

# LAPAROSKOPİK APENDEKTOMİ CERRAHİSİNDE İNTRATEKAL OLARAK KULLANILAN BUPIVAKAİN-FENTANİL VE BUPIVAKAİN-ALFENTANİLİN KARŞILAŞTIRILMASI

## COMPARISON OF BUPIVACAINE-FENTANYL AND BUPIVACAINE-ALFENTANIL USED INTRATHECALLY IN LAPAROSCOPIC APPENDECTOMY SURGERY

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### ÖZET

**AMAÇ:** Akut karın ağrısının en sık nedeni olan akut apandisit, apendiks vermiformisin akut enflamasyonudur. Spinal anestezi günümüzde en çok kullanılan bölgesel anestezi tekniklerinden biri olup, beyin omurilik sıvısına enjekte edilen lokal anestetik solüsyon ile sinir iletiminin geçici olarak kesilmesidir. Bu çalışmada çeşitli opioid ajanların (fentanil ve alfentanil) intratekal olarak lokal anesteziyle verilmesi sonucu multimodal analjezi oluşturuldu. Bu çalışmanın amacı, motor ve duyuşsal blok oluşturmak için intratekal olarak kullanılan bupivacaine-fentanil ve bupivacaine-alfentanil karşılaştırmaktır.

**GEREÇ VE YÖNTEM:** Bu çalışma bir üçüncü basamak sağlık kuruluşunda rastgele örneklem yöntemi ile klinik bir çalışma olarak planlandı. Çalışmaya genel cerrahi kliniğinde laboratuvar testleri ve klinik tanı yöntemleri ile apandisit tanısı almış 50 gönüllü hasta dahil edildi. Hastalar rastgele Grup I (10 mg hiperbarik bupivacaine (2cc) ve 25 mcg fentanil (0.5 cc)) ve Grup II (10 mg hiperbarik bupivacaine (2 cc) ve 250 mcg alfentanil (0.5 cc)) olmak üzere ikiye ayrıldı. Operasyon öncesinde her hastaya ağrı skorlaması için hasta kontrollü analjezi sistemi ve Görsel Analog Skala (GAS) kullanımı hakkında bilgi verildi. Farklı opioidlerle multimodal spinal anestezi uygulanan hastaların postoperatif analjezik ihtiyaçları karşılaştırıldı. Duyusal blok seviyeleri ilk 10 dakikada 2 dakikada bir, sonraki dönemlerde 5 dakikada bir iğne testi ile ölçüldü. Ameliyat başlangıcında 0. dakikada ve ameliyat sırasında 5-10-30. dakikalarda ortalama arter basıncı kaydedildi. Ayrıca postoperatif 1-2-6-12-24. saatlerde ortalama arter basıncı ve kalp hızı kaydedildi.

**BULGULAR:** Grup I'in postoperatif ilk analjezik gereksinim zamanı, Grup II'ye göre gecikti. Postoperatif 6., 12. ve 24. saat GAS ölçekleri Grup I'de Grup II'ye göre anlamlı olarak düşük bulundu. Ancak 2. ve 6. saat kalp hızları Grup I'de Grup II'den daha yüksek bulundu.

**SONUÇ:** Bupivacaine-fentanil verilen hastalarda, bupivacaine-alfentanil verilen hastalara göre analjezi süresinin daha uzun olduğu ve ameliyat sonrası ilk analjezi gereksinim süresinin çok geç kaldığı gösterilmiştir.

**ANAHTAR KELİMELE:** Alfentanil, Analjezi, Görsel analog skala, İntratekal fentanil

### ABSTRACT

**OBJECTIVE:** Acute appendicitis, which is the most common cause of acute abdominal pain, is an acute inflammation of appendix vermiformis. Spinal anesthesia is one of the most used regional anesthesia technique nowadays, and it is the temporary interruption of nerve conduction by local anesthetic solution injected into the cerebrospinal fluid. In this study we created multimodal analgesia by giving various opioid agent (fentanyl and alfentanil) intrathecally with local anesthetic. The aim of this study is to compare bupivacaine-fentanyl and bupivacaine-alfentanil that are used intrathecally to create motor and sensory block.

