia for total knee replacement surgeries

	Group A (Mean±SD)	Group B (Mean±SD)
	Morphine 150 mcg (n=54)	Morphine 200 mcg (n=53)
Male (n)	11	12
Female (n)	43	41
Mean age (years)	65.07 ± 7.06	61.1 ± 8.4
Mean weight (kgs)	70.6 ± 1 1.5	75.02 ± 1 3.09
Mean BMI (kg/m2)	25.1 ± 11.6	31.1 ± 5.5
American Society of Anesthesiologists classification	Grade I= 18 (33.3%) Grade II =27 (50%) Grade III =9 (16.6%)	Grade I= 1 (1.8%) Grade II= 24 (44.4%) Grade III=10 (18.5%)
Comorbidities		
Hypertension	37	31
Diabetes mellitus	16	15
Myocardial infarction	1	0
Cardiogenic shock	1	2
History of surgery		
PCI/CABG	2	2
Concomitant Medications		
NSAIDS	3	2
COX-2 selective inhibitors	54	53
Gabapentinoids	0	1

Table 2: Post-operative details obtained after administration of intrathecal morphine 150 mcg and 200 mcg after total knee replacement surgery

	Group A (Mean±SD)	Group B (Mean±SD)
The mean duration of surgery (minutes)	68.9 ±29.3	83.2± 36.8
Median temperature (F)	36.2 (34.5-37.1)	36.4 (34.8-36.8)
End of spinal anaesthesia Effect (In minutes)	267.5 ± 25.68	263.03 ± 30.79
Used of NSAIDS		
Need of analgesic (other than morphine)	57.4%	11.1%

Table 3: Pain assessment using Visual Analogue Scale (VAS) for Group A

Pain rating	0	1	2	3	4	5	6	7	8	9	10
Post-operative hours	No pain	Mild		Moderate		Distressing pain	Severe		Very Severe		Unbearable pain
6	54	0	0	0	0	0	0	0	0	0	0
12	50	1	2	1	0	0	0	0	0	0	0
18	40	0	11	3	0	0	0	0	0	0	0
24	14	0	35	2	2	0	0	0	0	0	0

Table 4: Pain assessment using Visual Analogue Scale (VAS) for Group B

Pain rating	0	1	2	3	4	5	6	7	8	9	10
Post-operative hours	No pain	Mild		Moderate		Distressing pain	Severe		Very Severe		Unbearable pain
6	52	0	1	0	0	0	0	0	0	0	0
12	44	0	6	2	1	0	0	0	0	0	0
18	40	0	9	2	2	0	0	0	0	0	0
24	11	2	31	2	4	0	0	0	0	0	0

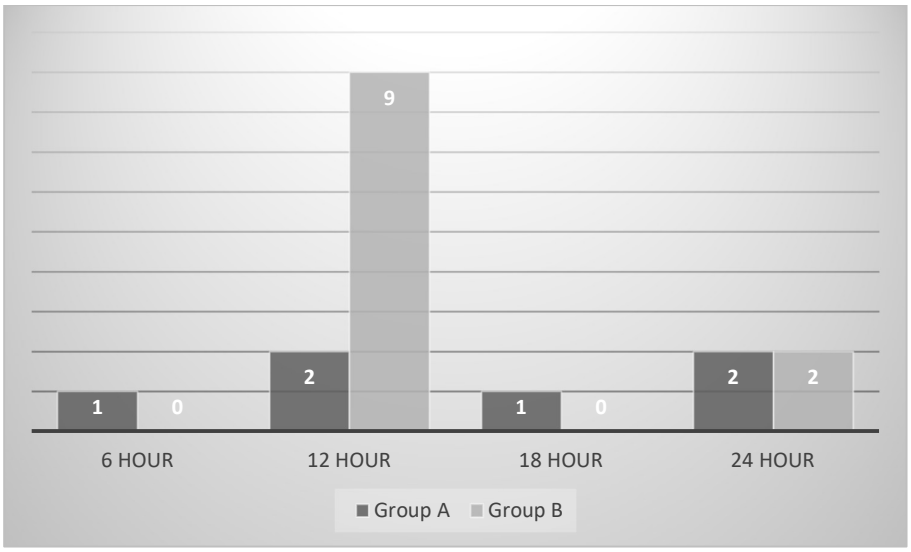

Figure 1: No of patients that required opioids, other than morphine at different time intervals in Group A and B

