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Epidural versus intravenous analgesia for pain control in kidney donors: a retrospective cohort study

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ABSTRACT

Aims: It's crucial to ensure that live kidney donors receive top-notch care, including postoperative pain control. Treatment options include intravenous intermittent analgesics, intravenous or epidural patient-controlled analgesia (PCA). In this study we aimed to compare these modalities with respect to their analgesic efficacy.

Methods: A retrospective analysis of fifty-eight live donor nephrectomy patients operated in a 7-year-period in a university hospital was performed. Investigational Review Board approval has been obtained. Data of the patients' postoperative analgesia methods, degree of kinship with the recipient, postoperative pain scores, and rescue analgesic and antiemetic use were obtained from the patients. The patients were divided into three groups according to the analgesia method used, including intravenous intermittent, intravenous PCA and epidural PCA. Correlation of postoperative pain scores with the analgesia technique was investigated, as well as with the degree of kinship of the donor and recipient.

Results: Enhanced control of postoperative pain was achieved through PCA, epidural PCA being the best. Moderate to severe pain at 6th postoperative hour in the intravenous intermittent, intravenous PCA, and epidural PCA groups was 76, 37, and 14%, respectively. Rescue analgesic use on the day of operation was 32% and 5% in the intravenous intermittent and intravenous PCA groups, with no rescue analgesic use in the epidural PCA group. Postoperative antiemetic consumption was also less with the epidural PCA (P=0.024 and P=0.027 for postoperative days 1 and 2, respectively). No correlation was detected between the pain and the degree of kinship.

Conclusion: Epidural PCA provides better postoperative pain control after live donor nephrectomy, compared with intravenous intermittent or PCA. Postoperative pain scores were not related to the degree of kinship.

Keywords: Analgesia, kinship, postoperative pain, renal transplantation

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INTRODUCTION

Kidney transplantation is the last step in the treatment of end-stage renal failure, but is the best option for these patients, increasing survival rate and the quality of life. The kidney can be obtained from either cadaveric, or live donors, but the last is the best way in increasing the number of transplants and increasing the chance of graft survival.[1] Cold ischemic time is decreased, and the recipient's preoperative condition is optimized in the case of live donation, thus increasing the chance of the patient and graft survival.[2,3]

The conventional way of nephrectomy was open through a big flank incision often including a rib resection. This has many disadvantages like hyperesthesia, risk of incisional hernia, prolonged recovery and poor cosmesis.[4] Considering these unwanted effects of open surgery, minimally invasive laparoscopy was introduced for donor nephrectomy, with advantages of less blood loss, less pain, faster recovery, and earlier discharge.[5] Still it involves some challenges from the anesthetist's point of view and need special management, including postoperative pain.[6-10]

Pain is a major challenge for the donor. Several analgesic techniques have been proposed to relieve pain in kidney transplant donors, including paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, patient-controlled analgesia (PCA) systems, epidural analgesia, transversus abdominis plane (TAP) block, skin and surgical cite local anesthetic infiltration, and acetazolamide, as well.[7,9,11]

The main objective of this study was to compare the pain scores of the kidney transplant donors that receive intravenous intermittent analgesia, intravenous PCA or epidural PCA. The secondary aim was to investigate the effect of the degree of kinship on the pain scores of the patients.

METHODS

Following the Institutional Ethics Board approval (Date: 03.01.2020, Decision No: 09.2020.127) data of 58 patients undergone live donor nephrectomy (LDN) between 2012-2019 in our Educational and Research Hospital were collected for the study. We have routine registration of the transplant patients in the Transplantation Committee of our institution. The patients' dossiers were collected from the hospital archive and their intraoperative follow-up forms, as well as ward nurse follow-up forms were obtained. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

We perform LDN for kidney transplant in our institution since 2012. Both open and laparoscopic techniques are performed, with the trend toward the latest. Analgesia is provided via intravenous (iv) intermittent analgesics, intravenous PCA or epidural PCA.

