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Analgesic Effect of Wound Infiltration with Morphine versus Dexketoprofen, Tramadol, and Bupivacaine in Lumbar Disc Surgeries

Research Article

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Abstract

Background and Purpose: Wound infiltration using local anesthetics, anti-inflammatory drugs and opioids can significantly improve postoperative analgesia. The purpose of this clinical study was to determine the most effective method of wound infiltration among morphine, tramadol, dexketoprofen and bupivacaine for postoperative analgesia in patients undergoing lumbar discectomy.
Methods: One hundred patients undergone elective lumbar discectomy operations were included. Patients were randomly allocated to one of five groups: wound infiltration with 10 mg morphine (group M), with 100 mg tramadol (group T), with 50 mg dexketoprofen (group D), with 100 mg bupivacaine (group B) or control group (group C). Pain scores using visual analog scale (VAS) at 15th min, 1st, 6th, 12th, and 24th hours postoperatively and 24-h analgesic requirements were recorded.
Results: No differences were determined between the four groups by means of demographic and clinical characteristics. In terms of patient satisfaction, Group M was significantly superior to groups D and B, respectively ($p<0.05$ for all). Post-hoc analyses revealed that the 15-min VAS score was significantly lower in Group M than in Group D; the 1-h VAS score was significantly lower than in groups T and A; the 6-h VAS score was significantly lower than in groups T, A and B, and the 24-h VAS score was significantly lower than in groups D and B, respectively ($p<0.05$). Tramadol consumption in the postoperative period was significantly lower in Group M than in Group B ($p=0.004$). There was significant reduction in other four groups according to Group C about the postoperative analgesic consumption.
Conclusion: The incision infiltration using morphine is superior when compared to tramadol, dexketoprofen, and bupivacaine for controlling postoperative pain in lumbar discectomies.

Keywords: Postoperative pain; Laminectomy; Morphine; Wound Infiltration.

Introduction

Pain after lumbar discectomy may cause unacceptable morbidity. Inadequate pain control leads to patient dissatisfaction and may also be associated with major morbidities, such as perioperative myocardial ischemia, pulmonary complications, altered immune function, and postoperative cognitive dysfunction [1]. In addition, the risk of thromboembolism may increase when early mobilization cannot be established due to pain. Sufficient analgesia in these patients, particularly in the first 24 h postoperatively, is very important in terms of morbidity and patient satisfaction. Various different methods (such as patient-controlled analgesia and intravascular (iv), intramuscular (im), epidural, and intrathecal drug administration) and drugs (such as non-steroidal anti-inflammatory drugs [NSAIDs]) are employed [1-4]. The most popular methods, epidural analgesia and patient-controlled analgesia, are both expensive and require trained personnel [5]. Infiltration into the muscles surrounding the incision site with various analgesic drugs at the end of surgery can establish more effective analgesia. Local anesthetics, NSAIDs, and opioids have been used for that purpose. The purpose of this study was to perform wound infiltration with four different drugs into the incision site in patients undergone elective lumbar disc surgery, and to determine the efficacy of each drugs by assessing patients' postoperative pain monitorization, analgesic drug requirements, and patient and physician satisfactions.

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Methods

This double-blinded, prospective, randomized clinical trial was conducted in the Education and Research Hospital, between May 2015 and January 2016. Local ethical committee approval was granted (date: 26.05.2015, no: KAEK 2015/10-79), and signed informed consent forms were received from all patients enrolled. One hundred twenty-five patients with ≥22 ages and American Society of Anesthesiologists (ASA) status I and II, and who were scheduled for elective lumbar discectomy under general anesthesia, were randomly assigned by block randomization method (with each block containing 1 case) to one of the five groups. Each groups contained 25 patients; Group M (morphine), Group T (tramadol), Group D (dexketoprofen trometamol), Group B (bupivacaine) and Group C (control).

