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Canlı Donör Hepatektomide Epidural Analjezinin Avantajı, Retrospektif Kohort Çalışma

Advantage of Epidural Analgesia in Living Donor Hepatectomy, a Retrospective Cohort Study

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ÖZ

Giriş: Canlı karaciğer donörü hastalarında postoperatif ağrının kontrolü hem hasta konforu hem de morbiditenin azaltılması açısından son derece önemlidir. Bu retrospektif kohort çalışmamızın amacı canlı karaciğer vericisi hastalarında intravenöz (IV) ve epidural temelli analjezi yöntemlerini hastaların postoperatif ağrı düzeyleri, analjezik ve antiemetik tüketimi açısından karşılaştırmaktı.

Yöntem: Etik kurul onayı alındıktan sonra kliniğimizde yedi yıllık süre içinde alınan karaciğer transplantasyon vericisinin verileri incelenmiştir. Hastaların demografik verileri, cerrahi ve klinik özellikleri, postoperatif ağrı skorları, analjezik ve antiemetik tüketimleri kayıtlardan ve dosyalardan elde edildi. Hastalar intravenöz ve epidural temelli analjezi yöntemi kullanımına göre sınıflandırılmış olup, demografik ve klinik özellikleri, intraoperatif opioid tüketimleri, postoperatif ağrı skorları, postoperatif analjezik ve antiemetik kullanım miktarları karşılaştırıldı. Verilerin incelenmesinde SPSS yazılımı kullanıldı.

Bulgular: Toplamda 28 hastanın verisi elde edilmiş olup, bunlardan beşi IV grupta, 23'ü ise epidural gruptaydı. Perioperatif opioid tüketimi IV grupta anlamlı olarak daha yüksekti (P = 0,009). Epidural grupta daha düşük postoperatif ağrı skorları eğilimi vardı. Postoperatif ikinci günde kurtarıcı analjezik kullanımı IV grupta anlamlı olarak daha yüksekti (P <0,041).

Sonuç: Canlı karaciğer vericisi hastalarında postoperatif ağrı kontrolü epidural analjezi ile daha iyi sağlanmaktadır. Epidural analjezi uygulanan hastalarda daha düşük intraoperatif opioid tüketimi, daha düşük postoperatif ağrı skorları, postoperatif ikinci günde daha az kurtarıcı analjezik tüketimi eğilimi olmaktadır.

Anahtar Kelimeler: hasta kontrollü analjezi, HKA, intravenöz, karaciğer, postoperatif ağrı

ABSTRACT

Objective: Control of postoperative pain in live liver donor patients is extremely important in terms of both patient comfort and reducing morbidity. The aim of this retrospective cohort study was to compare intravenous (IV) and epidural-based analgesia methods in live liver donor patients in terms of postoperative pain levels, analgesic, and antiemetic consumption.

Method: After ethics committee approval, the data of the liver transplantation donors obtained within a period of seven years in our clinic were examined. Demographic data, surgical and clinical characteristics, postoperative pain scores, analgesic and antiemetic consumption of the patients were obtained from the records and files. The patients were classified according to the use of intravenous and epidural-based analgesia methods, and their demographic and clinical characteristics, intraoperative opioid consumptions, postoperative pain scores, postoperative analgesic and antiemetic use amounts were compared. SPSS software was used to analyze the data.

Results: A total of 28 patients' data were obtained, five of which were in the IV group and 23 in the epidural group. Perioperative opioid consumption was significantly higher in the IV group (P = 0.009). There was a trend for lower postoperative pain scores in the epidural group. Rescue analgesic use on the second postoperative day was significantly higher in the IV group (P <0.041).

Conclusion: Postoperative pain control is better with epidural analgesia in live liver donor patients. Patients with epidural analgesia have lower intraoperative opioid consumption, tend to have lower postoperative pain scores, and less rescue analgesic consumption on the second postoperative day.

