Original Article

Comparison of intrathecal morphine versus erector spinae block for postoperative analgesia in patients with end-stage kidney disease undergoing kidney transplantation: A randomised clinical study

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ABSTRACT

Background and Aims: Intrathecal morphine (ITM) or erector spinae plane (ESP) block reduces postsurgical pain in patients who underwent kidney transplantation surgeries. We aimed to compare the effectiveness of both modalities in terms of duration and quality of postoperative analgesia along with postoperative fentanyl consumption. **Methods:** We conducted a randomised study and analysed 60 patients posted for elective live-related kidney transplantation surgery. They were randomised into two groups. Group M patients received ITM, whereas Group E patients received ESP block. We standardised the postoperative analgesia for both groups with intravenous fentanyl-based patient-controlled analgesia. The primary outcome was to compare the quality of analgesia using the numerical rating scale score between the groups. The secondary outcome was to observe the effect of both modalities on the duration of analgesia, postoperative fentanyl consumption, rescue analgesics requirement, catheter-related bladder discomfort and any complications. **Results:** We found significantly lower pain scores at rest and while coughing in Group M at all time intervals, except at 24 h while coughing. The mean time to first analgesia requirement was significantly longer in Group M than in Group E ($P = 0.002$). No significant difference was found in postoperative consumption of total fentanyl ($P = 0.065$) and rescue analgesia in both groups. In Group M, there was significantly more nausea, vomiting and pruritus ($P = 0.001$). **Conclusions:** ITM provides long-lasting postoperative analgesia at the cost of higher side effects than ESP block.

Keywords: Analgesia, fascial plane block, erector spinae plane, intrathecal morphine, kidney transplantation, opioid, patient-controlled analgesia, postoperative pain

INTRODUCTION

Effective postoperative analgesia after a kidney transplantation is an essential component of enhanced recovery following surgery. Inadequate pain control after surgery can be associated with agitation, delirium, prolonged intensive care unit stay and delayed recovery and discharge.[1] Currently, there is an increasing trend of regional analgesia techniques as they have numerous advantages like reduced requirement of intravenous (IV) analgesics and opioids and minimal adverse effects with enhanced recovery after surgery. Several regional analgesic modalities have been practised to control post-surgical pain in kidney transplant recipients, which include intrathecal morphine (ITM),

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epidural analgesia, surgical site infiltration of local anaesthetics or fascial plane blocks.[2] In recent studies, the role of ITM and erector spinae plane (ESP) block as postoperative analgesia has been evaluated in kidney transplant recipients, and they are good postoperative analgesic techniques. However, no study has compared these modalities' analgesic quality and duration and procedure/drug-related adverse effects.[3-5]

Major surgery significantly alters a patient's immune and metabolic functions due to surgical stress, which can further lead to organ dysfunction. The optimal control of postoperative pain is vital for early recovery and ambulation in patients who underwent kidney transplant surgeries.[6,7]

We hypothesised that the ESP block would provide good postsurgical pain relief with minimal adverse effects compared to ITM after kidney transplantation. Our primary objective was to compare the analgesia with regards to the numerical rating scale (NRS) pain score over 24 h between ITM and ESP block. The secondary outcome was to observe the effect of both modalities on the duration of analgesia, postoperative fentanyl consumption, rescue analgesics requirement, catheter-related bladder discomfort (CRBD) and any procedure or drug-related complications in patients who had undergone kidney transplantation.