**MATERIAL AND METHODS:** This study was planned as a clinical study using the random sampling method in a tertiary care hospital. 50 voluntary patients who were diagnosed with appendicitis by laboratory tests and clinical diagnosis methods in the general surgery clinic were included in the study. The patients were randomly assigned into two group, Group I (10 mg hyperbaric bupivacaine (2cc) and 25 mcg fentanyl (0.5 cc)) and Group II (10 mg hyperbaric bupivacaine (2 cc) and 250 mcg alfentanil (0.5 cc)). The patients were randomly assigned into two group, Group I and Group II. Before the operation, each patient was informed about the use of the patient-controlled analgesia system and visual pain scale (VPS) for pain scoring. It was compared the postoperative analgesic needs of patients who underwent multimodal spinal anesthesia with different opiates. Sensorial block levels were measured by pinprick test every 2 minutes in the first 10 minutes and every 5 minutes in later periods. It was recorded mean arterial pressure at the beginning of the surgery at 0th minute and at 5-10-30<sup>th</sup> minutes during the surgery. In addition, mean arterial pressure and heart rate were recorded at 1-2-6-12-24<sup>th</sup> hours postoperatively.

**RESULTS:** Postoperative first analgesic requirement time of Group I was found to be late than Group II. Postoperative 6th, 12th and 24th hours visual pain scales were found to be significantly lower in Group I than Group II. But 2nd and 6th hours heart rates were found higher in Group I than Group II.

**CONCLUSIONS:** It was shown that the duration of analgesia was longer and postoperative first analgesia requirements time were so late in patients who were given bupivacaine-fentanyl than the patients given bupivacaine-alfentanil.

**KEYWORDS:** Alfentanil, Analgesia, Intrathecally fentanyl, Visual pain scale

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## INTRODUCTION

Acute appendicitis is an acute inflammation of appendix vermiformis (1). The main cause of acute appendicitis is obstruction of the appendix lumen. Fecalith is responsible for 40% of uncomplicated appendicitis, 65% of non-perforated gangrenous appendicitis and 90% of perforated appendicitis (2). Appendicitis is the most common cause of acute abdominal pain and abdominal surgeries in all age groups (3 - 5).

Appendectomy operations can be performed as laparoscopic and open surgery. The choice of the appendectomy method in adults usually depends on the experience of the surgeon.

Studies have shown that laparoscopic surgery compared to the open surgery provides better cosmetic results, reduces the risk of wound infection, shortens the length of hospital stay and reduces the postoperative pain. Laparoscopic appendectomy is recommended for uncomplicated appendicitis as well as complicated and perforated appendicitis (6 - 7). Also, laparoscopic appendectomy is accepted the safest approach for obese patients (8). In pregnant patients, open appendectomy is thought to be the safest approach (9). If provided the surgical experience and the equipment is available, laparoscopic technical is considered safe and equally efficient compared to the open technical and it is seen as the first-choice procedure for most cases of suspected appendicitis (3). Regional anesthesia applications are becoming increasingly widespread today because of its advantages like patients' awareness during operation, continuation of spontaneous breathing, protection of airway reflex, longer postoperative analgesia (10). Spinal anesthesia is one of the most used regional anesthesia technique nowadays, is a temporary interruption of nerve conduction by local anesthetic solution injected into the cerebrospinal fluid (11). Bupivacaine is a local anesthetic agent in the amide structure. It is one of the longest acting local anesthetic and its latent time is short (12). Its anesthetic efficacy starts in 3 - 4 minutes and continues for 3-4 hours in spinal anesthesia (11-13). The terms opioid, narcotic analgesic and narcotic anesthetic are used to identify drugs

that exhibit opioid agonist activity by specifically binding to opioid receptors (14). Fentanyl is short acting lipophilic opioid and analgesic efficacy increases at doses 6.25 mcg or more (15). Intrathecal fentanyl in addition to bupivacaine has been used in several studies in the 10 - 25 µg dose range (15 - 18). Alfentanil is a fast and short-acting fentanyl analogue that offers clinically significant advantages over fentanyl during outpatient anesthesia (19). Intrathecal multimodal analgesia is one of the postoperative pain management method (20).