We have standard protocols in our institution for the intra- and postoperative management of kidney donors. General anesthesia was used routinely, with intravenous induction, endotracheal intubation and volatile-narcotic based maintenance. Invasive arterial blood pressure monitorization was performed in the recipients. Intraoperative fluid management was performed using hemodynamics and the fluid balance of the patient. Postoperative analgesia was provided by one of the three methods: 1) Intermittent intravenous analgesia, where morphine 0.1 mg kg^{-1} ideal body weight (IBW) and paracetamol 1 g intravenously are given perioperatively, followed by paracetamol 1 g every 6 hours (q 6 h); 2) Intravenous PCA, where paracetamol 1 g intravenously is given perioperatively, followed by iv PCA system (CADD-Legacy, Smiths Medical, USA) used by the patient with 0.4 mg mL^{-1} solution of morphine without continuous infusion, a demand dose of 15 µg kg^{-1} and a lockout of 10 min; 3) Epidural PCA, where paracetamol 1 g iv is given perioperatively, followed by epidural PCA system (CADD-Legacy, Smiths Medical, USA) through lower thoracic epidural catheter used by the patient with 0.125% bupivacaine and 3 µg mL^{-1} fentanyl with loading dose 10 mL, infusion 4 mL h^{-1}, demand dose 5 mL and lockout 30 minutes. Meperidine 0.5 mg kg^{-1} IBW was used as rescue analgesia in all the three groups.

Live donor nephrectomy is performed either open, or laparoscopically in our institution. For open surgery mini-incision retroperitoneal open procedure with the patient in lateral extended position is used. For laparoscopic, live donor nephrectomy in lithotomy position is done. Left nephrectomy is routinely performed unless there are anatomical reasons for the right nephrectomy.

The patients' demographic data, including age, sex, weight, height, American Society of Anesthesiologists (ASA) physical status; type of surgery (open vs laparoscopic); degree of kinship with the recipient; duration of surgery and intraoperative narcotic analgesic amount used was obtained from the intraoperative follow-up forms. Morphine equivalent was used as the amount of narcotic analgesic to standardize the data. Intraoperatively used tramadol and meperidine were converted to morphine equivalent in a ratio of 10:1.

The patients' numerical rating scale (NRS) pain scores measured at postoperative 6^{th}, 24^{th}, 48^{th} and 72^{nd} hours were obtained from the ward nurse follow-up forms, as well as meperidine rescue analgesic and antiemetic amounts for the postoperative days zero, one, two and three (PO0, PO1, PO2 and PO3). The obtained data were divided into three groups regarding the postoperative analgesia technique; as the patients receiving intravenous intermittent analgesia (Group iv), those having intravenous PCA (Group ivPCA) and those having epidural PCA (Group epiPCA). The patients' pain scores, postoperative analgesic and antiemetic consumptions were compared between the groups. Correlation between the demographics of the patients, degree of kinship and surgical technique in the groups was investigated.

Statistical Analysis

Data analysis was performed using Statistical Package for the Social Sciences 22.0 software (SPSS, IBM, USA). Data were presented as frequency, percentage, mean and standard deviation. Normal distribution was tested by Shapiro-Wilk test. Categorical variables were analyzed by Chi-Square test. Continuous variables were analyzed by One-way ANOVA with Tukey Post-hoc test or Kruskal-Wallis H test with Bonferroni adjusted Mann-Whitney U test for three and more groups. Pearson correlation coefficient was used for correlations between continuous variables. A P-value <0.05 was considered to be statistically significant.

RESULTS

Data of a total of 58 patients with the age range of 26-70 years (44.19±10.58) were analyzed, of whom 25 (43.1%) were males, and 33 (56.9%) females. The demographic characteristics, ASA physical status, surgical technique, degree of kinship, operation duration and intraoperative morphine consumption of the patients are presented in Table 1. The demographic variables and ASA physical statuses of the patients in all the three groups were similar. Forty patients had laparoscopic surgery, which comprised 69% of all the operations. No significant difference was observed between the groups regarding the surgery type. Left nephrectomy was performed in 56 out of the 58 patients. Degree of kinship was comparable between the groups, as well. Significant difference was observed in the operation duration between the groups, with the Group iv having the longest (Table 1). Intraoperative narcotic consumption did not show any significantly difference between the groups.

The patients' postoperative pain intensities are presented in Table 2.

The patients' postoperative rescue analgesic use is presented in Table 3. Group iv had the most rescue analgesic use among the study groups. Only one, if at all patients needed rescue analgesic in the Groups ivPCA and epiPCA.