METHODS

After getting approval from the institutional ethics committee (MGMC&H/IEC/JPR/2022/1149, dated 22 November 2022) and written informed consent for use of patient data for research and educational purposes from the participating patients, a randomised comparative study was conducted on patients with end-stage kidney disease posted for kidney transplantation surgery. This study was registered in the Clinical Trials Registry-India (CTRI/2023/01/049068, accessible at www.ctri.nic.in). It was conducted from March 2023 to August 2023, according to the principles of the Declaration of Helsinki, 2013 and good clinical practice. Sixty kidney transplant recipients of either gender, aged 20–60 years, were recruited. Exclusion criteria for the study were patient refusal for participation, history of allergy to study drugs, any contraindication to subarachnoid and peripheral nerve blocks (like bleeding diathesis, neurological dysfunction and any recent systemic/local infection), incomprehensiveness to use patient-controlled analgesia (PCA) device, history of drug abuse and recent use of psychoactive or analgesic medications. Recruited patients were randomised using a computer-generated random number table into two groups. Allocation concealment was done using sealed, opaque, serially numbered envelopes kept with anaesthesia nurses who did not participate in the study and only opened them before the surgery. Group M patients received preservative-free ITM 200 μg, and Group E patients received ESP block with 20 ml of 0.5% ropivacaine. The analgesic blocks or intrathecal injections were executed by an independent, experienced anaesthetist who was not further involved in this study. The outcome assessor was the only person blinded to the group allocation. All patients underwent thorough preanaesthetic evaluation, and the analgesic intervention, PCA device use, and pain interpretation were explained using the numeric rating score. On the day of surgery, all patients received palonosetron 0.075 mg IV, oral alprazolam 0.25 mg and immunosuppressants at least 2 h before shifting to the operating room. In the operating room, standard anaesthesia monitoring, such as non-invasive blood pressure, pulse oximetry and electrocardiograph, were attached. Baseline vital parameters were noted.

Patients in Group M received 200 μg morphine (0.2 ml) intrathecally along with 1.8 ml sterile normal saline (total volume 2 ml). The procedure was done under all aseptic precautions. A 25-gauge Quincke needle was inserted in intervertebral space L3–L4 or L4–L5 in a sitting position. In Group E, patients received ESP block at T10 level on the same side of surgery in a lateral position under ultrasound guidance (M-TURBO FUJIFILM Sonosite, Inc., Bothell, WA, USA). A linear transducer probe (13–6 Hz) was placed 3 cm lateral to midline longitudinally, and back muscles were visualised, including the trapezius superiorly, rhomboid major in the middle and the erector spinae muscle below with the T10 transverse processes. A 10-cm, 22-gauge needle was inserted towards the transverse process, keeping craniocaudal direction using the plane technique till it touched the transverse process tip after crossing all three muscles after the needle tip was localised by visible fluid spread, thereby lifting the erector spinae muscle away from the transverse process. A total of 20 ml of 0.5% ropivacaine was injected after negative aspiration of blood. The ultrasound-guided ESP block was performed by a trained anaesthesiologist with more than 1 year of experience in ultrasound-guided nerve blocks.

All patients were administered IV midazolam (0.02 mg/kg) and fentanyl (2 μg/kg), followed by an induction dose of propofol 2 mg/kg IV. The trachea was intubated 3 min after administration of IV cisatracurium (0.2 mg/kg), and anaesthesia was maintained with isoflurane in a mixture of nitrous oxide and oxygen (50:50) and IV cisatracurium infusion at the rate of 0.1 mg/kg/h. Urinary catheterisation was performed in all patients. After the surgery, residual neuromuscular blockade was reversed using IV neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). Post-extubation, patients were shifted to the kidney transplant unit (KTU). Fentanyl IV PCA was attached for postoperative pain control, and instructions regarding the use of the PCA device were given to the patient. Fentanyl IV PCA pump settings were: baseline infusion- nil, demand dose- 1 ml (10 μg) bolus, lockout interval between two doses- 10 min and maximum allowed doses/hour-four. In the postoperative period, vital parameters (heart rate, blood pressure, respiratory rate, oxygen saturation) were noted. The primary outcome of our study was to compare the postoperative quality of analgesia using an 11-point NRS scoring system with 0 meaning no pain and 10 meaning worst pain for static and dynamic pain (on coughing) for measuring pain intensity. NRS was measured at 0, 1, 3, 6, 12, 18 and 24 h after shifting the patient to KTU. IV paracetamol 500 mg was used as a rescue analgesic if the NRS score was ≥ 4, with the dose not exceeding 2 g in 24 h. As a secondary outcome, the time of first analgesia request by the patient, total fentanyl consumption in 24 h postoperatively, any complications like opioid-related side effects and CRBD were recorded. CRBD was assessed at 0, 1, 3, 6, 12, 18 and 24 h after surgery using the scoring system: where 0: no discomfort, 1: mild discomfort reported only upon questioning, 2: moderate discomfort where patient describe having an urge to pass urine without any questioning and 3: that the patient was in severe discomfort where he had the urge to pass urine with behavioural responses like an attempt to pull out the catheter or flailing limbs.[8]

