Transversus Abdominis Plane Block for Analgesia in Renal Transplantation: A Randomized Controlled Trial

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BACKGROUND: The transversus abdominis plane (TAP) block has proven effective in reducing opioid requirements and pain scores for some procedures involving the lower abdominal wall. In this study we assessed its efficacy in patients with end-stage renal failure undergoing cadaveric renal transplantation.

METHODS: Sixty-five adult renal transplant recipients were prospectively randomized to receive a standard general anesthetic technique supplemented with levobupivacaine 0.375% 20 mL TAP block or sham block with 20 mL 0.9% saline. Both groups received patient-controlled morphine analgesia and acetaminophen. Patient assessment occurred in the postanesthetic care unit and at 2, 4, 6, 12, and 24 hours. The primary outcome was total morphine consumption in the first 24 hours after renal transplantation. Other outcomes assessed included pain scores, presence of nausea or vomiting, excessive sedation, and respiratory depression.

RESULTS: Morphine requirements did not differ between the 2 groups, 31.6 ± 5.6 mg in the TAP group and 32.6 ± 5.5 mg in the control group (95% confidence interval [CI], −8.96 to 7.09, $P = 0.817$). Pain scores also did not differ significantly at any time point after surgery. Nausea was reported in 53% of the TAP group and 24% of the control group. The relative risk of nausea associated with treatment was 2.2 (95% CI, 1.1 to 4.3, $P = 0.017$). No patient exhibited excessive sedation or respiratory depression.

CONCLUSIONS: The addition of a TAP block to the analgesia regimen for renal transplantation did not reduce morphine requirements. (Anesth Analg 2012;115:953–7)

Options for effective postoperative analgesia after renal transplantation are limited by considerations relating to the recipient's premorbid condition and the pharmacokinetic impact of the recipient's impaired renal excretory function. In addition, an initial period of graft dysfunction, and the desire to avoid hypotensive episodes that may compromise the return of graft function, limit the available choices. The pharmacokinetics of morphine in renal transplantation are well described, and its accumulation can lead to undesirable side effects, including respiratory depression, hypoxia, and even psychosis.[1–3] The use of nonsteroidal anti-inflammatory drugs is avoided after renal transplantation because of their potential adverse effects on renal hemodynamics.[4] Preoperative coagulopathy often precludes a neuraxial block, and surgical time can be prolonged, leading to conversion to general anesthesia.[5] A 2003 survey of all 27 United Kingdom renal transplant centers revealed that the majority used an opioid patient-controlled analgesia (PCA) regimen, with epidural being the only regional anesthetic technique reported.[6] More recently, the combination of intercostal and ilioinguinal–iliohypogastric nerve blockade has been reported to reduce both postoperative pain and opioid consumption after renal transplant,[7] and a small pilot study of transversus abdominis plane (TAP) block and a retrospective review of the use of a continuous TAP block reported similar results.[8,9]

A TAP block, by blocking the lower 6 thoracic and first lumbar nerves as they course through the neurofascial plane that exists between the transversus abdominis and internal oblique muscles, provides analgesia for procedures involving the abdominal wall. TAP blocks have been used in a number of lower abdominal surgical procedures, with investigators reporting reductions in pain scores and opioid requirements.[10–12] Renal transplantation predominantly involves an oblique incision in the right or left lower abdominal wall, with extraperitoneal graft positioning. This prospective, randomized, placebo-controlled study evaluated the efficacy of TAP blocks in patients undergoing renal transplantation. Our hypothesis was that the addition of a TAP block to the analgesia regimen of PCA morphine and regular acetaminophen would reduce 24-hour morphine consumption and improve analgesia after renal transplantation.

METHODS

After local institutional ethics committee approval, 65 adult patients, with end-stage renal disease undergoing cadaveric renal transplantation, were included. Written informed consent was obtained preoperatively for all participants. Exclusion criteria included contraindications to the use of morphine or levobupivacaine, age <16 years and an inability to use a PCA device. The primary study endpoint was

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total morphine consumption for 24 hours after renal transplantation, and secondary outcomes included pain scores, and the incidence of nausea or vomiting, excessive sedation, and respiratory depression.

Preoperatively, monitoring of electrocardiogram, noninvasive arterial blood pressure, and oxygen saturations (Spo_2) was instituted. All patients received a standardized anesthetic technique including the administration of fentanyl 1 to 1.5 $\mu g\ kg^{-1}$, propofol 2 to 3 mg kg^{-1}, and atracurium 0.5 mg kg^{-1}. Anesthesia was maintained with sevoflurane and nitrous oxide in oxygen after tracheal intubation. Intraoperatively, all patients received IV acetaminophen 1 G, morphine 0.1 mg kg^{-1}, and ondansetron 4 mg, while postoperatively, a morphine PCA was provided for 24 hours, in addition to acetaminophen 1 G orally every 6 hours.

