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Comparison of effects of epidural bupivacaine and intravenous meperidine analgesia on patient recovery following elective abdominal aortic surgery

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Background: The efficacy of epidural anesthesia and analgesia in management of perioperative stress has been established. Perioperative pain management strategies decrease surgical complications and aid recovery. In this study, we aimed to document and compare the efficacy of epidural bupivacaine and intravenous meperidine on recovery of patients with elective abdominal aortic surgery performed under general anesthesia.

Material/Methods: Patients undergoing elective abdominal aortic surgery between February 2009 and November 2011 were studied prospectively. Patients were randomized into epidural bupivacaine (n=40) and intravenous meperidine (n=40) groups regarding postoperative analgesia strategy. The preoperative demographic characteristics, perioperative outcomes, postoperative adverse effects of analgesia strategy, time to initiate oral intake, sedation scores, visual analogue scale results, and mobility scores were compared.

Results: The mean ages of the patients were 61.7±8.1 in the epidural group and 59.4±9.7 in the intravenous group ($p>0.05$). The preoperative demographic characteristics of the patients were comparable between the groups. There were no statistically significant differences between groups regarding anesthesia times, intubation times, intensive care unit stay, hospital length of stay, postoperative vomiting, and postoperative cardiac, renal, and cerebral complications. Postoperative nausea was more prevalent in the meperidine group ($p<0.05$). In the epidural group, time to begin oral intake was shorter, sedation scores and visual analogue scale results were lower, and mobility scores were higher ($p<0.05$ each).

Conclusions: Epidural analgesia allowed earlier recovery compared to intravenous analgesia in patients undergoing elective abdominal aortic surgery, but did not affect postoperative outcomes and complications.

Key words: anesthesia • epidural • bupivacaine • meperidine • aortic aneurysm • abdominal • peripheral arterial disease • surgical procedures • operative

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Background

In patients undergoing surgery, multiple factors have been reported to affect postoperative recovery and discharge condition of the patient. Despite advances in anesthesia, surgery, and postoperative care, the adverse effects of postoperative pain on recovery could not be prevented. In recent years, a 'stress-free anesthesia and surgery' strategy has been developed to avoid these adverse effects and to decrease surgical morbidity and mortality [1]. Efforts to decrease postoperative stress by means of postoperative pain management are employed to prevent catabolic state and organ dysfunction caused by endocrine-metabolic and inflammatory mediators [2].

Studies aiming to decrease surgical stress have documented the importance of anesthesia strategy. Epidural anesthesia and analgesia were reported to be very effective in decreasing perioperative surgical stress and surgical complications, and improving recovery [3,4].

In this prospective study, we aimed to compare the effects of epidural bupivacaine and intravenous meperidine on quality of recovery and postoperative outcomes in patients undergoing elective abdominal aortic surgery with general anesthesia for abdominal aortic aneurysm (AAA) repair or aortoiliac occlusive disease.

Material and Methods

The study followed the Declaration of Helsinki on medical protocol and was approved by the Institutional Medical Ethics Committee. Written informed consent was obtained from every patient.

Due to strict policies of the health insurance agencies in Turkey, in AAAs, endovascular repair procedures are only allowed in patients with severe comorbidities. In this study, patients with AAA eligible for endovascular repair were not included. American Society of Anesthesiology patient classification status II and III patients who underwent elective abdominal aortic surgery for either AAA repair or aortoiliac occlusive disease between February 2009 and November 2011 were included in the study.

Patients with contraindications for epidural anesthesia, abnormal coagulation tests (international normalized ratio >1.5, partial thromboplastin time >45 s and platelet count <80.000/mm^3), use of thrombolytic or potent antiplatelet agents within 1 week prior to surgery, and patients with cardiac ischemic changes on ECG were excluded from the study. In total, 80 patients were included in the study. The patients were then randomized as follows: each patient was given a number according to chronological order beginning from 1. Intravenous analgesia with meperidine was used in odd numbered patients (n=40), and epidural analgesia with bupivacaine was used in even numbered patients (n=40).

All patients were administered 10 mg diazepam (PO) prior to the night before surgery and 0.05 mg/kg (IV) midazolam on the day of surgery. The epidural anesthesia was performed in the operating room on the day of surgery, prior to anesthesia induction. Epidural anesthesia was performed with an 18 G Tuohy needle (Espocan®+Docking System+Perifix® Soft Tip, B. Braun Melsungen AG, D-34209 Melsungen, Germany) with median approach from L2-3 or L3-4 space, and hanging drop technique was used. Three ml of 1% lidocaine was tested through the epidural catheter. In 1 patient, we failed to insert the catheter due to anatomical considerations and the patient was excluded from the study. The epidural catheter was removed after 72 hours.