Respiratory depression (respiratory rate <10/min), if noted, was managed by giving supplemental oxygen or IV naloxone if required. Postoperative nausea and vomiting were managed by ondansetron 4 mg IV bolus, and pruritus was treated by administering dexamethasone 8 mg IV.

The sample size was calculated using G power for sample size calculation and by using the method of comparison of two independent means. Based on our experience, by anticipating a relatively large effect size of 0.74 in NRS between both groups (Group M and Group E), the final sample size was calculated to be 60 subjects (30 in each group) with a 5% level of significance and 80% power.[9]

All data was compiled and analysed using MS Excel (R) Office 365, GraphPad Prism 8.4.2 with Statistical Package for Social Sciences version 24.0 (SPSS Inc., Chicago, IL, USA). All descriptive statistics were shown as proportions or percentages for categorical variables (gender distribution, complications) and mean and standard deviation (SD) for continuous variables (age, weight, height, duration of surgery and anaesthesia, duration of analgesia). Fisher's exact test or Chi-square test was used to compare proportions (gender, complications). All the continuous variables mentioned above were analysed using the Mann–Whitney test or Student's *t*-test (independent group or unpaired data) along with the Wilcoxon signed-rank test or paired *t*-test (for paired data) based on the normality of the data. A *P*-value less than 0.05 was considered significant.

RESULTS

Seventy-one patients, fulfilling the eligibility criteria, were enroled in this study during preoperative assessment. Sixty patients were included in the study, and 11 were removed as per the exclusion criteria [Figure 1].

Demographic profile (age, gender, height and weight) and surgical duration were not significantly different between the two groups [Table 1].

Group M patients showed better pain relief and decreased static and dynamic pain scores at all time intervals, except dynamic pain scores at 24 h ($P > 0.05$) [Figure 2].

Table 1: Demographic characteristics in both groups

Variables	Group M (*n*=30)	Group E (*n*=30)
Age (years), Mean (SD)	34.07 (11.77)	32.71 (8.28)
Gender (male/female), *n*	25/5	24/6
BMI (kg/m^2), Mean (SD)	22.55 (3.33)	21.05 (2.33)
Duration of surgery (min), Mean (SD)	173.61 (31.44)	183.58 (27.61)
Duration of anaesthesia (min), Mean (SD)	217.01 (24.66)	215.34 (18.76)

Data expressed as mean (SD) or numbers. *n*=Number of patients, Group M=Intrathecal morphine group, Group E=Erector spinae plane block group, BMI=Body mass index, SD=Standard deviation

