J Surg Med. 2019;3(7):485-489.
DOI: 10.28982/josam.574416

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

The effects of epidural bupivacaine administration for postoperative pain after major abdominal surgery

Majör abdominal cerrahide epidural bupivakain uygulamasının postoperatif ağrı üzerine etkileri

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Abstract

Aim: Postoperative pain is a major problem after major abdominal surgery and conventional intramuscular analgesic therapy is usually not enough. We investigated the effectiveness and timing of epidural patient control analgesia on intraoperative analgesic consumption and postoperative pain, after major abdominal surgery.

Methods: We studied 41 patients prospectively. This was a prospective cohort study. The patients, after ethics committee approval, who were planned to have major abdominal surgery, aged between 35 and 75, were included to the study. 37 patients' data were included to the study; because two patients were excluded because of motor block developed during research, and 2 patients were excluded because catheter tips were migrated from the epidural space. Epidural catheters were applied to all patients, at proper levels for the surgery, preoperatively. In the first group; bupivacaine infusion was administered postoperatively, via patient controlled analgesia (PCA) machine. In the second group 25 mg bupivacaine bolus was administered before surgery and bupivacaine infusion via PCA was administered at the postoperative period. In the third group 25 mg bupivacaine bolus was administered preoperatively and bupivacaine infusion was administered intra and postoperatively via PCA. Pain levels of the patients were evaluated by using numeric rating scale (NRS). In NRS, patients were asked to evaluate their pain levels between 0 to 10, as 0; no pain and 10 is the worst pain ever.

Results: In all groups postoperative NRS levels were below 4, and sufficient postoperative analgesia was provided. In the third group significant lower analgesia scores and lower intraoperative analgesic consumptions were achieved (P<0.05). In this group arterial blood pressures were lower than the other groups, but they were not lower than the physiologic limits.

Conclusion: Epidural bupivacaine administration is a safe and effective method for postoperative pain management for patients who will have major abdominal surgery.

Keywords: Epidural analgesia, Bupivacaine, Major abdominal surgery

Öz

Amaç: Majör abdominal cerrahi sonrası, postoperative analjezi önemli bir problemdir ve konvansiyonel intramüsküler analjezik tedavisi genellikle yetersizdir. Biz bu çalışmada, majör abdominal cerrahide, hasta kontrollü epidural analjezi uygulanım zamanının ve şeklinin, intraoperatif analjezik ihtiyacı ve postoperatif ağrı üzerine etkilerini araştırdık.

Yöntemler: 41 hasta prospektif olarak çalışıldı. Bu, prospektif kohort bir çalışmadı. Elektif majör abdominal cerrahi uygulanacak yaşları 35-75 arasında değişen 41 hasta etik komite izni alınarak çalışmaya dahil edildi. Motor blok gelişmesi sebebiyle iki hasta ve epidural kateterin yerinden çıkması sebebiyle iki hasta çalışmadan çıkarıldı. 37 hastadan elde edilen veriler değerlendirmeye alındı. Bütün gruplara preoperatif, cerrahiye uygun dermatomda blok oluşturacak şekilde epidural kateter takıldı. 1. gruba bupivakain infüzyonu postoperatif dönemde hasta kontrolü analjezi (HKA) aleti ile uygulandı. 2. gruba cerrahi başlamadan 25 mg bupivakain bolus uygulamasının ardından postoperatif HKA aletine bağlandı. 3. gruba ise cerrahi öncesi 25 mg bupivakainin bolus uygulamasının ardından intraoperative ve postoperative dönemde HKA aleti ile bupivakain uygulandı. Hastaların ağrı düzeyleri "numeric rating scale (NRS)" ile değerlerlendirindi. NRS'de hastalara, 0: hiç ağrı yok, 10: bugüne kadar hissedilen en şiddetli ağrı olacak şekilde, ağrılarına 1 ile 10 arasında bir değer vermeleri istendi.