In this study we created multimodal analgesia by giving various opioid agent (fentanyl and alfentanil) intrathecally with local anesthetic. We aimed to compare the postoperative analgesic needs of patients undergoing multimodal spinal anesthesia with different opiates.

## MATERIAL AND METHOD

50 volunteer patients who were diagnosed with appendicitis by laboratory tests and clinical diagnosis methods in the general surgery clinic, aged 20-60 years with American Society of Anesthesiologists Classification I-II (ASA I-II) without contraindication for spinal anesthesia, scheduled for laparoscopic appendectomy operation were included in the study.

The patients were randomly assigned into two group, Group I and Group II. Before operation each patient was informed about the use of patient-controlled analgesia system and visual pain scale (VPS) for pain scoring. In operating room all patient was monitored using electrocardiography (ECG), noninvasive blood pressure. Before spinal anesthesia 10 - 15 ml/kg intravenous serum saline infusion was started.

Group I received 10 mg hyperbaric bupivacaine (2 cc) and 25 mcg fentanyl (0.5 cc), and Group II received 10 mg hyperbaric bupivacaine (2 cc) and 250 mcg alfentanil (0.5 cc) intrathecally.

Patients who did not accept spinal anesthesia, with diagnosed cardiovascular and pulmonary disease, with a history of allergy to local anesthetics or opioids, with history of using medication that effects cardiac output and hemodynamic response, with bleeding disorders, with local infection, with a history of peripheral or

autonomic neuropathy and with a history of perforated appendicitis were excluded from the study. Spinal anesthesia was performed for all patient with a 26 G spinal needle at the lumbar (L3-L4) intervertebral space with median approach. Group I was injected with hyperbaric bupivacaine and fentanyl, which was prepared in the same injector, within 30 seconds. Group II was injected with hyperbaric bupivacaine and alfentanil, which was prepared in the same injector, within 30 seconds. The patient was placed in the supine position within 10 seconds. Decrease in systolic blood pressure (SBP) $>20\%$  of baseline or decrease in SBP $<90$  mm/hg was defined as a hypotension. Heart rate below 60 bpm (beats per minute) was considered bradycardia. Heart rate above 100 bpm was considered as tachycardia. Sensorial block levels were measured by pinprick test every 2 minutes in the first 10 minutes and every 5 minutes in later periods. We recorded mean arterial pressure at the beginning of the surgery at 0th minute and at 5-10-30<sup>th</sup> minutes during surgery. We also recorded mean arterial pressure and heart rate at postoperative 1-2-6-12-24<sup>th</sup> hours.

In postoperative period, VPS one of the individual pain assessment methods, was used to evaluate the pain of the patient. The patients were asked to give a score of 0 in the absence of pain and a score of 10 in the case of severe pain. Between these situations the patients were asked to give a score corresponding to the number between 0 and 10 and this score were recorded. VPS was performed to all patients at postoperative 1-2-6-12-24<sup>th</sup> hours and postoperative first analgesic requirement times recorded as minutes. No patient needed naloxone in postoperative period and all patients were breathing spontaneously.

#### Ethical Committee

This study was approved by Erciyes University Faculty of Medicine Clinical Drug Research Ethical Committee (Approval number 2013/512; July 30, 2013) and written informed consent was obtained from all volunteer participating in the study. The study was registered at <http://clinicaltrials.gov> (registration number: NCT04196946) under the name of Mehtap Balci on December 10, 2019.

#### Statistical Analysis

IBM Statistical Package for the Social Sciences (SPSS) Statistics 24.0 software program was used in statistical analysis of data. Suitability of data for normal distribution was determined by Kolmogorov-Smirnov test. It was determined that the data did not show normal distribution. From this reason non-parametric Mann-Whitney U test was used to compare two independent group averages. Values of  $p < 0.05$  were considered statistically significant. All values expressed as mean $\pm$ standart deviation (mean $\pm$ sd).

