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ARAŞTIRMA / RESEARCH

Comparison of the effects of intrathecal fentanyl and intrathecal morphine on postoperative pain for inguinal hernia repair

İnguinal herni tamiri sonrası postoperatif ağrı üzerinde intratekal fentanil ve intratekal morfinin etkilerinin karşılaştırılması

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Abstract

Purpose: The aim of this study was to compare the effects of intrathecal fentanyl and intrathecal morphine combined with spinal anesthesia on postoperative pain control for inguinal hernia repair.

Materials and Methods: Fifty patients aged 18-60 years with American Society of Anesthesiologists physical status I-II scheduled for elective inguinal hernia repair surgery were enrolled in this prospective randomized double-blinded study. Patients received spinal anesthesia with either 25 mcg fentanyl plus 12.5 mg heavy bupivacaine intrathecally (group F, n=25) or 0.1 mg morphine plus 12.5 mg heavy bupivacaine intrathecally (group M, n=25).Hemodynamic parameters, time to first analgesic requirement, postoperative pain scores, the number of analgesic requirements and side effects over postoperative 24 h were recorded.

Results: Pain scores were significantly lower in group M compared with group F in the postoperative 24 h. The time to first analgesic requirement was higher in group M than group F. Analgesic requirement was higher in group F than group M for postoperative 24 h.

Conclusion: We concluded that the addition of 0.1 mg morphine intrathecally to 12.5 mg heavy bupivacaine provides improved postoperative analgesia, especially after postoperative 12 h than 25 mcg fentanyl for inguinal hernia repair under spinal anesthesia.

Key words: Spinal anesthesia; morphine; fentanyl; postoperative analgesia

Öz

Amaç: Çalışmamızın amacı inguinal herni onarımı geçiren hastalarda intratekal fentanil ve intratekal morfin ile uygulanan spinal anestezinin postoperatif ağrı etkilerini karşılaştırmaktır.

Gereç ve Yöntem: Elektif inguinal herni onarımı geçirecek olan 18-60 yaşları arasında, Amerikan Anesteziyologları Derneği fizik durum I-II'ye sahip olan 50 hasta, prospektif, randomize çift kör çalışmamıza dahil edildi. Hastalara 12.5 mg heavy bupivakaine ilave olarak bir grupta 25 mcg fentanil (grup F, n=25) ve diğer grupta 0,1 mg morfin (grup M, n= 25) intratekal yolla uygulandı. Hemodinamik ölçümler, postoperatif ilk analjezik gereksinimi için geçen süre, postoperatif ağrı skorları, analjezik gereksinim sayısı ve yan etkiler 24 saat içinde kaydedildi.

Bulgular: Postoperatif 24 saatte ağrı skorları, grup F ile karşılaştırıldığında grup M'de belirgin olarak düşüktü. Postoperatif ilk analjezik gereksinim için geçen süre, grup M'de grup F'ye göre belirgin yüksekti. Postoperatif 24 saat için kümülatif analjezik gereksinim sayısı grup F'de grup M'e göre belirgin yüksekti.

Sonuç: İnguinal herni tamiri geçirecek hastalarda spinal anestezi amacıyla intratekal 12,5 mg heavy bupivakaine 0,1 mg morfin eklenmesi, 25 mcg fentanil eklenmesine göre özellikle postoperatif 12 saat sonra daha etkili analjezi oluşturmuştur.

Anahtar kelimeler: Spinal anestezi, morfin, fentanil, postoperatif ağrı

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INTRODUCTION

Inguinal hernia repair (IHR) is one of the most common procedures in general surgery[1]. Postoperative pain can lead to a prolonged length of hospital stay caused by delayed ambulation. Spinal anesthesia is extensively used for both intraoperative anesthesia and postoperative analgesia management in IHR with the adverse effect concerns. The combination of intrathecal (IT) opioid and local anesthetic has been studied in these cases[2-5]. IT morphine can produce a long-lasting postoperative pain relief[6]. However, it can be limited to use due to its side effects including nausea, vomiting, pruritus, respiratory depression, and urinary retention[6,7]. The incidence of respiratory depression with fentanyl may not increase significantly despite an increased risk of pruritus[6]. Nevertheless, there is no study comparing morphine and fentanyl added to a local anesthetic for postoperative pain control with spinal anesthesia in IHR.