Bulgular: Bütün gruplarda NRS değerleri 4'ün altındaydı ve yeterli analjezi sağlandı. 3.grupta, diğer gruplara göre anlamlı olarak daha düşük ağrı skorları ve intraopertif analjezik tüketimi görüldü (P<0.05). Bu grupta, fizyolojik sınırlar içinde olmakla beraber, daha düşük kan basıncı değerleri gözlendi.

Sonuç: Bu sonuçlar ile HKA ile epidural bupivakain, majör abdominal cerrahi uygulanacak hastalara, analjezik tedavisi olarak kullanılabilir.

Anahtar kelimeler: Epidural analjezi, Bupivakain, Majör abdominal cerrahi

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Ethics Committee Approval: Ethics committee approval was received from local Ethics Committee.
Etik Kurul Onayı: Etik kurul onayı lokal Etik Kurulu'ndan alınmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 7/8/2019
Yayın Tarihi: 08.07.2019

How to cite / Atıf için: Çetintaş Y. The effects of epidural bupivacaine administration for postoperative pain after major abdominal surgery. J Surg Med. 2019;3(7):485-489.

Introduction

Patients, who will have major abdominal surgery, need serious pain management at the postoperative period. Many trials revealed that, conventional pain management with intramuscular analgesics is insufficient for many patients [1,2]. For this reason, epidural analgesia and patient controlled analgesia have been in used for postoperative pain management recently. Epidural analgesia is a good choice for pain management and it has also some more advantages. Early gastrointestinal function improvement, less postoperative pulmonary complications, less myocardial ischemia incidence, better mobilization, less thromboembolism risk and less chronic pain syndromes are among these advantages [3]. When risks, costs and advantages of epidural analgesia are considered, this technique must be used in selected patients. Epidural analgesia is useful for patients who are expected to have serious postoperative pain and also have high risk for postoperative pulmonary complications.

Preemptive analgesia is described as an effective postoperative analgesia therapy, which blocks sensitization of central nervous system that causing increase of nociceptive perception [4]. Animal studies revealed that, pain therapy started before tissue trauma, is more effective for postoperative pain therapy [5-7]. But clinical studies showed weak positive or negative results [8-10].

In this study, we aimed to determine the effects local anesthetics administered from epidural catheter, on postoperative pain and analgesic consumption.

Materials and methods

After ethics committee approval, 41 patients from ASA II-III were enrolled to the study. The study was planned as a preliminary study so the number of the patients is low. After promising results we plan to continue the study. The study was planned as prospective, randomized and double-blinded. Patients who were planned for elective major abdominal surgery were enrolled to the study (Table 1). The patients who have contraindications for epidural catheterization, coagulation abnormalities, skin infection at catheterization site, local anesthetic allergies and serious renal or hepatic dysfunction were excluded from the study.

Patients were divided into three groups randomly. The patient's group was determined by choosing one of the sealed envelopes containing one of the group numbers. After the monitoring of blood pressure and heart rate, 0.07 mg/kg midazolam and 0.01 mg/kg atropine intramuscular were given for premedication. After 500 ml of colloid infusion, an epidural catheter was inserted from appropriate level for surgery, ranging thoracic 7 to 12, directing 4-6 cm cephaloid. The catheter was tested by 3 ml of 2% lidocaine, and then the patient was taken to the operation room.

In all groups, 4-6 mg/kg thiopental or 0.3 mg/kg etomidate, 0.1 mg/kg vecuronium and 1.5 mg/kg lidocaine were given for anesthesia induction. 50% N_2O and 0.8% MAC isoflurane mixture were given for anesthesia maintenance and vecuronium was given when needed. After anesthesia induction all patients were monitored with central venous catheter and urinary catheter. During operation, 0.5 mg alfentanil was added, if there were symptoms of inadequate anesthesia or analgesia. Total alfentanil dose was recorded.