Table 1. Demographic and surgical characteristics, physical statuses, intraoperative morphine consumption, and degree of kinship of the patients

	Group iv (n=25)	Group ivPCA (n=19)	Group epiPCA (n=14)	P
Sex				0.466
Male	10 (40.0)	7 (28.0)	8 (32.0)	
Female	15 (45.4)	12 (36.4)	6 (18.2)	
Age (years)	42.6±9.0	44.9±11.3	46.1±12.4	0.569
BMI (kg m^{-2})	26.5±4.0	27.2±4.4	26.9±4.1	0.835
ASA				0.720
I	17 (40.5)	15 (35.7)	10 (23.8)	
II	8 (50.0)	4 (25.0)	4 (25.0)	
Surgical technique				0.265
Open	5 (27.8)	8 (44.4)	5 (27.8)	
Laparoscopic	20 (50.0)	11 (27.5)	9 (22.5)	
Degree of kinship				0.769
1°	17 (40.5)	14 (33.3)	11 (26.2)	
≥2°	8 (50.0)	5 (31.3)	3 (18.8)	
Operation time (minutes)	226.2±34.5^{A}	199.5±63.2^{A,B}	170.0±47.5^{B}	0.002*
Intraoperative narcotic (mg)**	4.8±1.4	4.9±1.0	5.0±0.0	0.871

Note: Categorical data are given as frequency (percentage). Continuous data are given as mean±standard deviation. BMI, body mass index. ASA, American Society of Anesthesiologists physical status. iv, intravenous. ivPCA, intravenous patient-controlled analgesia. epiPCA, epidural patient-controlled analgesia. *P<0.05, and different capital letters in each row indicate significant differences between the groups. **Measured in morphine equivalents.

Table 2. Postoperative pain intensity of the patients

Postoperative times	Pain intensity	Group iv (n=25)	Group ivPCA (n=19)	Group epiPCA (n=14)
6th hour				
	None	-	-	3 (21.4)
	Mild	6 (24.0)	12 (63.2)	9 (64.3)
	Moderate	16 (64.0)	7 (36.8)	2 (14.3)
	Severe	3 (12.0)	-	-
24th hour				
	None	-	2 (10.5)	1 (7.1)
	Mild	19 (76.0)	11 (57.9)	9 (64.3)
	Moderate	6 (24.0)	6 (31.6)	4 (28.6)
	Severe	-	-	-
48th hour				
	None	4 (16.0)	4 (21.1)	5 (35.7)
	Mild	17 (68.0)	10 (52.6)	6 (42.9)
	Moderate	4 (16.0)	5 (26.3)	3 (21.4)
	Severe	-	-	-
72nd hour				
	None	16 (64.0)	15 (78.9)	12 (85.7)
	Mild	8 (32.0)	4 (21.1)	2 (14.3)
	Moderate	1 (4.0)	-	-
	Severe	-	-	-

Note: Data are given as number of the patients and their percentage in the parentheses. Pain intensity is presented as mild: Numerical Rating Scale (NRS) score 1-3; moderate: NRS score 4-6; and severe: NRS score 7-10. "None" stands for no pain, i.e. NRS score 0. iv, intravenous. ivPCA, intravenous patient-controlled analgesia. epiPCA, epidural patient-controlled analgesia.

Table 3. Postoperative rescue analgesic use for the patients

Postoperative days	Group iv (n=25)	Group ivPCA (n=19)	Group epiPCA (n=14)
PO0	8 (32.0)	1 (5.3)	0 (0)
PO1	3 (12.0)	1 (5.3)	1 (7.1)
PO2	6 (24.0)	1 (5.3)	1 (7.1)
PO3	2 (8.0)	0 (0)	0 (0)

Note: Data is represented as number of the patients having rescue analgesic and their percentage in the parentheses. PO0, PO1, PO2, PO3; postoperative day zero, one, two and three, respectively. iv, intravenous. ivPCA, intravenous patient-controlled analgesia. epiPCA, epidural patient-controlled analgesia.

Postoperative antiemetic use of the patients is presented in the Table 4. Significant difference was observed between the groups on the PO1 and PO2.