All patients had been scheduled for surgery by the neurosurgery department with a diagnosis of single-level disc herniation. They were informed about the visual analog scale (VAS) in the preoperative period (no pain: 0-1, mild pain: 2-3, moderate pain: 4-5, severe pain: 5-6, very severe pain: 7-8, unbearable pain: 9-10). After data including demographic variables and ASA values were obtained, monitorization regarding electrocardiogram, non-invasive blood pressure, heart rate, and peripheral oxygen saturation (SpO2) was established. Venous access was maintained on the back of the right hand (18 G) and the right forearm (16 G). Intravenous infusion of 0.9% NaCl solution was initiated at a rate of 8 ml/kg. Following 3 minutes of oxygenation with 100% O_2 (7 ml/min), general anesthesia was administered to all patients with the same protocol (induction; propofol, 2.5 mg/kg, fentanyl, 1.5 µg/kg; and atracurium, 0.6 mg/kg were given intravenously. Patients were intubated through the orotracheal route). After the patient was placed in prone position, maintenance anesthesia consisting of O_2/N_2O:45/55%; Sevoflurane, 1.5%; and atracurium, 10 mg/30 min was introduced. Intravenous bolus of 50 µg fentanyl was administered in cases of 20% rises in blood pressure and heart rate. Time periods of the operation (start and termination) were recorded. Analgesic drugs were not used during the last 30 minutes of the surgery. Anesthetic gases were stopped after the start of subcutaneous tissue saturation. All surgical procedures were performed by the same team. All drugs were diluted with 10 ml of saline solution except bupivacaine. The surgeon who would use the injector was blind to the content. At the end of the surgery, before cutaneous sutures, around the incision site, intramuscular 10 mg morphine (morphine HCl, 0.01 gr/1 ml ampoule, Osel, Turkey) was administered in Group M, intramuscular 100 mg tramadol (Contramal® 100 mg/2 ml ampoule, Abdi İbrahim, Turkey) was administered in Group T, intramuscular 50 mg dexketoprofen trometamol (Arveles® 50 mg/2 ml ampoule, Spain) was administered in Group D, and intramuscular 50 mg bupivacaine hydrochloride (Marcaine® 0.5%, 5 mg/ml, 20 ml/vial, AstraZeneca) was administered in Group B. At the end of surgery patients were monitorized in the post-anesthesia care unit (PACU). Patients' pain statuses were assessed using VAS and the data was recorded by a blinded anesthetist at 15th min, 1st, 6th, 12th, and 24th hours. Analgesia with iv paracetamol was provided to patients with VAS scores above 4. Patients with VAS scores of 5 or above were given im 100 mg tramadol, and the amounts of drugs used were recorded. The satisfaction of patients and surgeons (1: very poor, 2: poor, 3: good, 4: very good) were assessed by a blinded anesthetist after 24th h.

Patients without history of an allergy to opioids, local anesthetics, or NSAIDs and chronic pain were included. Patients, who did not use any analgesics in the previous 24 h, and drug infiltration to the incision site, were included in the study. Patients who had neurological deficits, chronic pain such as neuropathy, received premedication, had history of an allergy to opioids, local anesthetic, or NSAIDs, chronic disorders such as diabetes mellitus, cardiovascular, pulmonary, hepatic, renal, or metabolic diseases were not included in the study. Additionally, patients whose ASA III or above, refusing the procedure, bleeding over 20 ml during surgery, operation time was over 90 min and developing complications associated with anesthesia or surgery were excluded.

Statistical Analysis

The sample size estimation was based on the mean ± SD of a similar study by Kamaz et al., [6].

In a one-way ANOVA study, sample sizes of 25, 25, 25, 25, and 25 are obtained from the 5 groups whose means are to be compared. The total sample of 125 subjects achieves 100% power to detect differences among the means versus the alternative of equal means using an F test with a 0.05 significance level. The size of the variation in the means is represented by their standard deviation which is 0.95. The common standard deviation within a group is assumed to be 0.50.

Results were expressed as mean ± SD for continuous variables and as percentages for countable variables. The chi square and Mann Whitney U tests were used for analyzing differences among demographic variables. Visual Analog Scale (VAS) and patient-physician satisfaction scores were compared using one-way analysis of variance and post-hoc Bonferroni tests. SPSS v.20 was used for statistical analyses.

Results

There were no differences between the five groups in terms of demographical characteristics, ASA risk classification, smoking status, and duration of surgery (Table 1). No significant difference was present between the groups in terms of physician satisfaction while one-way ANOVA revealed a significant difference in terms of patient satisfaction (p=0.001). Bonferroni post-hoc analysis revealed significant differences between Group M and GroupD (p=0.011) and between Group M and Group B (p<0.0001) (Table 2). Post hoc analysis of VAS values at 15th min revealed significant difference between groups M and A (P=0.036). Also, significant post hoc differences in VAS values were found at postoperative 1st h between groups M and T (p=0.025) and between groups M and D (p=0.001). Similarly, statistically significant difference in terms of 6th h VAS scores was determined between Group M and the other groups (P<0.0001). At postoperative 12th h, statistical difference was observed between groups M and B (p=0.001). At postoperative 24th h, significant differences were determined between groups M and D (p=0.017), groups M and B (p<0.0001), groups T and D (p=0.001), and groups T and B (p<0.0001) Patient satisfaction was found statistically significant between the groups M and B, groups M and C, groups T and C, and groups A and C (p=0.002, p<0.0001, p<0.0001, and p=0.002, respectively). Physician satisfaction was statistically significant between Group C and all other groups (p<0.0001). The VAS score at the 15th minute was statistically significant between Group C and all other groups (p<0.0001). The VAS score on the 1th hour was statistically significant between groups M and A, groups M and C, groups T and A, and groups B and C (p=0.002, p<0.0001, p<0.0001, and p<0.0001, respectively). The VAS score on the 6th hour was found statistically significant between the groups M and T, groups M and A, groups M and B, and groups M and C (p<0.0001, p<0.0001, p=0.009, and p=0.027, respectively). The VAS score on the 12th hour was statistically significant between groups M and B, groups M and C, groups T and B, and groups T and C, and groups A and C (p=0.013, p=0.001, p=0.029, and p=0.001, and p=0.043, respectively). The VAS score on the 24th hour was found statistically significant between the groups M and A, groups M and B, groups T and A, groups T and B, and groups T and C (p=0.021, p<0.0001, p=0.001, p<0.0001, and p=0.006, respectively)(Table 2).