In the first group (Group 1, n=12); 5 ml of isotonic solution was given from epidural catheter at the arrival to the operation room. After 20 minutes, anesthesia induction was given. At the end of the operation; at the postoperative care unit (PACU), the patients were monitored with noninvasive blood pressure, ECG and pulse oximetry (SpO_2). 10 ml of loading dosage, 5 ml infusion and 5 ml of bolus dose of 0.125% bupivacaine with 20 minutes lockout time, with a PCA (acute pain manager - APM, Abbot ®) was started right after. The patient's pain levels were evaluated with numeric rating scale (NRS). In NRS, patients were asked to evaluate their pain levels between 0 to 10, as 0; no pain and 10 is the worst pain ever. The NRS levels, total analgesic consumption, sedation level (0: fully awake, 1: arousable on calling, 2: arousable with painful stimulus, 3: no response) were evaluated by another anesthesiologist who does not know the patient's group, at 0^{th}, 30^{th}, 60^{th}, 90^{th}, 120^{th} minutes and 3^{th}, 4^{th}, 6^{th}, 12^{th}, 24^{th} and 48^{th} hours. Blood pressure levels, heart rates, respiratory rates, SpO2 levels and complications were recorded at the same time. If the patient's NRS level is higher than 4, additional 25 mg bupivacaine bolus was given from epidural catheter. Despite the additional dose, if the patient still had pain, the patient was excluded from the study and parenteral opioids were given for pain management. At postoperative 24^{th} hour, if the patient's NRS was 0 hasn't any complications, and then the patient was disengaged from PCA and transferred to the regular ward. If the patient had pain, 25 mg bupivacaine was given from the epidural catheter and recorded. At the regular ward, pain management continued with NSAI drugs, by the doctor in charge at the regular ward. At postoperative 48^{th} hour, if the patient had no pain the epidural catheter was withdrawn.

In the preoperative bolus group (Group 2, n=13), after the same premedication with group 1, epidural catheter was inserted. At the operating room, 25 mg bupivacaine bolus was given as loading dose, 20 minutes before anesthesia induction. Same anesthesia induction and maintenance was administered. Alfentanil was given during the operation if necessary and recorded. At the PACU, PCA was started in the same way, and pain management was started. Postoperative analgesic therapy and follows were recorded by a different anesthesiologist who is unaware of the patient's group.

In the intraoperative infusion group (Group 3, n=16), after epidural catheterization, 25 mg bolus bupivacaine was given and bupivacaine infusion via PCA was administered through operation. When the patient arrived to the PACU, bupivacaine consumption was recorded and the memory of PCA machine deleted. The patients were followed as the same way with the other groups, by a different anesthesiologist, at the postoperative period.

Statistical analysis

Data were analyzed with "One Way ANOVA" test for one way variance, by "SPSS 23.0 for Windows" computer program. Tukey test was used for differences between groups. $P<0.05$ value was accepted as significant.

Results

Demographic data, ASA classifications, operation times and operation types were similar between groups (Table 1, 2). There weren't any significant differences between heart rates at the postoperative period.

Arterial blood pressure values in the third group, at 60th minutes were lower than group 1 (P=0.028) and group 2 (P=0.016). And at 4th hour again in the third group, arterial blood pressure values were significantly lower than group 1 (P=0.032) and group 2 (P=0.024). Again in the third group, blood pressure at 30th minutes were lower than group 2 (P=0.021). And also at 90th minutes in the third group, arterial blood pressure levels were lower than group 2 (P=0.017) (Table 3). But these levels were within the physiologic range so we did not intervene. There weren't any significant differences between other blood pressure levels.

There weren't any differences between arterial oxygen saturation levels and respiratory rates between the groups. But one patient from the first group and two patients from second group, needed oxygen therapy via oxygen mask, since their SpO2 levels were below 90, at the early postoperative period. The patient's from the first group, NRS level during first two hours was 5 and sedation score was 1. The two patients' from the second group, NRS levels were 4 and sedation scores were 1. And in the intraoperative period, all these three patients received one mg alfentanil. This amount of alfentanil was higher than the mean levels of alfentanil consumption in all groups. After additional analgesic therapy and a complete recovery from anesthesia, SpO_2 levels were better and inhaler oxygen therapy was no longer needed.