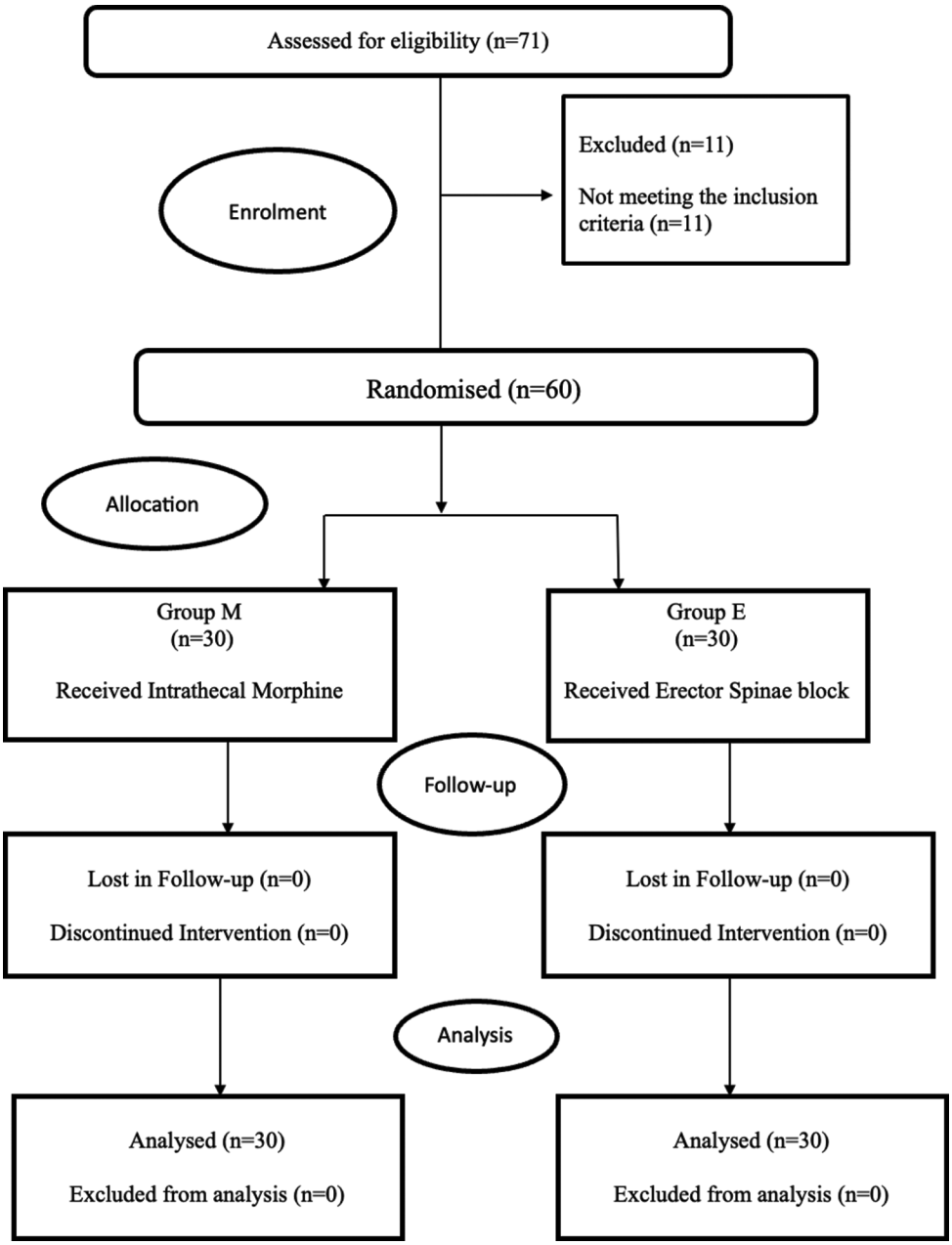

Figure 1: Consolidated Standards of Reporting Trials (CONSORT) flow diagram

The mean (SD) time to first analgesia requirement after the patient was shifted to KTU was significantly longer in Group M than in Group E ($P < 0.001$). Postoperative total fentanyl consumption ($P = 0.065$) and requirement of rescue analgesic ($P = 0.336$) were lesser in Group M in comparison to Group E, but the difference was statistically insignificant [Table 2].

The incidence of CRBD at 0, 1, 3, 6, 12, 18 and 24 h was lower in Group M than in Group E, with $P = 0.001$, 0.024, 0.013, 0.049, 0.026, 0.035 and 0.039, respectively, which were all statistically significant [Table 3].

A total of 13 patients complained of postoperative nausea and vomiting in Group M, while only two patients had nausea and vomiting in Group E ($P = 0.001$). Respiratory depression was observed in four patients in Group M and one patient in Group P ($P = 0.160$). Pruritis was observed in seven patients in Group M, while no patient had pruritus in Group E ($P = 0.001$).