Table 4. Postoperative antiemetic use for the patients

Postoperative days	Group iv (n=25)	Group ivPCA (n=19)	Group epiPCA (n=14)	P
PO0	16 (64.0)	14 (73.7)	6 (42.9)	0.190
PO1	18 (72.0)	9 (47.4)	4 (28.6)	0.024*
PO2	13 (52.0)	8 (42.1)	2 (14.3)	0.027*
PO3	5 (20.0)	3 (15.8)	1 (7.1)	0.301

Note: Data represent number of the patients receiving antiemetic and their percentage in the parentheses. PO0, PO1, PO2, PO3; postoperative day zero, one, two and three, respectively. iv, intravenous. ivPCA, intravenous patient-controlled analgesia. epiPCA, epidural patient-controlled analgesia. *P<0.05.

Table 5 demonstrates the correlations of the patients' age, sex, BMI, degree of kinship, and surgical technique with the analgesia technique and postoperative pain scores. A negative correlation was observed between age and PO1 postoperative pain scores.

Table 5. Correlations of the patients' age, sex, BMI, degree of kinship, and surgical technique with the postoperative pain scores and postoperative rescue analgesic intake

	Analgesia technique	Postoperative pain scores			
		PO0	PO1	PO2	PO3
Age	0.140	-0.193	-0.277*	-0.160	-0.147
Sex	0.162	0.186	-0.195	0.107	-0.040
BMI	0.056	-0.030	-0.208	-0.141	-0.155
Degree of kinship	0.095	-0.069	0.109	-0.017	-0.026
Surgical technique	0.214	0.135	0.006	-0.063	0.102

Note: Data are represented as Pearson correlation coefficient. BMI, body mass index. PO0, PO1, PO2, PO3; postoperative day zero, one, two and three, respectively. *P<0.05.

DISCUSSION

This study investigated the efficacy of different analgesic techniques for postoperative pain relief in renal donor patients, and the factors affecting postoperative pain. The main finding of the study was that the patients with epidural PCA had better pain control after the operation. If we consider NRS of three as a threshold number for rescue analgesic application at the early postoperative period, three quarters of the patients in iv intermittent and about one third in the intravenous PCA groups had NRS scores above it at the 6th hour postoperatively. However, only 14% of the patients in the epidural PCA group had the pain scores above three at that time (see Table 2). This difference decreased at the 24th hour measurements and thereafter. The patients in the epidural PCA group did not receive any narcotics perioperatively. This can be advantageous in sparing the natural well-known side effects of the opioids, like nausea, vomiting, pruritus, urinary retention, bowel disfunction; but most importantly, sedation and respiratory depression.[12,13] Of these we only had the data of nausea of the patients, as metoclopramide was given "pro re nata" in these states, and the significantly lower number of antiemetic use in the epidural PCA group was concordant with that data.

Forty patients had laparoscopic operation, which comprised 69% of the nephrectomies. Minimally invasive laparoscopic donor nephrectomy was first introduced in 1995.[5] Since then many different minimally invasive approaches have evolved, like mini-incision muscle-splitting open technique; anterior vertical, posterior transcostal, transverse mini-incision technique; finger assisted technique, microinvasive technique; and video-assisted minilaparotomy.[4] Laparoscopic donor nephrectomy is a preferred method in many centers and even considered gold standard for donor nephrectomy.[14] It may be associated with

prolonged surgical times, especially in the early periods with unexperienced surgical team, but less pain, reduced narcotic use and so their side-effects, short hospital stay and early return to work are remarkable.[15] There is trend towards minimally invasive techniques, but this can be dangerous.[5] A recent article has stated that no deaths occurred since 1991 in open donor nephrectomies, but there have been several mortalities and graft losses after laparoscopic techniques.[16] We perform both techniques in our institution. Unfortunately, we had experienced one mortality; a 38-year-old female had serious postoperative hemorrhage and could not survive. This patient had also laparoscopic nephrectomy.

Left kidney is generally preferred because of anatomic reasons, but in the literature the percentage of left kidney preference varies between 45-94%.4 In our study all but two patients had left nephrectomy and so the left kidney preference was 97%.