There weren't any differences between sedation scores between the groups. All patients were lightly sedated in the early postoperative period.

Lower pain scores were recorded in group 3, according to the other groups (Table 4). NRS pain scores in group 3, at 30th, 60th, 90th, 120th minutes and at third, 4th, 6th, 12th and 24th hours were significantly lower than the other groups. There weren't any difference between the first and the second group. NRS scores were recorded as 5 in the first and second groups in the first 90 minutes postoperatively, after 90 minutes the NRS scores were below 4. At 48th hour, all patients' NRS scores were below 2 and none of them needed analgesic therapy any more.

There weren't any significant differences between bupivacaine consumption between the groups.

Two patients from the third group received 25 mg of bupivacaine boluses from epidural catheter, because NRS scores were above 4. Since these patients' pain levels didn't change after the boluses of bupivacaine, the patients were excluded from the study, assuming that the epidural catheters were migrated from the epidural space. Parenteral opioids were used for the rest of their pain management.

Intraoperative alfentanil consumption was significantly lower in the third group, then the other two groups (P=0.012). Mean values of intraoperative alfentanil consumption was 0.42 (0.37) mg in the first group, 0.31 (0.40) mg in the second group and 0.02 (0.2) mg in the third group. Also in the third group patients' intraoperative isoflurane consumption was lower. Since study protocol didn't include isoflurane consumption, we couldn't assess it properly.

Postoperative nausea and vomiting was detected in one patient from the first group and one patient from the third group. They were successfully treated with 10 milligrams of metoclopramide.

Partial motor blockage at one extremity was observed at 3 patients from group 2 and three patients from group 3. Bupivacaine infusions were paused and epidural catheters were withdrawn 2 centimeters back. After the resolving of motor blockage, the epidural catheter was checked again and bupivacaine infusion was started. But, one patient from group 2 and three patients from group 3, developed motor blockage again, so they were excluded from the study. Epidural catheters were removed and parenteral opioids were used for the rest of their pain management.

In this trial, none of the patients developed complications like epidural hematoma, epidural abscess, pruritus or neurologic damage. Urinary retention was not observed because all patients were urinary catheterized for 24 hours postoperatively.

Table 1: Type of operation and number of patients

	Group 1	Group 2	Group 3
Total gastrectomy	4	5	4
Subtotal gastrectomy	1	2	0
Whipple	2	1	2
Hepatic cyst hydatid	0	0	2
Biliodigestive bypass	1	2	1
Esophagectomy	1	0	0
Colon resection	2	1	2
Palliative bypass	1	1	2

Table 2: Demographic data of the patients

	Group 1	Group 2	Group 3	*P*-value
n	12	12	13	
Age (year)	64.2 (9.1)	56 (14.6)	55 (16)	0.101
Height (cm)	169 (3)	167 (4)	170 (2)	0.086
Weight (kg)	66 (2)	65 (3)	69 (2)	0.052
Sex (F/M)	5/7	4/8	4/9	0.851
Operation time (min)	190.5 (39.4)	147.2 (49.2)	203.7 (101.4)	0.062
ASA	II-III	II-III	II-III	0.126

Table 3: Mean arterial pressures (MAP) values of groups

	Group 1	Group 2	Group 3	*P*-value
0 min	113 (7)	122 (6)	112 (10)	0.252
30th min	116 (6)	125 (5)	101 (8)□	0.025
60th min	104 (5)	111 (4)	96 (5)*	0.014
90th min	110 (4)	119 (3)	92 (7)□	0.021
120th min	109 (5)	109 (4)	102 (9)	0.070
3th hour	104 (4)	111 (3)	105 (5)	0.069
4th hour	114 (6)	125 (5)	106 (4)*	0.016
6th hour	112 (5)	118 (4)	115 (5)	0.244
12th hour	110 (4)	115 (3)	113 (6)	0.357
24th hour	119 (2)	120 (1)	121 (2)	0.701
48th hour	123 (2)	121 (2)	122 (2)	0.527