DISCUSSION

We observed no significant difference in terms of postoperative quality and duration of analgesia between the ESP and ITM groups. However, ITM

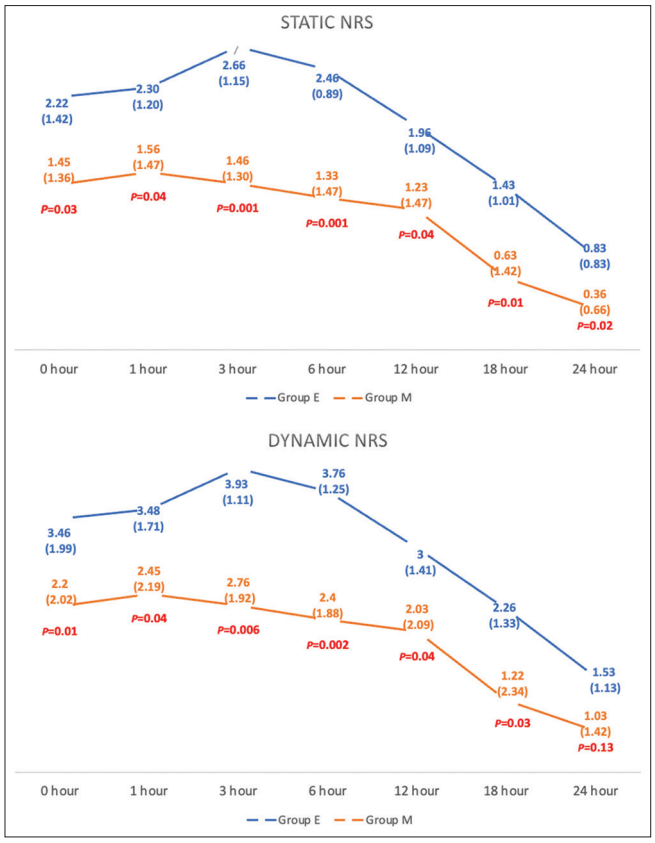

Figure 2: Static and dynamic numerical rating scale (NRS) score trends postoperatively in both groups. Data expressed as mean (standard deviation). Group M = intrathecal morphine group, Group E = erector spinae plane block group

Table 2: Perioperative analgesic consumption

Variables	Group M (*n*=30) Mean (SD) (95% CI)	Group E (*n*=30) Mean (SD) (95% CI)	*P*
Time of first analgesia request (min)	67.0 (42.0) (51.9, 82.1)	33.1 (20.7) (25.7, 40.5)	<0.001
Total fentanyl consumption (μg)	187.6 (66.9) (163.6, 211.5)	221.6 (73.0) (195.4, 247.7)	0.065
Total rescue analgesia consumption (mg)	634.3 (667.6) (395.4, 873.2)	801.0 (663.3) (563.6, 1038.3)	0.336

Data expressed as mean (SD) (95% CI). *n*=Number of patients, Group M=Intrathecal morphine group, Group E=Erector spinae plane block group, CI=Confidence interval, SD=Standard deviation

Table 3: CRBD trends postoperatively

Time point	Group M (*n*=30) Mean (SD) (95% CI)	Group E (*n*=30) Mean (SD) (95% CI)	*P*
0 h	0.36 (0.55) (0.16, 0.55)	0.93 (0.73) (0.66, 1.19)	0.001
1 h	0.53 (0.68) (0.28, 0.77)	0.96 (0.76) (0.68, 1.23)	0.024
3 h	0.43 (0.62) (0.20, 0.65)	0.86 (0.68) (0.61, 1.10)	0.013
6 h	0.30 (0.55) (0.10, 0.49)	0.62 (0.67) (0.38, 0.86)	0.049
12 h	0.20 (0.48) (0.02, 0.37)	0.56 (0.72) (0.30, 0.81)	0.026
18 h	0.13 (0.41) (0.01, 0.27)	0.36 (0.61) (0.14, 0.57)	0.035
24 h	0.06 (0.25) (0.02, 0.14)	0.26 (0.44) (0.10, 0.41)	0.039

Data expressed as mean (SD) (95% CI). *n*=Number of patients, Group M=Intrathecal morphine group, Group E=Erector spinae plane block group, CI=Confidence interval, CRBD=Catheter-related bladder dysfunction, SD=Standard deviation

reduced the incidence of CRBD at the cost of certain side effects.