#### RESULTS

This study included 50 patients who were diagnosed as non-complicated appendicitis, between the ages of 20 - 60 years and preferred preoperative spinal anesthesia. 50 patients have completed the study. Patients were randomly divided into two groups: 25 patients in Group I and 25 patients in Group II. Patients in Group I received (2 cc) 10 mg intrathecal hyperbaric bupivacaine+25 mcg fentanyl (0.5 cc) and patients in Group II received (2 cc) 10 mg intrathecal hyperbaric bupivacaine+250 mcg alfentanil (0.5 cc) for laparoscopic appendectomy anesthesia and postoperative analgesia. In Group I there were 13 male and 12 female patients. In Group II there were 12 male and 13 female patients. The average age of Group I was  $35.64 \pm 8.65$  and average age of Group II was  $35.96 \pm 8.04$ . No significant differences were detected when both groups were compared for ages ( $p = 0.705$ ). There was no statistical significance in weight, body mass index data between the two groups (**Table 1**).

**Table 1:** Comparison of average values between groups

Groups		N	Mean $\pm$ SD	p
Group I	Age	25	35.64 $\pm$ 8.65	0.705
	Length (cm)	25	169.40 $\pm$ 9.07	0.443
	Weight (kg)	25	73.40 $\pm$ 16.16	0.749
	BMI kg/m <sup>2</sup>	25	25.44 $\pm$ 4.87	0.282
Group II	Age	25	35.96 $\pm$ 8.04	0.705
	Length (cm)	25	167.80 $\pm$ 8.27	0.443
	Weight (kg)	25	75.12 $\pm$ 12.97	0.749
	BMI kg/m <sup>2</sup>	25	26.76 $\pm$ 4.70	0.282

BMI: Body mass index

The average operation time was determined  $39.24 \pm 9.39$  minutes in Group I and  $40.48 \pm 5.45$  minutes in Group II. There was no significant difference between the two groups in terms of mean operation time ( $p = 0.226$ ). Laparosco-

pic surgery was started at 0<sup>th</sup> minutes in both groups and the mean systolic and diastolic blood pressures measured at 0-5-15-30<sup>th</sup> minutes and were compared between the two groups.

There was no significant difference between mean systolic and diastolic blood pressures in Group I and Group II at 0<sup>th</sup> minute ( $p=0.27$ ,  $p=0.16$ , respectively). The mean systolic blood pressure at 5<sup>th</sup> minute was  $92.20\pm 6.80$  in Group I and  $98.16\pm 10.33$  mmhg in Group II ( $p<0.05$ ).

The mean diastolic blood pressure at 5<sup>th</sup> minute was  $64.60\pm 7.32$  in Group I and  $70.52\pm 8.34$  in Group II ( $p<0.05$ ). When the mean systolic and diastolic blood pressures of two groups evaluated at 5<sup>th</sup> minute, the mean systolic and diastolic blood pressure of Group I was significantly lower than that of Group II ( $p<0.05$ ). There was no significant difference between two groups in the mean systolic and diastolic blood pressure at 15<sup>th</sup> and 30<sup>th</sup> minutes (**Table 2**).

**Table 2:** Intraoperative systolic-diastolic blood pressure comparison

Groups	N	Mean±SD	p
Group I	Intraoperative Systolic 5 <sup>th</sup>	25 92.20±6.80	0.019*
	Intraoperative Diastolic 5 <sup>th</sup>	25 64.60±7.32	0.003*
	Intraoperative Systolic 15 <sup>th</sup>	25 87.92±7.73	0.041
	Intraoperative Diastolic 15 <sup>th</sup>	25 62.84±8.80	0.316
	Intraoperative Systolic 30 <sup>th</sup>	25 87.12±8.27	0.317
	Intraoperative Diastolic 30 <sup>th</sup>	25 58.44±8.38	0.732
Group II	Intraoperative Systolic 5 <sup>th</sup>	25 98.16±10.33	0.019*
	Intraoperative Diastolic 5 <sup>th</sup>	25 70.52±8.34	0.003*
	Intraoperative Systolic 15 <sup>th</sup>	25 92.56±10.41	0.041
	Intraoperative Diastolic 15 <sup>th</sup>	25 65.48±11.89	0.316
	Intraoperative Systolic 30 <sup>th</sup>	25 88.60±7.34	0.317
	Intraoperative Diastolic 30 <sup>th</sup>	25 59.08±7.71	0.732

\*Mann-Whitney U test, There was a significant difference between the groups,  $p<0.05$ .