Keywords: patient-controlled analgesia, PCA, intravenous, liver, postoperative pain

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INTRODUCTION

Living liver donation has become a good option for liver transplantation. Especially in developing countries, living liver donation is an important source for liver transplantation due to the shortage of cadaveric donors. Living donation has advantages such as elective planning of the procedure, optimization of the recipient and shorter ischemia time. However, this procedure is not without risk and is associated with significant patient morbidity and even mortality (1,2). Improvements in both surgical and anesthetic techniques have made living liver transplantation safe (3,4). Nevertheless, postoperative pain remains a leading cause of morbidity. The source of pain in these patients may be subcostal incision, rib retraction, diaphragm irritation and visceral in origin (5).

Opioids have often been preferred for donor analgesia after living liver transplantation because they are a good option for the control of moderate to severe postoperative pain. Intravenous patient-controlled analgesia with opioids (IV-PCA) has become the standard for postoperative pain control in many centers. However, the lack of effect of this method on pain caused by movement and the side effects of opioids such as nausea, vomiting, sedation, pruritus, constipation, urinary retention, and most importantly respiratory depression have been the reasons limiting the use of IV-PCA. Epidural analgesia has become a good alternative for the control of postoperative pain and has been found superior to IV-PCA in many surgical groups due to its efficacy and low side effect profile (3,6). The effects of thoracic epidural anesthesia on the cardiovascular, respiratory, and gastrointestinal systems are well known (7). Many studies have shown that epidural analgesia provides better analgesia for up to 72 hours postoperatively after intraabdominal surgery compared with IV-PCA, is associated with lower opioid consumption, less pulmonary complications, earlier return of bowel function, shorter hospital stay and higher quality of life (8,9,10).

The aim of this retrospective cohort study was to compare postoperative intravenous (IV) or epidural-based analgesia methods in living liver donor patients in terms of postoperative pain levels, analgesic, and antiemetic consumption.

MATERIALS AND METHODS

This retrospective study was approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee (Protocol No: 09.2021.295, Date: 05.03.2021). For the study, postoperative pain scores, analgesic consumption and side effects of liver transplant donors operated in our clinic between 2014 and 2021 were analyzed. Our clinic is a center that had actively performed liver transplantation from living donors until 2021. The data of 28 patients over a seven-year period were obtained from hospital electronic records and files. For postoperative pain control, three patients had IV intermittent, two had IV-PCA, and the remaining 23 had epidural patient-controlled analgesia (EPI-PCA). Patients were routinely evaluated by the surgeon and referred to the anesthesiologist. In the anesthesia evaluation, in addition to the patient's preparation for surgery, the epidural or IV-PCA plan was formulated based on a risk/benefit assessment.

Perioperative pain management for living donor hepatectomy was determined by a standardized protocol. Patients scheduled for thoracic epidural had an epidural catheter inserted in a sitting position before induction of anesthesia. The epidural catheter was inserted at the 7th and 11th thoracic vertebral levels (T7-T11) after reviewing the patient's computed tomography (CT) images. A test dose of 3 mL 1.5% lidocaine and 15 µg adrenaline was administered to exclude intrathecal and intravascular placement.

In addition to electrocardiography (ECG), peripheral oxygen saturation (SpO_2) and noninvasive blood pressure monitoring, a radial artery catheter, internal jugular vein catheter and urinary catheter were inserted. After induction with propofol, remifentanil and nondepolarizing muscle relaxant, volatile-narcotic based anesthesia maintenance was provided. Patients whose postoperative analgesia plan was IV intermittent or IV-PCA were given intraoperative opioid infusion in the amount determined by the patient's primary anesthesiologist. Generally, remifentanil was used as an IV infusion in the range of 0.1-0.5 µg kg^{-1} min^{-1}. The use of epidural infusion intraoperatively has become standard in our clinic because it reduces central venous pressure and therefore reduces surgical blood loss. Epidural infusion is usually started within the first hour of surgery, and after a loading dose of 10 mL of 0.15% bupivacaine and 50 µg fentanyl, a standard basal dose of EPI-PCA infusion is continued. This protocol was applied to our patients. All patients received intraoperative acetaminophen 1 g IV and ondansetron 4 mg IV as antiemetic.

At the end of surgery, patients were transferred to the Intensive Care Unit (ICU) and continued with one of three postoperative analgesia techniques. Patients using intravenous patient-controlled analgesia (IV-PCA) received a standardized protocol dose of 1 mg mL^{-1} morphine solution (no infusion, 1 mL bolus, 10 min lockout time, 30 mL 4 h limit), and tramadol 1 mg kg-1 IV if needed. Patients using epidural patient-controlled analgesia (EPI-PCA) also received a standardized protocol dose of 0.125% bupivacaine and 3 µg mL-1 fentanyl solution (4 mL h^{-1} infusion, 5 mL bolus, 20 min lockout time). All patients received acetaminophen 1 g IV every 6 hours. Nonsteroidal anti-inflammatory drugs were not preferred. Tramadol dose was recorded as morphine equivalent for ease of evaluation (10 mg tramadol = 1 mg morphine equivalent).

Patient demographic data, postoperative pain scores (Numeric Rating Scale), postoperative analgesia method, and the amount of additional analgesic needed were recorded. Numeric Rating Scale (NRS) was evaluated from "0" (no pain) to "10" (most severe imaginable pain). The pain was also classified into mild (NRS 1-3), moderate (NRS 4-6) and severe (NRS 7-10). Duration of operation, surgical side, and antiemetic use were also recorded.

Statistical Package for the Social Sciences was used for statistical analysis (SPSS 27.0, IBM, USA). Data were presented as frequency, percentage, mean and standard deviation. Normal distribution was evaluated by Shapiro-Wilk test. Categorical variables were analyzed by Chi-Square test. In addition to complementary statistical methods, Independent Sample t-test was used for group comparisons of variables with normal distribution and Mann Whitney U test was used for group comparisons of variables without normal distribution. $P < 0.05$ was considered statistically significant.

RESULTS

Demographic and clinical characteristics of the patients are presented in Table 1. There were no significant differences between the groups in terms of demographic characteristics, body mass index (BMI), degree of consanguinity, surgical site, and duration of operation. Perioperative IV opioid consumption was significantly higher in the IV group (P = 0.009).

Table 1. Demographic and Clinical Characteristics of the Patients.

		IV and IV-PCA Group (n = 5)	EPI-PCA Group (n = 23)	P
Sex	Male	5 (%25,0)	15 (%75,0)	0,281
	Female	-	8 (%100,0)	
Age (year)		35,2 ± 9,9	28,9 ± 9,5	0,149
BMI	Normal	3 (%18,8)	13 (%81,2)	0,999
	High	2 (%16,7)	10 (%83,3)	
Degree of kinship	Mother/ father	3 (%60,0)	2 (%40,0)	-
	Sister/ brother	2 (%12,5)	14 (%87,5)	
	Other	-	7 (%100,0)	
Surgical side	Left	5 (%20,8)	19 (%79,2)	0,999
	Right	-	4 (%100,0)	
Operation duration (minutes)		385,0 ± 70,3	433,5 ± 57,4	0,133
Perioperative IV opioid (mg ME)		7,0 ± 3,1	2,4 ± 2,5	0,009*

Note: Categorical data are presented as number (percentage). Continuous data are presented as mean ± standard deviation. *P <0.05 IV, intravenous; IV-PCA, intravenous patient-controlled analgesia; EPI-PCA, epidural patient-controlled analgesia; BMI, body mass index; ME, morphine equivalents.

The postoperative pain severity scores of the patients are presented in Table 2. Statistical comparison could not be made due to the paucity of data. However, moderate pain was observed in 80% of the IV group and approximately 50% of the epidural group in the first two postoperative days. It is noteworthy that pain scores decreased in both groups in the following days.

The postoperative rescue analgesic use of the patients is presented in Table 3. There was no significant difference between the groups except on PO2 day when the use of rescue analgesics was significantly higher in the IV group, (P = 0.041).

Postoperative antiemetic use of the patients is shown in Table 4. There was no significant difference between the groups in terms of antiemetic use.

Table 2. Postoperative Pain Intensity of the Patients.

Postoperative day	Pain intensity	IV and IV-PCA Group (n = 5)	EPI-PCA Group (n = 23)
PO0	None	-	-
	Mild	1 (%20,0)	11 (%47,8)
	Moderate	4 (%80,0)	12 (%52,2)
PO1	None	-	1 (%4,3)
	Mild	1 (%20,0)	11 (%47,8)
	Moderate	4 (%80,0)	11 (%47,8)
PO2	None	-	1 (%4,3)
	Mild	4 (%80,0)	12 (%52,2)
	Moderate	1 (%20,0)	10 (%43,5)
PO3	None	-	2 (%8,7)
	Mild	3 (%60,0)	16 (%69,6)
	Moderate	2 (%40,0)	5 (%21,7)
PO4	None	-	5 (%21,7)
	Mild	4 (%80,0)	16 (%69,6)
	Moderate	1 (%20,0)	2 (%8,7)
PO5	None	1 (%20,0)	12 (%52,2)
	Mild	4 (%80,0)	9 (%39,1)
	Moderate	-	2 (%8,7)

Note: Data are presented as number (percentage). IV, intravenous; IV-PCA, intravenous patient-controlled analgesia; EPI-PCA, epidural patient-controlled analgesia; PO0, PO1, PO2, PO3, PO4, PO5, postoperative days 0-5.

Table 3. Postoperative Rescue Analgesic Use of the Patients.

Postoperative day	IV and IV-PCA Group (n = 5)	EPI-PCA Group (n = 23)	P
PO0	2 (%40,0)	2 (%8,7)	0,135
PO1	1 (%20,0)	3 (%13,0)	0,999
PO2	4 (%80,0)	6 (%26,1)	0,041*
PO3	2 (%40,0)	1 (%4,3)	0,073
PO4	2 (%40,0)	1 (%4,3)	0,073

Note: Data are presented as number (percentage).*P <0,05. IV, intravenous;IV-PCA, intravenous patient-controlled analgesia; EPI-PCA, epidural patient-controlled analgesia;
PO0, PO1, PO2, PO3, PO4, PO5, postoperative days 0-4.

Table 4. Postoperative Antiemetic Use of the Patients.

Postoperative day	IV and IV-PCA Group (n = 5)	EPI-PCA Group (n = 23)	P
PO0	4 (%80,0)	21 (%91,3)	0,459
PO1	2 (%40,0)	18 (%78,3)	0,123
PO2	2 (%40,0)	16 (%69,6)	0,315
PO3	1 (%20,0)	12 (%52,2)	0,333
PO4	3 (%60,0)	13 (%56,5)	0,999
PO5	1 (%20,0)	3 (%13,0)	0,999

Note: Data are presented as number (percentage). IV, intravenous; IV-PCA, intravenous patient-controlled analgesia; EPI-PCA, epidural patient-controlled analgesia; PO0, PO1, PO2, PO3, PO4, PO5, postoperative days 0-5.

DISCUSSION

In this study, we compared postoperative intravenous or epidural-based analgesia methods in living liver donor patients in terms of postoperative pain levels, opioid consumption, and nausea. The main objective of our study was that perioperative morphine consumption was lower in the epidural analgesia group. In addition, postoperative pain scores tended to be lower in the epidural analgesia group.

Aydogan et al. compared IV morphine and EPI-PCA with morphine for the control of postoperative pain in patients with living liver donors (11). In their study, they observed lower pain scores and less morphine consumption in the 12th and 24th hours postoperatively with epidural analgesia compared with IV. In our study, moderate pain was observed in 80% of the IV group and approximately 50% of the epidural group in the first two postoperative days and these results were consistent with those of Aydogan et al. Due to the small sample size, a comparison test between the two groups was not performed and descriptive statistics are presented. Epidural analgesia not only controls pain effectively but also improves respiratory functions (12). In their study, Atalan et al. observed more effective analgesia as well as lower atelectasis scores and preserved pulmonary function tests in living liver donor patients who received epidural analgesia (13). These results are associated with lower intensive care unit length of stay and probably lower incidence of pneumonia (12,13).