The anesthesia was inducted with etomidate 0.2 mg/kg, vecuronium 0.1 mg/kg, and fentanyl 0.1 mg/kg. Maintenance was done with 1 MAC isoflurane (Primus, Drager), 50% oxygen, and remifentanil (1 µg/kg bolus followed by 0.5 µg/kg infusion). All patients were monitored with electrocardiography, invasive blood pressure monitorization by radial artery catheterization, central venous pressure monitorization by internal jugular venous catheterization, oximetry, urine output, capnography, and bispectral index. A nasogastric tube was inserted after intubation.

Operative strategy

Transperitoneal approach was performed in every patient. Aortic graft interposition procedure was performed in AAA cases. In cases with aortoiliac occlusive disease, bilateral groin incisions were made for exploring femoral arteries, and aorto-bifemoral bypass procedure was performed. Dacron vascular grafts were used in every patient. A postoperative drain was not inserted into the retroperitoneal area.

Postoperative analgesia

In the intravenous group, for patient-controlled analgesia (PCA) (Abbott Pain Management Provider™ Abbott Laboratories, North Chicago, IL, 60064, USA), a solution of meperidine (Aldolan®, Liba Ilac Laboratuvarları A.S, Istanbul, Turkey) with a concentration of 5 mg/ml was prepared; lock-out was set as 10 minutes, and loading and infusion doses were set as 0.1ml/kg. In the epidural group, PCA was maintained as follows: a solution of bupivacaine (Marcaine®, Astra-Zeneca Ilac Sanayi, Istanbul, Turkey) with a concentration of 1.25 mg/ml was prepared; lock-out was set as 20 minutes, and loading and infusion doses were set as 0.1 ml/kg. In both groups, patients were given bolus doses at the end of surgery and taken to the intensive

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Table 1. Preoperative demographic characteristics of patients.

	Intravenous group (n: 40)	Epidural group (n: 40)	p value*
	Mean ±SD	Mean ±SD	
Age (years)	59.4±9.7	61.7±8.1	0.266
Weight (kg)	78.3±12.0	76.1±14.6	0.465
Height (cm)	169.7±6.4	170.1±5.8	0.814
	n (%)	n (%)	p value**
Male gender	39 (97.5)	38 (95.0)	1.000
Diabetes Mellitus	15 (37.5)	15 (37.5)	1.000
Hypertension	22 (55)	17 (42.5)	0.263
Coronary artery disease	10 (25)	10 (25)	1.000
COPD	6 (15)	7 (17.5)	0.762
Stroke	4 (10)	1 (2.5)	0.359***
Dyslipidemia	13 (32.5)	7 (17.5)	0.121
Smoking	36 (90)	33 (82.5)	0.330
Alcohol use	6 (15)	3 (7.5)	0.481

* Independent samples t-test; ** chi-square test; *** Fisher's exact test. COPD – chronic obstructive pulmonary disease.

care unit (ICU), and PCA was initiated and continued for 3 days. Patients were sedated with 5 mg/kg/hour propofol until extubation, and 500 mg acetaminophen 3 times a day was administered for 3 days. After cessation of PCA in both groups, 500 mg of acetaminophen was administered if required.

Extubation criteria were: ability to respond to verbal stimuli, body temperature >36.5°C, PO2 >70 mm Hg, PCO2 <50 mm Hg, and rate of respiration <20/min or pressure-aided ventilation <10 cm H_2O and stable hemodynamics.

All patients were mobile on postoperative day 1, all had mobility scores over or equal to 6 and all recordings within the first 3 postoperative days were noted. Mobility scores were graded as: 0, not able to move; 1, able to sit in bed; 2, able to stand in bed; 3, able to walk 25 m; 4, able to walk 50 m; 5, able to walk 75 m; 6, able to walk more than 100 m; 7, able to walk more than 100 m and able to climb 1 flight of stairs; and 8, able to walk more than 100 m and able to climb 2 flights of stairs [5].

In the first 3 postoperative days, pain was monitored using the visual analogue scale (VAS) [6,7] and sedation was monitored by a 4-point sedation scale [8]. The 4-point sedation scale was graded as 0: fully awake, 1: mild sedation (drowsy, but easily awakened), 2: moderate sedation (mostly sleepy, but easily awakened), 3: severe sedation (somnolence, awakened with difficulty).

Oral intake was initiated based on physical examination findings. When passage of flatus was observed and bowel motility was evaluated as satisfactory by the physician, the nasogastric tube was removed. Oral intake was initiated with fluids and progressively solid diet was given.