Statistically significant differences were also observed among the groups in terms of consumption of postoperative analgesia (p=0.038). In addition, no difference was present among the other four groups except group C in terms of postoperative consumption of paracetamol and tramadol consumption, but an increase was identified in consumption of postoperative both paracetamol and tramadol, particularly in Group B, between 12th and 24th hours. And also there was statistically significant difference between Group C and other 4 groups about paracetamol usage (p<0.0001). Statistically significant difference was present between the groups M and B (p=0.029) and Group C and other 4 groups (p<0.0001) regarding tramadol usage (Table 3).

Discussion

Lumbar discectomy is one of the most common procedures in neurosurgery and single-level lumbar herniations are generally treated using microsurgery. Although microsurgery is advantageous in terms of postoperative pain, pain is nevertheless a significant problem in the early postoperative period (particularly the first 24 h) in these patients [2, 3, 7]. This study showed that in the postoperative pain control, morphine was superior to tramadol, dexketoprofen, and bupivacaine in incisional infiltration during lumbar disc herniectomy.

Patients with lumbar herniation expect their pain to improve following surgery to which they agree because of unbearable pain. It is therefore very important in psychological terms to provide effective analgesia immediately following surgery in these patients. The most painful period for patients experiencing general anesthesia is generally the first 12 h postoperatively. If extreme pain is relieved using an appropriate method in this early postoperative period, it can also be controlled more easily in the subsequent period, because the patient's concerns over pain will have been alleviated [8, 9]. Opioids are most commonly used for postoperative pain control in patients undergoing lumbar herniectomy. However, all patients cannot tolerate opioids due to their side-effects [10]. Various studies have shown that analgesic infiltration around the incision is the most effective and simplest method of acute postoperative pain (both at rest and during

Table 1. Demographic data, ASA, smoking status and operation times of study population.

Characteristics	Group M	Group T	Group D	Group B	Group C	p
	n=25	n=25	n=25	n=25	n=25	
Age (year) (mean±SD)	43.92 ± 13.35	48.48 ± 13.07	48.56 ± 12.86	47.04 ± 15.30	47.20 ± 10.73	0.598
Weight (kg) (mean±SD)	77.76 ± 20.56	76.48 ± 10.16	79.72 ± 7.44	75.04 ± 10.67	75.20 ± 9.71	0.627
Height (cm) (mean±SD)	169.60 ± 6.81	168.88 ± 7.96	171.96 ± 7.28	168.48 ± 6.24	169.28 ± 8.12	0.313
Gender (M/F)	14/11	15/10	16/9	13/12	14/11	0.844
ASA (I/II)	17/8	13/12	15/10	18/7	16/9	0.47
Smoking, n(%)	7 (28)	14 (56)	12 (48)	8 (32)	36 (9)	0.144
Operation time (min)	52.60 ± 7.79	54.20 ± 6.56	52.20 ± 7.51	54.40 ± 6.51	54.40 ± 6.50	0.61

ASA, American Society of Anesthesiologists; SD, standard deviation.

Table 2. Median Visual Analog Scale (VAS) scores and patient-physician satisfaction during the postoperative period.

Time	Group M	Group T	Group D	Group B	Group	p
	n=25	n=25	n=25	n=25	Cn=25	
15th min	1.52 ± 1.50	2.60 ± 1.95	2.72 ± 1.24	2.32 ± 1.49	5.6 ± 1.32	0.036
1st h	1.40 ± 1.0	2.28 ± 0.84	2.60 ± 1.19	1.88 ± 1.17	4.1 ± 1.2	0.001
6th h	1.68 ± 0.75	2.72 ± 0.79	2.80 ± 0.58	2.48 ± 0.77	2.4 ± 1.5	<0.0001
12th h	2.28 ± 0.68	2.36 ± 1.19	2.68 ± 0.80	3.32 ± 1.07	3.6 ± 1.6	0.001
24th h	2.12±0.93	1.84±0.99	3.16 ± 1.34	3.60 ± 1.44	3.0 ± 1.0	<0.0001
Patient satisfaction	3.52 ± 0.65	3.16 ± 0.62	2.96 ± 0.54	2.80 ± 0.65	2.24 ± 0.78	0.001
Physician satisfaction	3.76 ± 0.43	3.52 ± 0.58	3.60 ± 0.58	3.56 ± 0.51	2.76 ± 0.73	0.403

Table 3. Postoperative consumption of analgesic drugs.