*: between groups 3 and the others, □: between groups 3 and 2

Table 4: Mean numeric rating scale (NRS) of pain scores of groups

	Group 1	Group 2	Group 3	*P*-value
0 min	5.1 (1.4)	4.2 (1.6)	3.2 (1.3)	0.062
30th min	4.5 (1.1)	5.2 (1.3)	2.0 (1.5)*	0.009
60th min	4.2 (1.3)	4.8 (1.5)	2.5 (1.3)*	0.012
90th min	3.3 (1.2)	4.2 (1.1)	2.0 (1.3)*	0.019
120th min	3.8 (1.4)	3.5 (1.3)	1.5 (1.2)*	0.034
3th hour	3.5 (1.3)	3.1 (1.2)	1.3 (1.2)*	0.021
4th hour	3.5 (1.2)	3.0 (1.3)	1.0 (1.3)*	0.038
6th hour	3.2 (1.3)	3.1 (1.1)	1.0 (1.3)*	0.023
12th hour	2.8 (1.2)	2.7 (1.4)	1.2 (1.4)*	0.041
24th hour	2.0 (1.2)	2.5 (1.2)	0.6 (1.1)*	0.031
48th hour	0.5 (1.3)	1.6 (1.2)	0.7 (1.0)	0.055

*: between groups 3 and the others

Discussion

A quality postoperative analgesia is one of most important goals of anesthesia. Despite all this interest,

postoperative analgesia is usually inadequate [1,2]. Earlier studies showed that epidural analgesia is more effective then intravenous or intramuscular opioids [11-13]. Epidural analgesia also has some more advantages. Early resolving of gastrointestinal function, lower postoperative pulmonary complications, lower myocardial ischemia incidence, better mobilization, lower thromboembolism risk and less chronic pain problems are some of these advantages.

Studies comparing patient controlled epidural analgesia with conventional epidural infusion or bolus techniques showed that, patient controlled epidural analgesia is a better analgesia therapy and a safer technique with higher patient satisfaction [14,15]. Liu et al. [16] reported in a study, better analgesia with less complications with patient controlled epidural analgesia then epidural infusion or epidural bolus analgesia techniques, conducted on 454 abdominal, 165 gynecological, 126 urologic, 108 vascular, 90 thoracic, 83 orthopedic, and 4 plastic, total 1030 patients. Pruritus 12-28%, nausea 6-32%, hypotension 3-8%, sedation 9-24%, motor blockage 4-12%, respiratory depression 0.2-1.9% were found. There weren't any hematoma or abscess in the patients [16]. In our study, we found an adequate analgesia with no serious complications. We didn't see any pruritus, sedation or respiratory depression since we didn't use epidural opioids. We recorded nausea in one patient from group 1 and one patient from group 3 and successfully treated with metoclopramide.

We didn't see any serious hypotension since we gave enough intravenous fluid replacement before epidural catheterization and during epidural analgesia treatment. Blood pressure levels, in the third group at postoperative 60^{th} minute and 4^{th} hour were lower than the first and the second group. Blood pressure levels, in the third group at postoperative 30^{th} and 90^{th} minutes were lower than the second group. Since these blood pressure levels were within the physiological range, they didn't need any intervention. In the third group, patients were hypotensive despite enough fluid replacement during surgery, so we reduced dosage of the volatile anesthetic. Low dose of volatile anesthetics were used for anesthesia maintenance without any signs of awakeness. Intraoperative regional local anesthetics can adjunct to general anesthesia and lower the dosage of volatile anesthetics. Since our study protocol did not involve volatile anesthetic consumption, this effect needs to be studied in another study.