In this study, we aimed to compare the effect of morphine and fentanyl added to heavy bupivacaine on postoperative pain relief for inguinal hernia repair under spinal anesthesia. The primary endpoint of the study was the time to first analgesic requirement and secondary endpoints were pain scores and the amount of analgesic consumption.

MATERIALS AND METHODS

After receiving the Erciyes University Faculty of Medicine Clinical Drug Research Ethical Committee approval (Approval number: 2013/272 on April 2, 2013) and patients' written informed consent, 50 patients aged 18-60 years, with American Society of Anesthesiologists physical status I-II, undergoing elective inguinal hernia repair surgery were enrolled in this prospective randomized double-blinded study. Exclusion criteria were contraindications to spinal anesthesia (e.g. coagulopathy, vertebral abnormality and infection at intervention area), neurologic, cardiac, respiratory diseases, diabetes mellitus, hypertension, chronic opioid use, allergy to drugs used and patient refusal. Patients admitted to the preoperative preparation unit 30 min before surgery. An 18 gauge intravenous (IV) cannula was inserted and 10 ml/kg/h serum saline infusion was started. All patients were monitored using electrocardiography (ECG), non-invasive blood pressure (NIBP) and peripheral oxygen saturation (SPO2). Patients were randomly allocated into two groups to receive either 25 mcg fentanyl plus 12.5 mg of 0.5 % heavy bupivacaine in 3 ml total volume (group F, n=25) or 0.1 mg morphine plus 12.5 mg of 0.5 % heavy bupivacaine in 3 ml total volume (group M, n=25), respectively.

Randomization was performed using a list generated by a computer randomization program. The anesthesiologist in charge of the patient was unaware of the groups. The drugs studied were prepared by another anesthesiologist immediate before the block. Spinal anesthesia was performed for all patients in the sitting position with a 25-gauge spinal needle at the L3-4 or L4-5 intervertebral space in the midline.

Sensory block was assessed using pinprick dermatomal testing, while the motor block was assessed using a 4-point modified Bromage Scale (0= no motor block; 1= hip blocked; 2= hip and knee blocked; 3= hip, knee and ankle blocked). The loss of pinprick sensation at ≥T8 with a Bromage score ≥2 was the successful block for surgery.

Systolic (SBP) and diastolic (DBP) blood pressures, heart rate (HR) were recorded at the 1, 5, 15, 30 and 60 min during surgery. The decrease in SBP >20% of baseline was defined as hypotension and treated with an increase in fluid infusion or a dose of 10 mg IV ephedrine. Bradycardia (decrease in heart rate below 50 bpm) was treated with 0.5 mg IV atropine. SBP, DBP, HR, the time to the first analgesic requirement, visual analog scale (VAS) scores, the number of analgesic requirements and side effects (e.g. nausea, vomiting and other) were recorded over 24 h after surgery.

The primary outcome was the time to first analgesic requirement of patients. Secondary outcomes were pain score using a VAS evaluating the pain intensity (VAS: 0-without pain;10-maximum imaginable pain) and the number of analgesic requirements. If the pain score was ≥4, we administered intramuscular diclofenac sodium as a rescue analgesic. Patients with nausea and vomiting received 10 mg IV metoclopramide.

Statistical analysis

A sample size calculation was performed using G*Power 3.1.9.2 software by a pilot study. The mean (±SD) time to first analgesic requirement was 5.75± 2.44 and 4.05±1.27, in morphine and fentanyl-treated groups, respectively. We calculated

the minimum number of patients needed as 22 in each group with a power of 80% and a p-value of 0.05. Fifty patients were included in this study to compensate data loss. Data were statistically analyzed using SPSS version 22.0. Categorical data were presented as numbers (n) and percentage (%), numerical data were presented as the mean and standard deviation (as median and minimum-maximum where necessary). Nonparametric Mann-Whitney U test was used for the time to the first analgesic requirement, the number of analgesic requirements and a cumulative number of analgesic requirements. Chi-Square test and T-test were used in demographic data analysis. A value of $p<0.05$ was considered statistically significant.