Group I and Group II were compared in terms of heart rate at 0-5-15-30<sup>th</sup> minutes in operation and no significant difference was found. When we look at the sensorineural block levels of Group I and II after laparoscopic appendectomy, Group II had a mean dermatome level of  $7.80\pm 1.04$  and Group I had  $8.16\pm 1.17$ . No significant differences were detected when both groups were compared for sensorineural level ( $p=0.232$ ). Postoperative VPS applied to all patients at 1-2-6-12-24<sup>th</sup> hours and postoperative first analgesic requirement times of patient were recorded. When the postoperative first analgesic requirement times were compared between two groups, postoperative first analgesic requirement times of Group I was  $217.60\pm 29.47$  minutes and  $182.40\pm 32.69$  minutes in Group II. The first postoperative analgesia requirement time of the Group I receiving fentanyl as opioid agent was found to be signi-

ficantly later than the Group II receiving alfentanil ( $p<0.001$ ). When we looked postoperative 1-2-6-12-24<sup>th</sup> hours VPS values, no significant differences were found at postoperative 1-2nd hours but at 6-12-24<sup>th</sup> the VPS values of Group I (fentanyl group) were significantly lower than Group II (alfentanil group), ( $p<0.001$ ,  $p<0.05$ ,  $p<0.05$ , respectively), (**Table 3**).

**Table 3:** Postoperative visual pain scale comparison

Groups	N	Mean±SD	p
Group I	Postoperative VPS 1 <sup>st</sup>	25 0.84±1.10	0.107
	Postoperative VPS 2 <sup>nd</sup>	25 1.56±1.98	0.952
	Postoperative VPS 6 <sup>th</sup>	25 4.52±0.91	<0.001*
	Postoperative VPS 12 <sup>th</sup>	25 1.72±1.92	0.003*
	Postoperative VPS 24 <sup>th</sup>	25 0.84±1.02	0.008*
	Postoperative VPS 1 <sup>st</sup>	25 0.32±0.69	0.107
Group II	Postoperative VPS 2 <sup>nd</sup>	25 1.28±1.13	0.952
	Postoperative VPS 6 <sup>th</sup>	25 6.20±1.15	<0.001*
	Postoperative VPS 12 <sup>th</sup>	25 3.12±1.36	0.003*
	Postoperative VPS 24 <sup>th</sup>	25 1.76±1.23	0.008*

\*Mann-Whitney U test, There was a significant difference between the groups,  $p<0.05$ .

VPS: Visual pain scale

In postoperative period the effects of opioid administration on mean systolic and diastolic blood pressures and heart rates were evaluated in both groups. There was no difference between the two groups in terms of mean systolic and diastolic blood pressures (**Table 4**) at postoperative 1-2-6-12-24<sup>th</sup> hours. There was no difference in heart rates between the two groups at 1-12-24<sup>th</sup> hours. But the heart rates of the intrathecal fentanyl-treated group were significantly higher than the intrathecal alfentanil-treated group at the 2nd and 6th hours ( $p<0.001$ ,  $p<0.05$ , respectively).