Opioid-related hyperalgesia is an important cause of postoperative pain.Reducing intraoperative high-dose opioid consumption or administering anesthesia without opioids are appropriate strategies to prevent this condition, for which remifentanil is particularly blamed. Tseng et al. administered intraoperative dexmedetomidine infusion to living liver donor patients and observed less intraoperative opioid consumption, more effective pain control in the first 24 hours, and less opioid consumption in the 24th and 48th hours in these patients compared to the control group (14).

In our study, intraoperative morphine consumption was less in the epidural group. Since we routinely perform epidural drug loading at the beginning of surgery, this provides both effective analgesia and reduces intraoperative IV opioid consumption. When we looked at postoperative rescue analgesic use, patients in the epidural group used less medication than the IV group on the second postoperative day (P = 0.041). On the other days, patients in the epidural group tended to use less rescue analgesics, but we could not reach a statistically significant conclusion, probably due to the small sample size.

Abdominal wall catheters, transversus abdominis plane, erector spinae block have also been used to provide analgesia for living liver donors. Khan et al. used local anesthetic infusion via abdominal wall catheter for pain control after living liver donation (15). Although it was not as effective as epidural analgesia in relieving pain, they observed less pruritus, less sedation and shorter hospitalization period. Kıtlık et al. showed in their study that transversus abdominis plane block effectively reduced pain scores and morphine consumption in the first 24 hours after live liver donation (16). In their study, no difference was observed in the frequency of nausea compared with the control group. Continuous erector spinae block was also used for postoperative analgesia. Adelman et al. observed lower opioid consumption in their study in which bilateral continuous erector spinae block was used for pain control after hepatectomy (17). Again, Kang et al. compared bilateral continuous erector spinae block with intrathecal morphine for analgesia after laparoscopic hepatectomy (18). In their study, it was shown that erector spinae block was associated with similar opioid consumption but lower pain scores, lower nausea-vomiting and pruritus compared with intrathecal morphine. In our study, when we looked at the frequency of postoperative antiemetic consumption, no difference was observed between the intravenous and epidural groups in terms of postoperative nausea-vomiting.

Our study had some limitations. First, our study was a retrospective study and data were obtained from patient files and electronic records. Secondly, the sample size was small. We were able to collect data from 28 cases over a seven-year period. This is sufficient time to allow for changes in both anesthesia practice and surgical techniques. Moreover, the number of cases in the İV treatment group was very small. This was not a surprise because epidural analgesia is usually preferred for pain control in this surgery unless there are contraindications. This precluded us to perform an adequate comparison between the two groups (lV and epidural) regarding the pain scores. Finally, other side effects of opioids have not been evaluated. Since only nausea and vomiting were tracked in the patient registry files, information on other side effects could not be obtained. In such studies, obtaining other opioid-related side effects such as constipation, urinary retention, pruritus, and respiratory depression may also provide valuable information.

CONCLUSİON

Epidural analgesia provides better postoperative pain control in living liver donor patients. Patients with epidural analgesia have lower intraoperative opioid consumption, lower postoperative pain scores, and

less rescue analgesic consumption on the second postoperative day. Although it reduces perioperative opioid consumption, epidural analgesia has not been shown to be more advantageous in terms of nausea and vomiting.

Highlight Key Points:

• Pain control in living donor hepatectomy can be provided with intravenous intermittent, intravenous patient-controlled analgesia (IV-PCA) or epidural patient-controlled analgesia (EPI-PCA).

• Epidural analgesia provided better postoperative pain control in living liver donor patients.

• Patients with epidural analgesia have lower intraoperative opioid consumption, lower postoperative pain scores, and can have less rescue analgesic consumption.

Ethics Committee Approval: Marmara University Faculty of Medicine Clinical Research Ethics Committee (Issue:05.03.2021-09.2021/295 number)

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Conflict of Interest: None

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Informed Consent: As this is a retrospective study there is no informed consent.

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