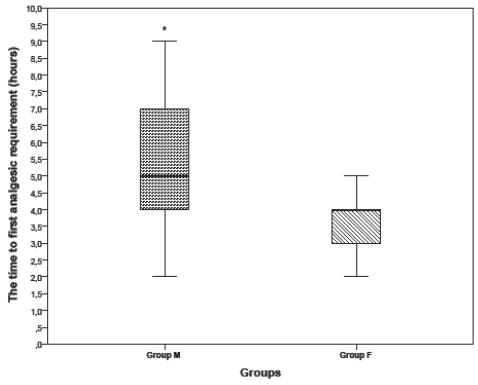

Figure 1. The time to first analgesic requirement for the groups.

*p=0.001, vs. group F Mann-Whitney U test was used. The time to the first analgesic requirement, time from sensory block to first analgesic use. Group M, 0.1 mg morphine plus 12.5 mg of 0.5 % heavy bupivacaine in 3 ml total volume; Group F, 25 mcg fentanyl plus 12.5 mg of 0.5 % heavy bupivacaine in 3 ml total volume. The box and whisker plots show median (horizontal line within the boxes), 5th and 95th percentiles (the upper limit and the lower limit of whiskers), 25 and 75 percentiles (upper and lower box edges).

RESULTS

Fifty-three patients were eligible for this study. Fifty patients have completed the study. There was no statistical significance in demographic and hemodynamic (SBP, DBP, and HR) data between the two groups. Demographic data (age, weight, height, gender, surgery time) are shown in Table 1. The median time to first analgesic requirement was significantly higher in group M compared with group F 5.0 (2.0-9.0) [mean±SD, 5.5±1.9] and 4.0 (2.0-5.0) [mean±SD, 3.7±0.8], respectively) (p=0.001) (Figure 1).

Table 1. Demographic data of the groups.

	Group M (n=25)	Group F (n=25)	*P* value
Age (year) [a]	56.2±8.1 53.0(45.0-71.0)	56.4±7.2 58.0(43.0-72.0)	0.942
Height(cm) [b]	171.6±9.4 172.0(156.0-185.0)	168.5±12.7 172.0(120.0-185.0)	0.420
Weight (kg) [a]	71.8±13.8 73.0(51.0-98.0)	73.4±10.6 75.0(39.0-85.0)	0.665
Gender (F/M) [c]	4/21	4/21	0.649
Surgery time (min) [b]	48.4±5.5 50.0(40.0-65.0)	50.9±10.7 50.0(40.0-98.0)	0.441

[a] Independent T test was used; [b] Mann-Whitney U test was used; [c] Chi-square test was used. Values are shown as mean±SD, median(min-max) and n (number of patients).

No statistical significance was found for the number of analgesic requirements in both groups (p>0.05). However, the cumulative number of analgesic requirements was significantly lower in group M than group F for 6, 12 and 24 h (p=0.02, p=0.001, and p=0.001, respectively). The percentage of patients with analgesic use is shown in Figure 2.

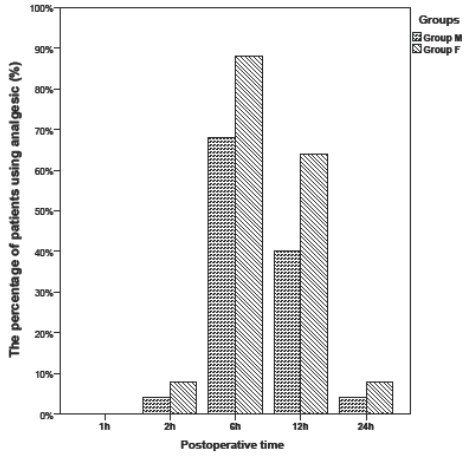

Figure 2. The percentages of patients with analgesic use over postoperative 24 h.