Patients were randomized to either a TAP or placebo block according to a computer-generated sequence contained in sealed, opaque envelopes. The investigator opening the envelope drew up either 20 mL of levobupivacaine 0.375% (TAP group) or 20 mL of 0.9% saline (control group) and subsequently took no further part in the study. The block was then performed by one of the investigating anesthesiologists, who was blinded, as were the nursing and surgical staff, to the patient's group randomization.

The TAP block was performed after induction of general anesthesia and before surgical incision, using the technique described by McDonnell et al.[12] The TAP was accessed using a 24-G 50-mm blunt-tipped needle (Plexufix®, B Braun, Melsungen AG, Germany) and a loss-of-resistance technique. Insertion point for the needle is the triangle of Petit bounded inferiorly by the iliac crest, anteriorly by the posterior border of the external oblique muscle, and posteriorly by the anterior border of latissimus dorsi muscle. After piercing the skin, the needle is advanced at right angles to the skin, until 2 separate losses of resistance are felt: the first "pop" felt being the entrance to the plane between the fascial extension of the external oblique and the internal oblique muscle; the second pop indicating entry into the plane between the internal oblique and transversus abdominis. Aspiration was performed to exclude vascular puncture and if negative an initial 1 mL was injected. Any resistance to injection or noticeable swelling of the lateral abdominal wall in the area of injection necessitated repositioning of the needle. The test solution, of either levobupivacaine 0.375% or 0.9% saline, was then injected.

In the postanesthesia care unit, PCAs were activated as follows: morphine sulfate 2 mg IV every 5 minutes until visual analog scale pain score (0 = no pain, 10 = worst possible pain) was 3 or less, and continued at the following settings for a 24-hour period: 1 mg bolus, 7-minute lockout, and 30 mg maximum 4-hourly dose.

Participant's age and weight were recorded. Total morphine consumption was recorded at 24 hours. Pain, at rest and on movement, was evaluated using a visual analog scale, by a blinded investigator, in the postanesthesia care unit and at 2, 4, 6, 12, and 24 hours, respectively. The following were also recorded, at similar time intervals: nausea, vomiting, sedation score, and respiratory depression. Nausea was scored as absent = 0, mild = 1, moderate = 2, severe = 3. Vomiting was either present or absent, and sedation was scored as per local hospital PCA protocol (0 = asleep; 1 = unrousable; 2 = somnolent, rousable with minor stimulus; 3 = calm, easily rousable; 4 = active; 5 = uncontrollable). Respiratory depression was recorded as present or absent, and was defined as respiratory rate <8 or Spo_2 <95%.

A reduction in 24-hour morphine consumption of 40% for sample size calculation was considered to be clinically relevant in this patient population. This figure was based on a small series of patients who had previously received a TAP block during renal transplantation in our institution, and on other published work showing up to 50% reduction in overall morphine consumption with the addition of a TAP block.[11,12] Experience from retrospective chart reviews in our own institution suggested that the 24-hour morphine consumption would be 45 ± 25 mg in the control group. Thus we calculated that a sample size of 31 per group would be necessary to demonstrate a 40% reduction in morphine consumption with an $\alpha = 0.05$ and $\beta = 0.2$.

Data were analyzed with StataSE release 11™ (StataCorp LP, College Station, TX). Pain scores were analyzed as continuous variables using the Wilcoxon Mann–Whitney test, and as binary variables comparing the presence of any pain between the groups. Multiple regression analysis was used to calculate morphine requirements and to explore relationships with age and weight, and logistic regression was used for analysis of binary endpoints.[13] Least squares regression models were checked for heteroskedasticity using the Breusch–Pagan/Cook–Weisberg test. Pearson goodness-of-fit tests were performed after logistic regression. In no case was there a significant violation of assumptions (all Ps > 0.15). Estimates of differences between groups and their confidence intervals were calculated from the regression models.

RESULTS

Thirty-two patients were randomized to the TAP group and 33 to the control group. One patient was excluded after informed consent had been given, but before randomization, because he was also scheduled for concurrent pancreatic transplant. There were no protocol violations. Demographic data did not differ significantly between groups apart from age, with patients in the TAP group being older by 7 years ($P = 0.036$) (Table 1).

There was no significant difference in total morphine consumption between the TAP and control groups (Table 2). Both age and weight were predictors of morphine requirement and were consequently adjusted for in all analyses of treatment effects. Total morphine consumption increased with increasing body weight (95% confidence interval [CI], 0.07–0.70; $P = 0.015$) and decreased with increasing age (95% CI, −0.71 to −0.12; $P = 0.006$); however, when adjusted for both of these variables, mean total morphine requirements did not differ between the groups (95% CI, −8.96 to 7.09; $P = 0.817$). There were no significant differences in pain scores between the TAP and control groups at 24 hours ($P = 0.137$) (Fig. 1), or in the prevalence of pain at any time point (data not shown).

Table 1. Baseline Patient and Surgical Data

	TAP (n = 32)	Control (n = 33)	Significance*
Sex (M/F)	20/12	23/10	0.726¶
Age (years)[a]	51.6 ± 13.2	44.6 ± 13.0	0.036
Weight (kg)[a]	71.9 ± 18.7	71.9 ± 11.8	0.470
Smoker	5	9	0.253¶
Cause of ESRD			
Unknown	6	1	
Hypertensive nephropathy	5	8	
Reflux nephropathy	4	4	
IgA nephropathy	3	5	
Diabetic nephropathy	3	1	
APCKD	2	6	
Other[b]	9	8	
Duration of surgery (minutes)[a]	230.3 ± 44.2	221.4 ± 55.2	0.474
Side of surgery	Right 25, left 7	Right 30, left 3	0.153¶
Complications of surgery[c]	3	0	0.131§
Urea (mmol/L^{-1}) D1 postop.[a]	16.7 ± 5.9	14.8 ± 5.0	0.180
Creatinine (μmol/L^{-1}) D1 postop.[a]	466.1 ± 180.4	445.4 ± 202.1	0.664

TAP = transverus abdominis plane; ESRD = end-stage renal disease; D1 postop. = first postoperative day at 24 hours posttransplant; APCKD = adult polycystic kidney disease.

[a] Mean ± SD.

[b] Other causes of ESRD included membranoproliferative glomerulonephritis n = 3(TAP); systemic lupus erythematosis (SLE) n = 1(TAP); Henoch Schonlein purpura n = 1(TAP); thrombotic microangiopathy n = 1(TAP) and n = 2(Control); amyloid n = 1(TAP); congenital hypoplastic kidneys n = 1(TAP) and n = 1(Control); chronic pyelonephritis n = 1(TAP) and n = 1(Control); polyarteritis nodosa n = 1(Control); tuberous sclerosis n = 1(Control); meningococcal sepsis n = 1(Control); and renal artery stenosis n = 1(Control).

[c] See last paragraph of RESULTS section for details.

*Significance based on t test, ¶chi-squared test, and §Fisher exact test.

Table 2. Morphine Requirements

	TAP (n = 32)	Control (n = 33)	Difference	P value
Morphine (mg)				
Intraoperative	6.6 (5.7–7.5)	7.1 (6.2–8.0)	−0.5 (−1.8 to 0.8)	0.448
PACU	4.0 (2.6–5.3)	3.1 (1.8–4.3)	0.9 (−9.0 to 7.0)	0.340
Total (24 hours)	31.6 (26.0–37.3)	32.6 (27.1–38.1)	−1.3 (−8.5 to 5.8)	0.817

Data are presented as mean, adjusted for age and weight, and 95% confidence interval. TAP = transversus abdominis plane; PACU = postanesthetic care unit.

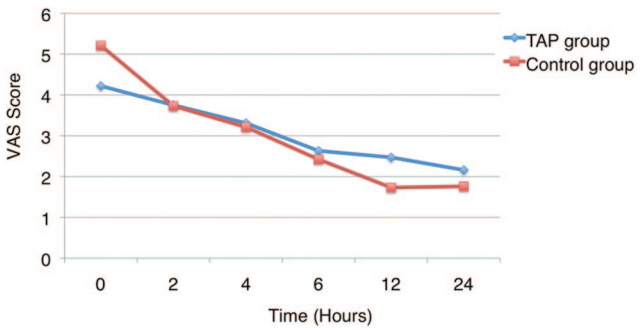

Figure 1. Mean postoperative visual analog scale (VAS) pain scores on movement in each group. P = ns at all time points. TAP = transversus abdominis plane.

Over the 24-hour observation period, nausea was reported in 53% of the TAP group and 24% of the control group. The relative risk of any nausea, associated with treatment, was 2.2 (95% CI, 1.1–4.3; P = 0.017). Vomiting occurred in 22% of TAP and only 6% of control participants in the first 24 hours after renal transplant, with a relative risk of 3.6 but a confidence interval spanning unity (95% CI, 0.81–61.1; P = 0.065). No excessive sedation or respiratory depression was observed during the study period.

One patient, from the TAP group, developed a mild weakness of left hip flexion, after a left-sided renal transplant. This was noted on day 1 postoperatively when the patient was first mobilized from bed to chair. On review by the transplant and orthopedic surgeons, weakness secondary to muscle retraction at the time of surgery was diagnosed, and was deemed not to be a complication of the TAP block. The observed weakness had completely resolved by 3 months postoperatively, at outpatient follow-up. Two intraoperative complications occurred in the TAP group: 1 patient required a transfusion of 2 units of packed red blood cells for bleeding during arterial anastomosis, and another developed an acute coronary syndrome with electrocardiogram changes that resolved postoperatively. Both made an uneventful recovery. There were no intraoperative complications in the placebo group.

DISCUSSION

We report that renal failure patients undergoing cadaveric renal transplantation who received a TAP block had comparable total morphine consumption to those in the control group. In addition, there was no difference in pain scores between the groups. These findings are in direct contrast with previously published postoperative analgesia data after TAP blocks, using the landmark technique, in patients undergoing cesarean delivery, open prostatectomy, and open large bowel resection.[10–12]

A retrospective review of single-shot TAP blocks in renal transplant recipients noted that the reduction achieved in intraoperative analgesia did not persist into the postoperative period.[9] TAP block, using the landmark technique, has also been shown to confer no additional benefits to postcesarean delivery patients either alone or in combination with intrathecal morphine.[14] Also, 2 randomized controlled trials, in patients receiving ultrasound-guided TAP blocks, reported no significant reductions in postoperative analgesia requirements.[15,16] Differences in study outcomes may be related to the fact that patients undergoing cesarean delivery in the Costello et al. trial received intrathecal morphine, the effects of which may well have outlasted those of the ropivacaine used in the TAP block. Griffiths et al. attribute the negative outcome for TAP block in their study of patients having gynecological cancer surgery to an obese population and heterogeneity in surgical insult.[16]

There are no data on the rate of partial or failed TAP block, and it is generally considered easy to perform, with a sensory block from T7 to L1 being achieved in volunteers given 20 mL of lidocaine 5%.[17,18] However, use of the landmark technique has been questioned because of a cadaveric study detailing the variability of size and position of the triangle of Petit.[19] Ultrasound imaging has also documented anatomical variability in this area,[20] and the authors of an editorial have called for ultrasound use on the grounds of precision and safety.[21] Ultrasound-guided TAP blocks have proved effective for both laparoscopic cholecystectomy and open appendicectomy.[22,23] Indeed, a recent large randomized controlled trial reported that in open inguinal hernia repair an ultrasound-guided TAP block provided better pain relief and reduced opioid consumption when compared with a conventional loss-of-resistance ilioinguinal–iliohypogastric nerve block.[24]

The volume of local anesthetic used in the study must also be considered: 20 mL may not be an adequate volume to block all the nerve roots in the TAP. A cadaveric study reported spread of 20 mL of dye from the iliac crest to the costal margin; however, this has subsequently been disputed.[18,25] Despite dye not reaching the costal margin, T11 was consistently dyed, and T10 was dyed in 50% of cadavers, suggesting that 20 mL is sufficient for lower abdominal surgery,[25] such as renal transplant.

The limitations of our study are lack of ultrasound guidance and lack of testing for sensory block in TAP patients. Use of an ultrasound-guided technique may have improved our block success rate or dermatomal spread. Unfortunately, cutaneous analgesia was not tested postoperatively in this study, as this would have unmasked the blinding process, and thus adequacy of block was uncertain.

Twenty-four-hour morphine requirements in renal transplant recipients vary widely in the reported literature.[7–9] A retrospective review of our institution's renal transplant recipients was undertaken, and an average 24-hour morphine consumption of 45 ± 25 mg was calculated before commencement of this study. These patients had received identical analgesia regimens to our 2 study groups, apart from the TAP block. The mean morphine consumption in our study control group, 32.6 ± 5.5 mg, was considerably less than this. This may also explain, in part, the negative outcome of this study. It can be argued that this may reflect the fact that subjects can alter their behavior simply because they are part of a study (Hawthorne effect).

The observed increase in nausea in the TAP group is difficult to explain. The study was not powered to detect a difference in this outcome, and the other side effects of opioids were not noted in either the TAP or control group.

In summary, the addition of a TAP block to the analgesia regimen for patients undergoing cadaveric renal transplantation did not confer any additional benefit on opioid requirements or pain scores in the first 24 hours postoperatively and was associated with no appreciable patient benefits. ■

DISCLOSURES

Name: Noelle M. Freir, MB, FCARCSI.
Contribution: This author helped design the study, conduct the study, analyze the data, and write the manuscript.
Attestation: Noelle M. Freir has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.
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Attestation: Caitriona Murphy has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
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Attestation: Anna Linnane has seen the original study data and approved the final manuscript.
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Contribution: This author helped design the study, conduct the study, and write the manuscript.
Attestation: Anthony J. Cunningham has seen the original study data and approved the final manuscript.
This manuscript was handled by: Terese T. Horlocker, MD.

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