**Table 4:** Postoperative systolic-diastolic blood pressure comparison

Groups	N	Mean±SD	p
Group I	Postoperative Systolic 1 <sup>st</sup>	25 104.80±11.59	0.146
	Postoperative Diastolic 1 <sup>st</sup>	25 67.20±9.25	0.201
	Postoperative Systolic 2 <sup>nd</sup>	25 106.00±12.07	0.478
	Postoperative Diastolic 2 <sup>nd</sup>	25 66.00±8.29	0.556
	Postoperative Systolic 6 <sup>th</sup>	25 108.20±13.83	0.467
	Postoperative Diastolic 6 <sup>th</sup>	25 68.20±6.10	0.149
	Postoperative Systolic 12 <sup>th</sup>	25 109.80±13.50	0.841
	Postoperative Diastolic 12 <sup>th</sup>	25 68.80±7.53	0.911
	Postoperative Systolic 24 <sup>th</sup>	25 115.20±10.75	0.408
	Postoperative Diastolic 24 <sup>th</sup>	25 72.40±6.31	0.992
	Postoperative Systolic 1 <sup>st</sup>	25 105.72±24.87	0.146
	Postoperative Diastolic 1 <sup>st</sup>	25 68.20±16.25	0.201
Group II	Postoperative Systolic 2 <sup>nd</sup>	25 109.00±17.50	0.478
	Postoperative Diastolic 2 <sup>nd</sup>	25 67.20±10.71	0.556
	Postoperative Systolic 6 <sup>th</sup>	25 110.80±12.96	0.467
	Postoperative Diastolic 6 <sup>th</sup>	25 71.40±8.10	0.149
	Postoperative Systolic 12 <sup>th</sup>	25 110.80±12.96	0.841
	Postoperative Diastolic 12 <sup>th</sup>	25 68.40±8.38	0.911
	Postoperative Systolic 24 <sup>th</sup>	25 112.40±14.72	0.408
	Postoperative Diastolic 24 <sup>th</sup>	25 72.20±7.78	0.992

## DISCUSSION

Postoperative pain is an acute pain that gradually decreases with tissue healing, accompanied by the inflammatory process associated with surgical trauma (21). One way to manage postoperative pain is to block pain before occurrence. Non-steroidal anti-inflammatory drugs, local anesthetics, opioids and ketamine can be used for this purpose (22). The way to reduce the severity and incidence of side effects

cts to analgesic therapy and to reduce postoperative analgesic consumption by prolonging the duration of analgesia is the combined use of each analgesic drug. For this purpose, in recent years, multimodal or balance analgesia has an important place in postoperative pain management (23). A study by Kang et al. showed that postoperative analgesic consumption was significantly lower in patients receiving multimodal analgesia and preemptive analgesia by periarticular injection for hip fractures in hemiarthroplasty surgery than the group not taking multimodal analgesia and preemptive analgesia (24). Cohen showed that liposomal-based bupivacaine used for multimodal analgesia in open colectomy surgery reduces postoperative narcotic consumption (25). The use of low-dose local anesthetics in spinal anesthesia may prevent cardiac side effects, but this practice may result in insufficient anesthesia. Because of this insufficiency some researchers recommend adding lipophilic opioids to local anesthetics in spinal anesthesia applications (16, 26). Intrathecal fentanyl has been used in several studies in addition to bupivacaine at doses of 10 - 25 mcg (15 - 18).

Ben David et al. showed that the administration of fentanyl with bupivacaine at a low dose like 7.5 mg was very successful in terms of anesthesia quality in day surgeon (27). Seewalet al. added that because of their research in 60 non-obstetric cases added to 0.5% bupivacaine increases the duration and quality of analgesia (18). Siddik-Sayyid et al. compared the intravenous administration of 12.5 mcg fentanyl with the same dose of fentanyl added to intrathecal hyperbaric bupivacaine and reported that no additional dose was needed in the intrathecal group, but additional dose was needed in the intravenous group. The study of Siddik-Sayyid et al. supports the preference of intrathecal opioid administration over intravenous administration (28).

In a randomized double-blind study, Cooper et al. examined the analgesic effects of intravenous fentanyl and epidural fentanyl after cesarean section. They found that the VPS of epidural fentanyl group was lower than the intravenous fentanyl group, even at the 8<sup>th</sup> and 12<sup>th</sup> post-

operative hours. In addition, they found that the average administered fentanyl dose was lower in the epidural group (29). Despite the ideal properties of alfentanil for epidural administration, there are very few studies. The distribution volume and total body clearance of alfentanil is smaller than that of fentanyl.

Alfentanil, one of the fastest analgesic onsets of opioids, has a peak effect in a short time, has a short half-life after bolus administration (30). During clinical use, opioids with fast half-life such as alfentanil, are generally selected for short procedures. Opioids with a longer half-life such as fentanyl and sufentanil are used for longer procedures (31 - 34).