The duration of surgery was significantly shorter in the group with epidural PCA, with the mean value of 170 minutes. Skin to skin time was reported between 117-180 minutes in the literature.[4] The duration of surgery in our study was comparable with the literature. The most plausible explanation for the shorter duration in the epidural PCA group was the trend in anesthesia towards neuraxial analgesic technique synchronously with the rising experience of the surgeons.

The consumption of rescue analgesics was higher in the intravenous intermittent analgesia group. Only few patients needed additional rescue analgesia in the PCA groups. Intermittent application of analgesics, especially "pro re nata" technique means that patients experience pain at certain intervals, and this condition is somewhat stressful, decreasing the quality of postoperative care. Uncontrolled postoperative pain may result in hemodynamic disturbances, psychological consequences. Many techniques are used for pain control in donor nephrectomy, like paracetamol, NSAIDs, opioids, epidural or neuraxial techniques, TAP block and local anesthetic infusions.[14,17-19] Yeap et al.[20] have used TAP block for postoperative analgesia in LDN and found a single injection TAP block with ropivacaine to be as effective as a catheter infusion. Erector spinae block have recently been demonstrated to provide good analgesia and reduce opioid consumption in LDN.[21] Gritsch et al.[22] have used quadratus lumborum block with liposomal bupivacaine for the pain management in laparoscopic LDN patients. The block was demonstrated to be a good adjunct for pain management in some patients with reduced opioid consumption in some patients. A recently described external oblique intercostal block may also be promising for pain control in LDN.[23] Deep neuromuscular blockade had been proposed as a method of reducing postoperative pain after laparoscopy.[24] Acetazolamide was also used to reduce pain after live donor nephrectomy.[11] There is no standard application to all the patients in our institution, and for the renal donor patients we use intravenous intermittent, intravenous PCA and epidural PCA analgesia. For all the groups we used meperidine 0.5 mg kg^{-1} for rescue analgesia. Nonsteroidal anti-inflammatory drugs are generally avoided in nephrectomy patients, because of their possible nephrotoxic effects, but they have good opioid sparing effects, and can be preferred for the treatment of postoperative pain for less than five days.[14] We do not prefer NSAIDs, considering their unwanted effects on gastrointestinal, hematologic systems, and kidneys, as well. In our study patients in the intravenous intermittent analgesic group needed more rescue meperidine, and this result emphasizes the importance of PCA systems in the pain management of live donor nephrectomy patients.

In this study we also measured the effect of the degree of kinship on postoperative pain. The patients can donate their kidney up to the 4^{th} degree relatives in our country, due to ethical and legal concerns. Most of the donations in our country is from first degree relatives, i.e. parents, siblings, children or spouses. We had 42 first degree relatives (parents, siblings, children, and spouses), which comprised 72% of all the donors. These findings are compatible with the literature.[25] We had two-sided H1 hypotheses at the beginning of the study; either less or more pain in the first-degree relatives. More pain in first degree relative donors could be explained by the added effects of their own perioperative physiological disturbances and the psychological effect of the recipient's condition. Lee et al.[25] have demonstrated a close relationship between trait anxiety and postoperative pain in liver donors. Non-drug therapies have been suggested to be added to the routine pain protocols after surgery.[26,27] On the other hand, the contrary could be the matter, and this may have been explained by the motivational effects of self-devotion of the donors to the people they appreciate. In our study no difference was observed between the groups regarding the degree of kinship. It is early to make solid judgement about the above-mentioned effects on postoperative pain and this needs validation by randomized controlled trials.

Limitations

The study had some limitations, firstly being retrospective in nature. Secondly, the treatment protocols in the intermittent iv analgesia group were not standardized, with patients having analgesics bis- ter- or quater in die, and sometimes as "pro re nata".

CONCLUSION

Epidural PCA has provided better postoperative pain control after live donor nephrectomy compared with intravenous intermittent and intravenous PCA. This effect was observed both for open and laparoscopic surgeries. Use of epidural PCA also resulted in less antiemetic use after the surgery. The degree of kinship was not related with postoperative pain scores. The hypothesis that we put forward regarding different postoperative pain scores in different degrees of relationship between donor and recipient can be studied in a larger population, with the inclusion of perioperative anxiety scales.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Marmara University Faculty of Medicine Clinical Researches Ethics Committee (Date: 03.01.2020, Decision No: 09.2020.127).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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