Pain scores were significantly lower in group M than group F in the postoperative 12 and 24 h (p=0.003

and p=0.001, respectively)(Figure 3). None of the patients in both groups had side effects intraoperatively. There was no respiratory depression in both groups. The occurrence of nausea and vomiting was 7 in group F and 2 in group M. Urinary retention was found in one patient of group F and 3 of group M. There was pruritus in 4 patients of group F and 6 in group M

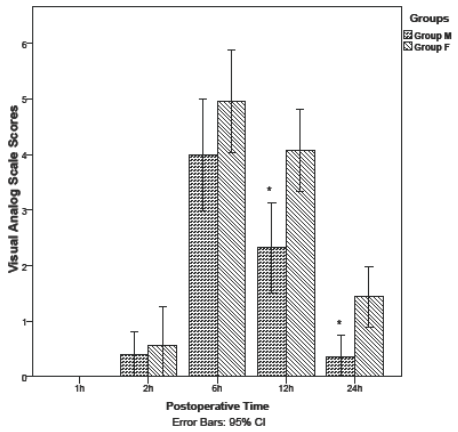

Fig 3. Visual Analog Scale scores over postoperative 24 h.

*p<0.05, vs. group F, Mann-Whitney U test was used.

DISCUSSION

In this study, we showed that the addition of 0.1 mg IT morphine to 12.5 mg of 0.5 % heavy bupivacaine for spinal anesthesia produces an effective postoperative analgesia with longer duration compared to adding 25 mcg IT fentanyl. Although there is a limited number of studies comparing the effects of IT morphine and IT fentanyl added to local anesthetic for postoperative pain control, there are no comparative results associated with inguinal hernia repair.

The addition of intrathecal opioids to local anesthetics for spinal anesthesia improves the quality of analgesia. Various doses of IT opioids added to local anesthetics were studied on postoperative pain. IT morphine and fentanyl added to intrathecal bupivacaine produce a prolonged analgesia and opioid-sparing effect. However, minimal effective doses of intrathecal morphine and fentanyl are still a research topic. Furthermore, there is no clear evidence of dose-responsiveness for benefit and risk[6]. The low hydrophobicity of morphine may be responsible for its slow clearance into the systemic circulation and long duration[8]. IT morphine can substantially reduce pain intensity for postoperative 12 h; however, there was no available data for advantageous outcomes of IT morphine on pain intensity at 24 h.[6]. A comparative study by Meco et al.[2]. reported that 0.1 mg IT morphine added to intrathecal 7.5 mg bupivacaine in spinal anesthesia for inguinal hernia repair can be a good alternative than that of 0.4 mg IT morphine. As similar to our results, they found the median first analgesia time as 5 h with 0.1 mg IT morphine. The different doses of fentanyl between 10 and 40 mcg added to hyperbaric bupivacaine for spinal anesthesia were studied in hernia repair surgery and the addition of 10 mcg fentanyl improved the quality and duration of analgesia. There was no further benefit with increased up to 40 mcg dose of fentanyl[5]. Some studies with fentanyl were performed to reduce the dose of local anesthetic used for IHR. The addition of 25 μg intrathecal fentanyl to low-dose levobupivacaine (5 mg) or low dose bupivacaine (7.5 mg) provided an adequate quality of spinal anesthesia and postoperative pain relief[9,10].

In studies comparing morphine and fentanyl added to local anesthetic for spinal anesthesia, morphine has been shown to have a longer duration of analgesia[11-15]. Morphine-induced respiratory depression is dose-related and centrally mediated[16,17]. IT morphine is associated with a significant risk of respiratory depression than that of IT fentanyl. The risk of respiratory depression is not pronounced at a dose of fentanyl between 10-40 mcg. There is an increased risk of postoperative nausea, vomiting, pruritus and urinary retention with IT morphine whereas fentanyl is associated with an increased risk of pruritus only[6]. Similarly, in our study, urinary retention was more pronounced in morphine group than fentanyl group. On the other hand, we found an increased incidence of nausea and vomiting in fentanyl group than morphine group.

The major weakness of our study is the lack of a placebo group. Several important factors including the patients' satisfaction, discharge times, and ambulation time were not evaluated in this study. Furthermore, we did not assess the severity of nausea/vomiting or pruritus and use a power analysis for these adverse events. Therefore, no

definite judgment can be made about the incidence of adverse events.

In conclusion, spinal anesthesia with the addition of 0.1 mg IT morphine to 12.5 mg of 0.5 % heavy bupivacaine for inguinal hernia repair provides an effective postoperative analgesia with longer duration compared to adding 25 mcg IT fentanyl.

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