Cooper et al. compared epidural bupivacaine 0.25% with epidural bupivacaine 0.125% and 0.005% alfentanil during delivery. They found that even lower doses of bupivacaine combined with alfentanil were used to prevent pain due to uterine contractions and they stated that the addition of local anesthetics to opioids provides an advantage in cesarean operations (35).

Barder et al. included 39 patients with ASA I who performed normal vaginal delivery in their study. They administered intrathecal bupivacaine+fentanyl to 20 patients, and bupivacaine+alfentanil to 19 patients. They found that fentanyl+bupivacaine treated group had higher postoperative VPS than bupivacaine+alfentanil treated group. They also found that postoperative perianal analgesia was less in group receiving alfentanil. The reason for this was attributed to high-dose alfentanil administration (36). Chauvin et al. in another study, they found that unlike morphine, growing epidural alfentanil dose does not increase its effectiveness. The reason for this is explained by the fact that, alfentanil receptors in the spinal cord are not dose dependent, they pass into the systemic circulation because of the dissolution of alfentanil in oil and there is very little alfentanil in the dura mater (37). In our study we applied VPS at 1-2-6-12-24<sup>th</sup> hours to all patients who underwent laparoscopic appendectomy under spinal anesthesia. We found that patients in Group I who received bupivacaine+fentanyl had lower VPS at 6<sup>th</sup>, 12<sup>th</sup> and 24<sup>th</sup> postoperative

hours compared to Group II who received bupivacaine+alfentanil. In contrast to the study by Barder et al., in our study the VPS's of the fentanyl group were lower. This may be due to the short half-life of alfentanil, our use of high-dose alfentanil and dose-dependent alfentanil receptors in the spinal cord. Hypotension due to spinal anesthesia is the most common complication. Sympathetic cardioaccelerator fibers of the heart exist from the thoracic (T)1 - 4 segments (38). When the sympathetic block reaches T1, the cardioaccelerator fibers will be affected, so the heart goes under the influence of nervous vagus. Due to the sympathetic blockade, systemic vascular resistance and cardiac output decrease. Hypotension causes a series of problems leading to cerebral ischemia, myocardial infarction, acute renal failure and cardiac arrest due to tissue hypoxia (39). Bradycardia is often accompanied by hypotension or hypoxia. It may also occur without dependence on them. In the literature, the frequency of bradycardia seen during spinal anesthesia varies between 8.9 -13%. If venous return is sufficient, if only the sympathetic of the heart is affected, it is seen that the heart rate decreases by 10% from the basal value (40). In our study, both systolic and diastolic blood pressure (especially diastolic blood pressure decreased more) decreased in bupivacaine+fentanyl group than the group treated with bupivacaine+alfentanil at intraoperative 5<sup>th</sup> minute. This may be since fentanyl has more sympathetic blocking effect than alfentanil. In the post-operative 2<sup>nd</sup> and 6<sup>th</sup> hours, the number of heart rate decreased more in the alfentanil group than fentanyl group. This may be, because of alfentanil is lipophilic and binds more to plasma proteins.

Despite the various methods used today, postoperative pain, which is still an important problem, can increase the stress and anxiety of the patients and overshadow the successful operation of the surgeon. Therefore, we recommend that postoperative pain be controlled from preoperative period. In the postoperative period after spinal anesthesia, the pain of the patient is less, the comfort of the patient increases. Economically, it reduces the length of hospital stay, reduces the risk of infection and thus reduces health care costs. If spinal anesthesia is

to be used, multimodal anesthesia should be preferred. In this study we demonstrated that co-administration of fentanyl with bupivacaine during multimodal anesthesia in laparoscopic appendectomy would provide more postoperative analgesia than the administration of bupivacaine+alfentanil, and the use of a second postoperative analgesic would be delayed in these patients.

However, in patients who received bupivacaine+fentanyl, the anesthesiologist should be careful because the hypotension may be seen in the 5<sup>th</sup> minute and the dose of iv fluid replacement which was started before spinal anesthesia, should be increased at the beginning of the operation.

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