Discharge criteria were: hemodynamic stability without arrhythmia, freely mobile and able to eat without any help, absence of fever and clinical manifestations of infection, normal urination and defecation, analgesia maintained with or without analgesics, able to walk more than 100 meters, able to climb more than 2 flights of stairs, and normal mental state.

Statistical analysis

Statistical analyses were performed using SPSS software for Windows version 17.0 (Statistical Package for the Social Sciences Inc, Chicago, IL, USA). Continuous variables were expressed as 'mean values ± standard deviation (SD)'. Categorical variables were expressed as number and percentages. Demographic characteristics and outcomes of the groups were compared using independent samples t-test for continuous variables, and, chi-square test and Fisher's exact test for categorical variables. Statistical significance was set as $p<0.05$.

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Table 2. Intraoperative variables and postoperative outcomes of patients.

	Intravenous group (n: 40)	Epidural group (n: 40)	p value*
	Mean ±SD	Mean ±SD	
Anesthesia time (min)	214.5±57.4	235.5±56.2	0.103
Intubation time (min)	234.5±145.1	254.0±130.8	0.530
ICU stay (hours)	20.0±3.9	21.9±9.5	0.256
Hospital length of stay (days)	6.7±2.2	7.0±2.4	0.604
Time to begin oral intake (days)	1.9±0.9	1.5±0.7	0.045
1st day sedation score	1.9±0.4	0.1±0.3	<0.001
2nd day sedation score	1.5±0.5	0	<0.001
3rd day sedation score	0.8±1.0	0	<0.001
1st day VAS	3.7±1.0	0.3±0.7	<0.001
2nd day VAS	3.4±0.9	0.2±0.6	<0.001
3rd day VAS	2.2±1.1	0.1±0.3	<0.001
	n (%)	n (%)	p value**
Nausea (%)	7 (17.5)	–	0.012
Vomiting (%)	1 (2.5)	–	1.000
Myocardial infarction	2 (5)	2 (5)	1.000
Renal failure***	3 (7.5)	2 (5)	1.000
Stroke	–	–	

* Independent samples t-test; ** Fisher's exact test; *** defined when peak creatinine value was 1.5 or greater times the preoperative value. ICU – intensive care unit; VAS – visual analogue scale.

Results

Eighty patients were included in the study; 40 were administered epidural bupivacaine (epidural group) and 40 were administered intravenous meperidine (intravenous group) PCA. The mean age of the patients was 61.7±8.1 in the epidural group and 59.4±9.7 in the intravenous group (p>0.05). The male: female ratio was 39: 1 in the epidural group and 38: 2 in the intravenous group (p>0.05). The preoperative demographic characteristics of the patients are shown in Table 1.

When intraoperative variables and postoperative outcomes were compared, anesthesia time, intubation time, ICU stay, hospital length of stay, and postoperative vomiting prevalence were similar between the groups. Postoperative myocardial infarction, renal failure, and stroke rates were not different between the groups. Postoperative nausea was more common in the intravenous group. In the epidural group, time to begin oral intake was shorter, mobility scores were higher, and sedation scores and VAS were lower during the first three postoperative days (p<0.05 each) (Table 2).

No complications related with epidural protocol (e.g., hematoma formation or infection) were observed during the study period. No mortality was observed during the study period.

Discussion

Postoperative pain is one of the most important factors increasing surgical stress. It causes endocrine-metabolic response, stimulates autonomic reflex, leads to nausea and ileus, and increases muscular spasm [9,10]. These responses lead to delayed recovery [9]. Even basic analgesic strategies improve recovery and decrease morbidity [11]. Thus, the search for a potent agent or strategy with minimal adverse effects has emerged.

Epidural anesthesia is defined as an acceptable method for postoperative pain management in patients undergoing abdominal surgery. It allows avoidance of systemic opioids and provides effective analgesia. Lower complication rates, reduced hospital stay, and decreased hospital costs have been

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reported with epidural analgesia, but there are controversial results regarding operative outcomes. The results do not appreciably differ in different abdominal surgical procedures [12].

In abdominal aortic surgical procedures, the use of epidural analgesia provided better pain relief, particularly in mobile patients in the first 3 postoperative, days when compared to systemic opioids. The occurrence of prolonged intubation, and cardiac, renal, and gastrointestinal complications were lower, but this strategy did not affect postoperative mortality [13]. In the Veterans Affairs Cooperative Study, the results of epidural analgesia and intravenous opioid analgesia were compared in patients undergoing abdominal surgery. They concluded that, following abdominal aortic surgery, the incidence of myocardial infarction, stroke, respiratory failure, and death was lower in the epidural analgesia group, and that epidural strategy provided better pain relief [3]. Conversely, Norris et al. [9] designed a randomized controlled trial comparing postoperative intravenous analgesia and epidural analgesia in abdominal aortic surgery. They documented no significant difference regarding pain relief (evaluated by VAS) and postoperative outcomes. Yie et al. [14] quantified pain relief by VAS in thoracoscopic lobectomy and found no difference between the epidural and intravenous groups. In our study, we demonstrated that epidural analgesia was more efficient in pain relief due to lower VAS results, but the intubation times, ICU stay, and rates of occurrence of postoperative myocardial infarction, renal failure, and stroke were not different between groups.