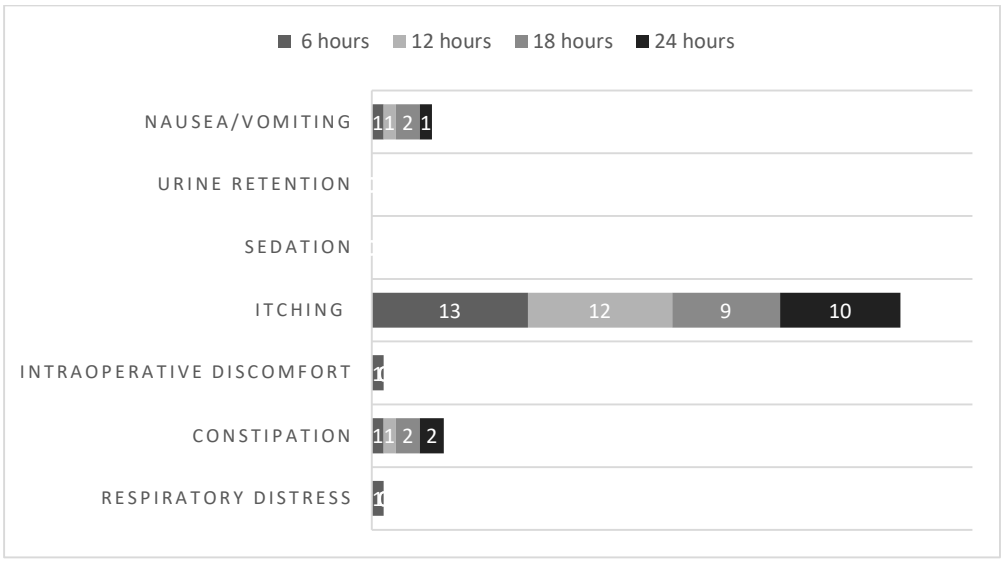

Figure 2: Post-operative side effects at a different time interval observed in Group A

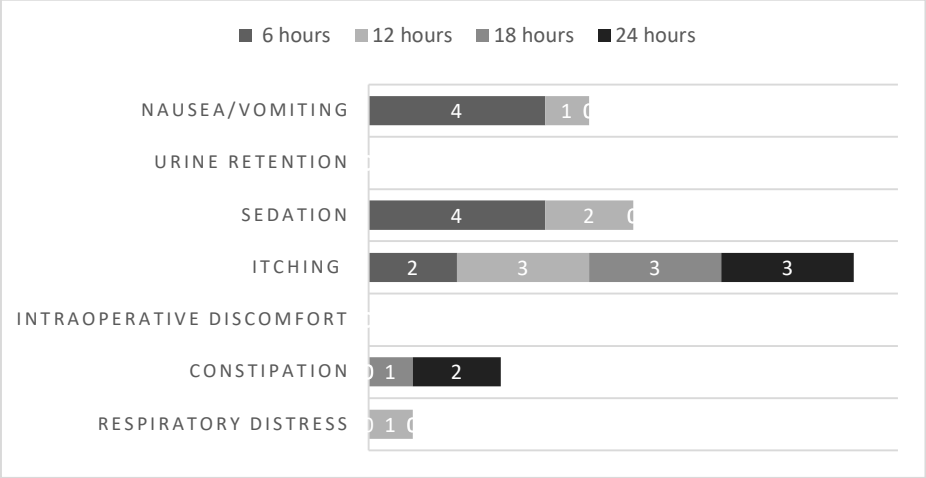

Figure 2A: Post-operative side effects at a different time interval observed in Group B

DISCUSSION

As per the VAS score, the post-operative pain experienced by the patients was mild to moderate. There is a significant difference in VAS score for using 150 mcg and 200 mcg of intrathecal morphine in total knee replacement surgeries **(Table 2)**. However, the one which benefits the patient and causes less distress should be a choice. Similar results were reported by Hassett *et al*. that evaluated the efficacy of intrathecal morphine in 100, 200 and 300 micrograms with 15 mg Bupivacaine. And found that, 200 µg and 300 µg intrathecal morphine provided comparable levels of postoperative analgesia. However, patients who received 100 µg had greater pain postoperatively, with higher pain scores and a greater requirement for supplemental morphine. There were no differences between groups with regard to post-operative Nausea Vomiting (PONV), pruritus, sedation, respiratory depression or urinary retention **[16]**. Conversely, Bowrey *et al* demonstrate that 500 µg intrathecal morphine produced better analgesia than 200 µg after knee replacement **[17]**. However, the risk of serious side effects, particularly respiratory depression is dose-dependent. Subsequently, ASA guidelines advocate that the lowest efficacious dose of neuraxial opioids be used to minimize this risk **[18]** respiratory distress is the most distressing side effect of intrathecal morphine. However, in our findings no respiratory distress was significant. The itching was evident in both groups and this complaint was resolved with tropical application and was not distressing.

The other peculiar finding of our study is the use of opioids (other than morphine) was 57.4% in group A and 11.1 % in group B. It can be said that with a slightly lower dose of morphine, the need for NSAIDs increases. Hence from the efficacy point, 200

micrograms of morphine is effective as compared to 150 micrograms as a post-operative analgesic for total knee replacement surgeries.

CONCLUSION

We conclude that 200 micrograms of intrathecal morphine is superior to 150 micrograms in total knee replacement surgery. Due to its potential benefits of lasting sedative effects, less requirement for analgesic other than morphine and NSAIDs has no major side effects. We, therefore, recommend that 200 µg intrathecal morphine can be used for postoperative analgesia in patients undergoing knee replacement.

Conflict of interest: none

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