At the early postoperative period, for two hours, inhaler oxygen therapy via mask was given to one patient from group 1 and to two patients from group 2, because their SpO_2 levels were below 90%. These patients' operation types and sedation scores were not different from the average of their groups. These patients' NRS scores were 5, so they were in pain. Also these patients' intraoperative alfentanil consumptions were above the average. We assumed that these patients were not breathing easily because either they were in pain or they had respiratory depression because of high dose of alfentanil. After additional analgesic therapy and a complete recovery from anesthesia, SpO_2 levels were better and inhaler oxygen therapy was no longer needed.

Maximum plasma concentration of bupivacaine, rarely reaches toxic levels. Bupivacaine is an optimal agent for epidural infusion, because it has long duration of action with less motor blockage. Recurrent partial motor blockage was seen in one patient from group 1 and one patient from group 2. So epidural infusions of these patients' were terminated and excluded from the study. Motor blockage ratio was found 16% and exclusion ratio from the study for this reason was found 5.5% in this study. These ratios are compatible with previous studies [16,17]. Quinn Hogan [18] tried to explain the reason of partial motor blockage in a study which was conducted on 20 female patients. He studied distribution of contrast agent with CT, which was given through epidural catheter. He showed that contrast agent distributed asymmetrically and asymmetrically distribution increased as the given contrast agent increased. He argued that this asymmetric distribution is why, asymmetric blockage develops.

Many animal studies reported that preemptive analgesia helps postoperative analgesia management. Preemptive analgesia conducted on animals, with regional local anesthetics and intrathecal opioids was found effective [5,6]. But clinical studies are contradictory. Cho et al. [9] studied 60 patients who had subtotal gastrectomy. They found that epidural morphine and ketamine given before anesthesia induction was more effective then given at the end of surgery. Nakamura et al. [19] studied on 90 abdominal hysterectomy patients. They showed that epidural local anesthetics suppress central sensitivity providing lower pain scores at the postoperative period. But Dahl et al. [20] reported that there wasn't any difference with epidural bupivakain and morphine applied 40 minutes before surgery, in a study, conducted on 32 patients who had major abdominal surgery. Again Rice et al. [10] reported in a study conducted on 40 children ageing 18 months to 11 years old that, caudal block with bupivacaine either applied preoperatively or postoperatively does not affect postoperative analgesia.

Lack of existence of any difference between application of preoperative or postoperative analgesics in some clinical studies, is not a reliable evidence that, preemptive analgesia does not exist. It must be emphasized that, central hyperexcitability must be prevented, to achieve preemptive effect. The high intense of stimulation seen in major surgery is not only because of surgical incision but also because of some chemicals released from injured tissue [21]. For this reason, preemptive analgesia must also prevent central sensitization by chemicals released from injured tissue.

We couldn't find any difference between preoperative bolus group (group 2) and postoperative group (group1) on postoperative analgesia. In the postoperative infusion group after preoperative bolus and intraoperative infusion of bupivacaine (group 3), postoperative pain scores were lower than the other groups. The reason why, there was no difference between preoperative bolus and postoperative infusion group was probably that, the surgery time was longer then the duration of action of preoperatively administered bupivacaine or preoperative bolus bupivacaine was insufficient to suppress central hyperexcitability. But in the third group, since intraoperative infusion was given after preoperative bolus, central hyperexcitability have been prevented and also duration of action was not an issue. And lower pain scores were achieved in this group. Dahl et al. [20] and Rice et al. [10] probably

couldn't find any preemptive effect because they couldn't be able to suppress central sensitization with one bolus dose given preoperatively.

In the third group, intraoperative alfentanil consumption was lower than the other groups because intraoperative bupivacaine infusion is an effective way to suppress pain, during surgery.

Effective pain management can be achieved with the suppression of transduction, transmission, modulation and perception of pain with multimodal approach.

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The National Library of Medicine (NLM) citation style guide is used in this paper.
Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine