

# Comparison of transversus abdominis plane block and intrathecal morphine for laparoscopic donor nephrectomy: Randomised controlled trial

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## ABSTRACT

**Background and Aims:** Postoperative pain following laparoscopic donor nephrectomy (LDN) is significant and no suitable analgesic technique is described. Opioid analgesia in standard doses is often suboptimal and associated with numerous adverse effects. Transversus abdominis plane (TAP) block has been evaluated in various laparoscopic procedures. Intrathecal morphine (ITM) has been seen to provide long-lasting analgesia of superior quality in laparoscopic colorectal procedures. **Methods:** The present study was undertaken to evaluate the analgesic efficacy of single-dose ITM 5 µg/kg for LDN. After ethics approval, 60 adult patients scheduled for LDN were randomised to receive intravenous fentanyl, ultrasound-guided TAP block or ITM for postoperative analgesia. Postoperative 24-h patient-controlled analgesia (PCA) fentanyl consumption, visual analogue scale (VAS) score and intraoperative fentanyl and muscle relaxant requirements were compared. Statistical analysis was performed using appropriate statistical tests by using Stata 11.1 software. **Results:** Haemodynamic stability at pneumoperitoneum and in the post anaesthesia care unit was significantly better in patients receiving ITM. Intraoperative rescue fentanyl requirement ( $P = 0.01$ ) and postoperative fentanyl requirement until 24 h ( $P = 0.000$ ) were significantly lower in the morphine group. Postoperative VAS at rest and on movement was significantly lower in the morphine group at all points of assessment ( $P = 0.000$ ). **Conclusion:** ITM 5 µg/kg provides better intraoperative and postoperative analgesia and reduces postoperative PCA fentanyl requirement in laparoscopic donor nephrectomy compared to TAP block or intravenous fentanyl.

**Key words:** Donor nephrectomy, intrathecal morphine, laparoscopy

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## INTRODUCTION

Renal transplantation is the definitive treatment for patients with end-stage renal disease on haemodialysis. Although cadaver donations are common, the supply is far outstripped by the demand and living donor renal transplant is a useful and feasible alternative. Further, 3-year survival rates of living donor grafts have been found to be superior to cadaver grafts.<sup>[1]</sup> Donor selection, previously stringent, presently extends to and includes partners, altruistic donors and 'paired'/pooled kidney transplants. Since the introduction

of laparoscopic donor nephrectomy (LDN), kidney donation has increased significantly due to the perceived 'minimally invasive' nature of the procedure.<sup>[2]</sup>

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Pain after LDN, however, is significant and results from somatic pain arising out of multiple port site and abdominal wall incisions in addition to visceral pain resulting from irritation of peritoneum and diaphragm, gas insufflation and postoperative gas retention.<sup>[3,4]</sup> This pain is intense and may not be completely treated by systemic opioids. The voluntary kidney donor is a special person who deserves excellent analgesia with minimal adverse effects. The transversus abdominis plane (TAP) block has been shown to produce effective, but short-lasting analgesia after LDN.<sup>[5]</sup> On the other hand, intrathecal morphine (ITM) in small doses provides excellent analgesia in patients undergoing caesarean section, laparoscopic cholecystectomy and colorectal surgery.<sup>[6-9]</sup> However, ITM has not yet been evaluated in LDN.

This present study aimed to compare the analgesic efficacy of ITM over TAP block and conventional intravenous opioid for LDN. Our hypothesis was that ITM would provide better intraoperative and postoperative analgesia in donor nephrectomy. The primary objective was to compare 24 h postoperative opioid (patient-controlled analgesia [PCA] fentanyl) requirement. The secondary objectives were to compare a) VAS scores at rest and on movement for 24 h, b) hemodynamic response to pneumoperitoneum and c) side effects: postoperative nausea and vomiting (PONV), pruritus and respiratory depression (Respiratory rate <12/min).

## METHODS

After obtaining institutional ethical committee approval (Ref no: IESC/T-24/03.01.2014, dated 9<sup>th</sup> January, 2014) and individual written informed consent, this prospective, randomised, open-labelled, controlled clinical trial was carried out on adult American Society of Anaesthesiologists (ASA)-I/II voluntary kidney donors scheduled for left trans-peritoneal laparoscopic nephrectomy. Exclusion criteria were refusal to participate; contraindications to spinal anaesthesia; incapable of handling PCA device; the history of PONV and chronic analgesic use. The trial is registered with the Clinical Trials Registry of India ([www.ctri.nic.in](http://www.ctri.nic.in)) - CTRI/2016/07/007110.

Computer-generated randomisation was done and allocation concealment was performed in sealed opaque envelope technique. A detailed pre-anaesthetic check-up was performed and all the patients were taught about the use of VAS and use of PCA device.

All patients received premedication with oral alprazolam (0.5 mg) on the morning of surgery. After application of routine ASA monitors and insertion of an intravenous (IV) cannula, the envelope bearing the serial number of the patient in the study was opened and the patient assigned to the group contained in it.

Patients in group M received 5 µg/kg (maximum 300 µg) preservative-free morphine in 1 mL normal saline through subarachnoid injection, administered after skin preparation with chlorhexidine and local anaesthetic infiltration, at L2-3 or L3-4 interspace in the left lateral position, with 25-G Sprotte needle. They were then turned supine and administered general anaesthesia (GA) with fentanyl 2 µg/kg, propofol 2–3 mg/kg and atracurium 0.5 mg/kg. Anaesthesia was maintained with air, oxygen and isoflurane. All patients were mechanically ventilated to maintain end-tidal carbon dioxide between 35 and 45 mmHg, and MAC between 0.7 and 1.1.

Patients assigned to Group T (TAP block) received ultrasound-guided (Sonosite, linear probe 6-13 Hz) bilateral TAP block in the triangle of Petit with 20 mL 0.375% ropivacaine with 1 µg/kg of clonidine on either side after induction of GA as described above.

Patients in Group C received GA as described above and served as controls. All three groups received fentanyl infusion at 1 µg/kg/h throughout the procedure. Any increase in baseline hemodynamic parameters (heart rate, systolic blood pressure, diastolic pressure) by ≥20% of baseline was treated by rescue bolus of 1 µg/kg fentanyl IV.

At the end of the surgery, all patients received IV paracetamol 1 g and ondansetron 4 mg. Neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg and trachea extubated. All patients were transferred to post-anaesthesia care unit (PACU) and connected to PCA device capable of delivering 25 µg fentanyl on demand, with lockout period of 10 min and maximum dose of 150 µg/h. Rescue morphine of 3 mg IV bolus was administered if patients continued to have pain in spite of maximum dose of PCA fentanyl.

Visual analogue scale (VAS) scores at rest and movement were assessed by a blinded investigator at awakening, every 2-h up to 6 h, and at 12 and 24 h. Patients with VAS >4 despite PCA were administered 3 mg morphine boluses every 10 min till the VAS

was <4. All patients were encouraged to ambulate and resume oral intake. At 24 h, the PCA was discontinued and the total amount of PCA fentanyl calculated before discharging patients to the ward.

No previous study has compared ITM with TAP block for LDN. Parikh *et al.* in 2013<sup>[10]</sup> reported that 24 h mean (SD) tramadol consumption after LDN was 103.8 (32.18) mg with USG guided TAP block. We hypothesised that ITM will reduce postoperative opioid consumption by 30%. So, with a power of 90% and alpha of 0.05, at least 17 patients would be required in each group to reject the null hypothesis. Considering a drop out of 20%,  $n = 20$  patients were recruited in each study group.

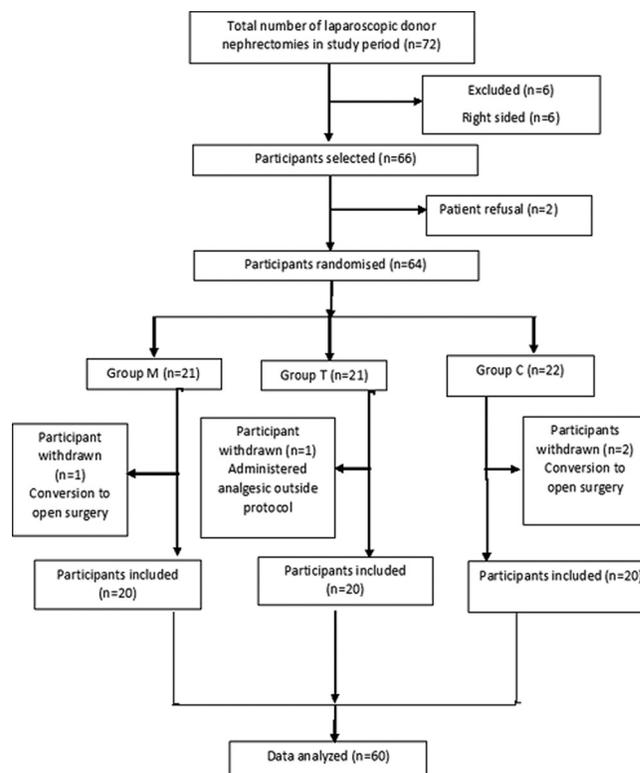
Statistical analysis was carried out by using Stata 11.1 software. Data were represented as mean with standard deviation and qualitative data was compared by applying Chi-square/Fischer's exact test. The quantitative data were compared by ANOVA followed by posthoc comparison by Bon-Ferroni method. To see the change over period of time in quantitative data, repeated measure analysis was applied followed by posthoc comparison by Bon-Ferroni method.  $P$  values <0.05 were considered significant.

## RESULTS

The study was conducted between January 2014 and July 2015. A total of 72 donor nephrectomies were assessed for eligibility during the study period, of which 60 were available for analysis. The consort diagram is shown in Figure 1. The mean age, weight, sex distribution, basal heart rate and blood pressure, ASA status and duration of pneumoperitoneum were comparable between the three groups [Table 1].

The maximum heart rate and mean arterial pressure after pneumoperitoneum were significantly lower in group M compared to group T and C. Intraoperative requirement of rescue fentanyl was lower in group M compared to other groups whereas requirement of muscle relaxant boluses was similar [Table 2].

On arrival in PACU, VAS scores at rest at 0, 2 and 6 hours were comparable in patients receiving TAP block and subarachnoid morphine. VAS scores in the control group were significantly higher at 0, 2 and 6 h compared to both TAP and subarachnoid morphine groups ( $P = 0.000$ ) [Figure 2]. VAS scores on movement and deep breathing were significantly lower at all observation



**Figure 1:** Consort diagram

points in patients receiving subarachnoid morphine (M) compared to control patients and those receiving TAP block ( $P = 0.0001$  at 1 and 2 h and  $P = 0.014$  at 6 h). At 12 and 24 h, VAS in the morphine group continued to be significantly lower ( $P = 0.000$  at both time points) than in group C and T, both at rest and on movement. VAS at 12 and 24 h were comparable between control and TAP patients [Figure 3].

Postoperative PCA fentanyl consumption and rescue morphine boluses were significantly lower in group M compared to other groups ( $P = 0.0001$ ) [Table 2].

The incidence of PONV and pruritus were similar between the groups and no patient had respiratory depression [Table 3]. Urinary retention could not be measured as all the patients were catheterised until the study follow-up period of 24 h.

## DISCUSSION

In the present study use of ITM 5  $\mu$ g/kg before induction provided better postoperative analgesia, decrease in 24-h PCA fentanyl consumption and rescue morphine boluses, less intraoperative fentanyl requirement and a better suppression of the haemodynamic response to pneumo-peritoneum in LDN.

There is considerable evidence in the literature that pain can be significant after most types of laparoscopic surgery and is most intense up to 24 h.<sup>[11]</sup> Pain following LDN can be due to a combination of port pain, the abdominal incision (to extract the kidney), pelvic organ nociception, diaphragmatic irritation, ureteric colic and urinary catheter discomfort. Severe postoperative pain can be an obvious disincentive for live kidney donation, so, a multimodal pain management plan should be discussed and agreed upon before surgery.<sup>[12]</sup>

Analgesic techniques like an epidural opioid, TAP block, paravertebral block and parenteral opioids have been assessed for efficacy in patients undergoing LDN.<sup>[5,13,14]</sup> To the best of our knowledge, this is the first study in which ITM was assessed for LDN.

Patients receiving ITM had consistent and significantly lower pain scores at rest throughout 24 h

postoperatively. VAS in this group had declined to and remained at a score of 1 from 6 h onwards till 24 h. The VAS at rest range over 24 h ranged 0–3 in group M, 1–3 in group T and 1–4 in group C respectively. Similarly, ITM could bring down VAS on movement to  $\leq 3$  but not the other groups.

Efficacy of ITM was established in other laparoscopic surgeries as well. Motamed *et al.*<sup>[8]</sup> observed that pain scores at rest and on coughing were significantly lower with ITM at all time points of observation in patients undergoing elective laparoscopic cholecystectomy. Morphine 150–200  $\mu\text{g}$  with bupivacaine in patients undergoing colorectal surgery has been found to significantly decrease opioid consumption in the first two postoperative days.<sup>[9,15]</sup> Thoracic epidural anaesthesia using bupivacaine-fentanyl infusion for 48 h has been used for ‘fast-tracking’ in hand-assisted LDN.<sup>[14]</sup> VAS scores at ambulation were superior in

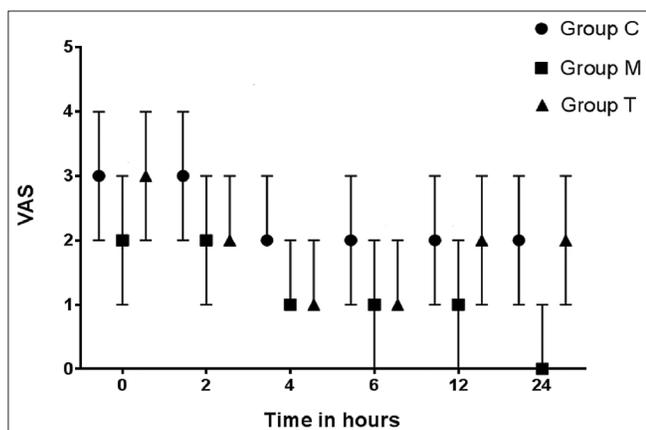


Figure 2: Visual analogue scale (VAS) at rest

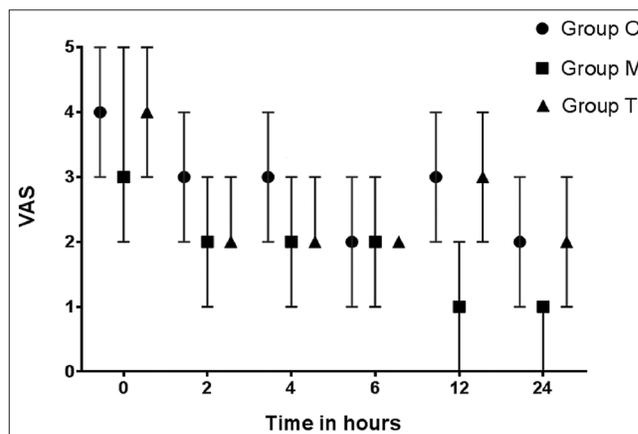


Figure 3: VAS on movement (deep breathing and turning)

Table 1: Demographic characteristics

| Parameter              | Group C (n=20) (Mean±SD) | Group M (n=20) (Mean±SD) | Group T (n=20) (Mean±SD) | P      |
|------------------------|--------------------------|--------------------------|--------------------------|--------|
| Age (years±S.D.)       | 41.25±11.79              | 45.1±9.91                | 42.65±11.29              | 0.5390 |
| Weight (kg±S.D.)       | 57.4±11.23               | 60±11.95                 | 60.85±9.27               | 0.5820 |
| ASA I/II               | 16/4                     | 17/3                     | 17/3                     | 1.00   |
| Pneumoperitoneum (min) | 144.7±17.02              | 150.15±11.09             | 146.3±7.58               | 0.3737 |

P<0.05 is considered significant

Table 2: Outcome parameters

| Parameter  | Group C        | Group M       | Group T       | P      |
|--|----------------|---------------|---------------|--------|
| Heart rate at pneumoperitonium (bpm; mean±SD)                              | 87.05±7.53     | 78.75±4.89    | 86.1±4.72     | 0.00   |
| Heart rate at PACU (bpm; mean±SD)  | 87±6.80        | 81.45±4.17    | 84.65±5.28    | 0.009  |
| MAP at pneumoperitonium (mmHg; mean±SD)                                    | 93.85±7.04     | 86.9±4.47     | 92.45±7.34    | 0.003  |
| MAP at PACU (mmHg; mean±SD)  | 92.1±6.50      | 86.15±4.98    | 89.1±6.58     | 0.011  |
| Intraoperative rescue fentanyl consumption Median (min-max) mcg            | 90.5 (0-240)   | 38.1 (0-140)  | 51 (0-210)    | 0.018  |
| Number of intraoperative muscle relaxant boluses required median (min-max) | 3 (3-4)        | 2 (2-2)       | 2 (2-3)       | 0.18   |
| 24-h PCA fentanyl consumption Median (min-max) mcg                         | 850 (650-1100) | 275 (100-450) | 525 (350-650) | 0.0001 |
| Number of rescue morphine boluses (min-max)                                | 2 (1-3)        | 0 (0-1)       | 1 (0-2)       | 0.0001 |

P<0.05 is considered significant. MAP – Mean arterial blood pressure; PACU – Post-anaesthesia care unit; PCA – Patient-controlled analgesia

**Table 3: Adverse effects and complications**

| Parameter              | Group C<br>n (%) | Group M<br>n (%) | Group T<br>n (%) | P     |
|------------------------|------------------|------------------|------------------|-------|
| PONV                   | 2 (10)           | 4 (20)           | 2 (10)           | 0.710 |
| Pruritus               | 1 (5)            | 4 (20)           | 1 (5)            | 0.344 |
| Respiratory depression | 0                | 0                | 0                | 0     |

*P*<0.05 is considered significant. PONV – Postoperative nausea and vomiting

the epidural analgesia group compared to the controls receiving PCA morphine. However, patients receiving epidural analgesia complained of more pain after its withdrawal, possibly due to enhanced pain perception. In the present study, ITM provided excellent analgesia for more than 24 h, and also did away with the logistics of epidural catheter placement and management of continuous infusion. Subarachnoid block is also technically easier to administer than a thoracic epidural, with fewer potential adverse effects. The finding that ITM is superior to TAP block has been established in multiple studies performed in patients undergoing caesarean section.<sup>[16-18]</sup> However, ITM has multiple mechanisms of analgesia and provides both visceral and somatic analgesia<sup>[15]</sup>; whereas TAP block essentially provides only somatic analgesia and may be considered as part of multimodal analgesia technique rather than a stand-alone comparator to ITM.

Patients receiving TAP block had minimal pain at rest and movement up to 6 h postoperatively with VAS comparable to the morphine group. Thereafter, VAS scores at rest and on movement increased similar to the control group, ostensibly due to the limited duration of action of TAP block. However, we had used a higher dose of the drug in TAP block (0.375% ropivacaine 20 ml each side) to increase the duration of action, as the comparator was ITM, which is known to provide longer-lasting analgesia even up to 24 h.

Aniskevich *et al.*<sup>[5]</sup> observed that bilateral TAP block with 0.5% ropivacaine in patients undergoing hand-assisted laparoscopic nephrectomy reduced overall pain scores at 24 h, with a trend toward decreased total morphine consumption. However, two recently published meta-analyses<sup>[19,20]</sup> on the efficacy of TAP block in patients undergoing colorectal surgery found that TAP block was not effective in relieving dynamic pain. Yu,<sup>[21]</sup> however, found TAP to be superior to local anaesthetic (LA) infiltration in a meta-analysis of four RCTs.

Patients in the control group experienced significantly worse pain than both morphine (*P* = 0.000 at all time points) and the TAP groups (*P* = 0.000 till 6 h)

throughout the period of study. Patients in all three groups used PCA fentanyl to keep VAS <4. PCA use likely resulted in lower pain scores than would have otherwise been recorded.

Median PCA fentanyl consumption was significantly reduced in group M compared to other groups effectively highlighting the opioid-sparing effect of ITM in the postoperative period. Opioid sparing by ITM has been reported by Wongyingsinn<sup>[15]</sup> in an RCT of patients undergoing laparoscopic colorectal surgery and by TAP block in patients undergoing hand-assisted LDN.<sup>[5]</sup>

There were a few limitations of the present study. First, the use of a bilateral TAP block may be questioned. Since the laparoscopic ports are placed on both sides of the abdomen, we chose bilateral technique. However, ipsilateral continuous catheter technique with contralateral port site infiltration could have been used. Second, the duration of analgesia with ITM was not determined.

## CONCLUSION

In conclusion, administration of low dose ITM reduces the haemodynamic response to pneumoperitoneum, provides superior postoperative analgesia up to 24 h, leading to a significant reduction in perioperative parenteral opioid consumption without a significant increase in side effects in patients undergoing live LDN under general anaesthesia. However, this should be tested in a larger population of LDN to validate our results.

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## Conflicts of interest

There are no conflicts of interest.

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