In this study, we observed a significant reduction of postoperative NRS score in both groups, M and E, up to 24 h in the postoperative period. A study by Jun *et al.*[10] in live-related kidney transplant surgeries, authors observed that ITM, compared to surgical site infusion of ropivacaine, was associated with a decrease in postsurgical pain up to 48 h. Still, the dose of ITM was higher (400 μg). A comparative study between bilateral single-injection ESP block and ITM in laparoscopic hepatectomy by Kang *et al.*[11] concluded that patients who received ITM had lower postoperative pain scores than those who received ESP block.

We found that the mean time to the first analgesic requirement was significantly longer in Group M than in Group E, providing the additional advantage of reduced rescue analgesic requirement. Similar results were reported by Sayed *et al.*[12] in their study of major abdominal surgeries. This can be attributed to a comparatively shorter duration of action of local anaesthetic agent than a longer-acting morphine, whose effect lasts throughout the postoperative period.

Postoperative consumption of fentanyl was higher in Group E compared to Group M. Still, it was statistically non-significant, which is in agreement with a study performed by Kang *et al.*[13], where postoperative opioid consumption was found to be significantly higher in the ESP block group. In our patients, we did not find statistically significant results, which may be attributed to using a lower dose of ITM (200 μg) in our study compared to 400 μg of morphine. A recent study by Dewey *et al.*[14] in paediatric liver transplant, recipients also concluded that the use of continuous ESP catheter technique resulted in lesser post-surgical opioid consumption. However, unlike our study, they compared the ESP technique with standard IV analgesia. However, Hamed *et al.*, in their study, concluded that in the initial 24 h, patients who received ITM had used significantly higher opioid or tramadol (101.71 [25.67] mg) compared to patients

who received ESP block (44 [16.71] mg) in caesarean section surgeries, which may be due to a lower dose of ITM (100 μg) compared to our study (200 μg).[15] Postoperative opioid consumption in the ITM groups varied among studies depending on the intrathecal dose of morphine used by the authors in kidney transplant recipients.

We observed a reduced requirement for rescue analgesics in the ITM group. In their study, Kim *et al.*,[16] observed that the rescue analgesic requirement was reduced in the ITM group up to 24 h following open nephrectomy, similar to our finding.

Our study found a significant reduction in the incidence of CRBD up to 24 h in the ITM group patients. We could not find any study to show the effects of ITM on CRBD in kidney transplantation. Russo *et al.*[17] conducted a pilot study (TORNADO) in patients undergoing robot-assisted laparoscopic prostatectomy where they found that ITM may help to prevent CRBD as well as to reduce pain perception, but ESP block at the thoracic level (T10) may not be effective in preventing CRBD due to pathophysiology involving sensory innervations from the sacral nerve roots.

In our study, we noticed less incidence of nausea, vomiting, and pruritus in the ESP group, which is similar to the observation made by Sayed *et al.*[12] in their study of patients undergoing major hepatopancreatic biliary surgery. We observed a high incidence of pruritus in patients in the ITM group who responded well to IV dexamethasone. Kim *et al.*[16] also found a high incidence of pruritus in the ITM group in patients undergoing open nephrectomy. The incidence of respiratory depression was higher in patients receiving ITM and was managed with supplemental oxygen without any significant consequences. In their study of patients undergoing living donor hepatectomy, Kang *et al.*[13] found similar adverse sequelae of ITM. Although the incidence was low, there is a small notable chance of late respiratory depression, particularly at higher doses of ITM.

Our study had a few limitations, including a small sample size and a centric study population with male prevalence. We included all end-stage kidney disease patients irrespective of their preoperative urine output. Patient satisfaction was not considered in this study. Lastly, we did not recruit any control group for comparison, as a classical control group is not ethical in pain studies. Future studies can focus on modified techniques like continuous catheters or adjuvant agents in ESP blocks.

CONCLUSION

Unilateral ESP block showed higher consumption of postoperative opioids compared to ITM after kidney transplantation, with minimal drug-related adverse effects.

Study data availability

De-identified data may be requested with reasonable justification from the authors (dr.vipin28@gmail.com) and shall be shared after approval as per the authors' institution policy.

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Conflicts of interest

There are no conflicts of interest.

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