Following abdominal surgery, restoration of gastrointestinal functions as early as possible is one of the main objectives of postoperative recovery [15]. Postoperative ileus is the major determinant of gastrointestinal functions and is one of the most important perioperative complications after abdominal aortic surgery [15,16]; together with postoperative nausea and vomiting, it is the most common factor causing patient discomfort and delaying rehabilitation. The etiology for postoperative ileus, nausea, and vomiting is multifactorial. Surgical stress response and inhibitory neural reflexes play major roles in the pathophysiology. Early oral intake and nutrition, early mobility, and epidural anesthesia may prevent these complications and improve recovery. But, controversial results have been published regarding early oral intake [15]. In a randomized clinical trial, Han-Geurts et al [15] reported that early oral intake does not decrease the duration of postoperative ileus following abdominal surgery.

It was reported that opioids have no effect on surgical stress response and have inhibitory effects on gastrointestinal system [17]. Therefore, substitution of opioids with local anesthetics and non-steroidal anti-inflammatory agents, and use of epidural analgesia strategies are suggested to attenuate these complications [11]. In our study, we also documented that epidural strategy allowed earlier oral intake. Nausea was less prevalent than in the intravenous meperidine group, but vomiting incidence was not different.

Postoperative pain prevents patient mobility following surgery, which also contributes to occurrence of postoperative ileus and thromboembolic complications. The most effective strategy in initiation of early mobility is efficient analgesia. Opioids provide pain relief in the immobilized patient and fail to provide analgesia in a mobile patient, whereas epidural analgesia provides efficient pain relief in the mobile patient [11]. However, Kehlet et al. [18], in their review, reported that epidural analgesia allowed earlier mobility in abdominal aortic procedures, but failed to prevent pulmonary and cardiac complications. On the other hand, Park et al. [3] in a randomized, controlled study, and Nishimori et al. [13] in a systematic review, documented decreased postoperative pulmonary and cardiac complications without documenting the relation with mobility. In our clinic we initiate early mobility in the morning of postoperative day 1. We documented that mobility scores were higher in the epidural group, which also shows that the epidural strategy is a better way of providing satisfactory analgesia in the mobile patient. Lower sedation scores in the epidural group also allowed earlier mobility. We hypothesized that by providing efficient analgesia and early mobility, we could prevent postoperative complications, but we failed to document this.

In our study, the mean length of hospital stay was 6.85 days when all patients were considered. This is much shorter than the length of stay in many published reports [3,11,15]. We believe this is explained by early mobility and nutrition protocols.

Occurrence of epidural catheter-related complications has been reported, such as epidural hematoma formation, local inflammation, or epidural abscess formation and neurological damage [19,20]. The anticoagulants used increase the risk of epidural hematoma formation, which may lead to spinal cord injury. In cardiac surgery, the dose of anticoagulants used is much higher than in vascular surgery, but even in those applications the incidence was reported to be 1/1528 cases with thoracal epidural interventions [21]. Shroeder et al. [22] documented an incidence of 1/6588 following epidural anesthesia in 112 000 patients with enoxaparin administration. Due to the German network for safety in regional anesthesia, the incidence was 1/6628 in the non-obstetric population [23]. The occurrence of infectious complications was reported to be more common with catheters removed after 4 days [19]. In our study, we did not encounter any complications related to the epidural catheter.

In our hospital, the patients with any abdominal aortic pathology, either in the epidural or intravenous group, are hospitalized

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on the day before the operation. Thus, the length of preoperative hospital stay is the same for each group, which does not provide additional cost benefit for the epidural group. Since the ICU and hospital length of stay of patients, and occurrence of major adverse events in both groups were comparable, no additional cost benefit was provided in any of the groups in our study.

Limitations

The study included patients with 2 different groups of pathologies: AAA and aortoiliac disease. The burden of peripheral arterial disease, which can affect postoperative pain depending on the extent of the disease, was not taken into account while evaluating the results.

Conclusions

Postoperative pain following abdominal aortic surgery is a major issue that causes patient discomfort and delays mobility and oral intake. Strategies for postoperative pain management will provide earlier mobility, nutrition, and improve recovery. Epidural analgesia allows earlier mobility and less sedation, but does not affect postoperative complication rates, intubation times, or ICU and hospital length of stay.

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