	Group M	Group T	Group D	Group B	Group C	p
	n=25	n=25	n=25	n=25	n=25	
Additional analgesia, n (%)	6 (24)	10 (40)	12 (48)	16 (64)	100 (25)	0.038
Paracetamol (mg)	240.0 ± 435.8	280.0 ± 458.2	440.0 ± 506.6	400.0 ± 500.0	1541.7 ± 588.2	0.396
Tramadol (mg)	0*	20.0 ± 40.8	12.0 ± 33.1	32.0 ± 47.6*	124.0 ± 43.6	0.016
Paracetamol consumption, n (%)	6 (24)	7 (28)	11 (44)	10 (40)	24 (96)	0.387
Tramadol consumption, n (%)	0 (0)	5 (20)	3 (12)	8 (32)	25 (100)	0.018

$^{\alpha}$, in particular, no patients in Group M required tramadol (p=0.016). Two-way chi square analysis performed to determine which three of the five groups were responsible for this difference identified groups M and B, groups M and C as the source (p=0.004, p=0.001).

movement) control [2, 7, 11]. This technique can also reduce postoperative opioid and other analgesic requirements and their associated side-effects [3]. Several methods have been employed for analgesia after lumbar disc surgery, including opioids, opioid derivatives, NSAIDs, and local anesthetic agents [3, 4, 12].

Local anesthetic agents have been widely used in many surgical operations to reduce incision pain. In our study, based on previous research, bupivacaine, a long-term local anesthetic, was used below (at 100 mg) the recommended maximum dose (2-3 mg/kg) [2, 13]. Rahmanian et al., [2] injected 150 mg (30 ml, 0.25%) bupivacaine into the muscles around the incision at the end of lumbar discectomy and compared pain status at 6th and 15th h with control group, but reported no significant difference. Another study, however, concluded that bupivacaine reduced pain scores in the early postoperative period and lowered morphine consumption [8, 14]. In another double-blinded study, 100 mg (10 ml, 0.5) bupivacaine was injected into the incision area, and a significant decrease in pain scores was observed, particularly in the first postoperative 4 h [15]. In parallel to these studies, VAS scores were shown to increase after the 5th hour in Group B in our study, and analgesic consumption increased after that time.

Dexketoprofen trometamol is a centrally acting NSAID with potency similar to that of μ-opioid agonists and widely used in recent years. In a number of studies in different pain models, it has been proven to have a good analgesic efficacy and tolerability profile after oral and iv or im administration [16, 17]. In one study, 50 mg dexketoprofentrometamol was administered twice im at a 12-h interval and reduced morphine consumption in the postoperative period by one-third compared to a control group [18]. In our study, a single dose of dexketoprofen trometamol that provides safe and effective analgesia by infiltration, was found to be effective as morphine and tramadol. In another study, dexketoprofen was administered orally before and after surgery and resulted in a significant decrease in postoperative opioid consumption [19]. In addition, a single dose of dexketoprofen trometamol has been shown to provide sufficient analgesia over a 24 h period in dental surgery [20].

Tramadol hydrochloride is a synthetic analog of codeine that acts through the mechanisms of action of both opioids (weak μ-opioid receptor agonist) and non-opioids (noradrenalin, which prevents reuptake of serotonin). Tramadol has effects similar to those of local anesthetics onperipheral nerves and has been shown to block nerve transmission. It is an effective analgesic when added as an adjuvant to local anesthetic agents, or when used alone (im, iv, and intrathecally). It can also modify the effects of local anesthetics by directly or indirectly affecting sodium channels, thus contributing to more effective analgesia [3, 5, 21, 22]. Ozyılmaz et al., [3] compared tramadol and levobupivacaine in wound infiltration in lumbar discectomies and showed that tramadol significantly reduced analgesic requirements. Another study in which tramadol was injected im into the incision site in cases of pediatric herniectomy reported that injection into the wound site was more effective than both tramadol administered im and more effective than bupivacaine administered around the wound site [23].

Opioids, which have been used for thousands of years for pain relief and pleasure, are today highly important and essential for anesthetic procedures. Additionally opioids, and particularly morphine, are frequently used for pain control in the perioperative period due to their anxiolytic, sedative, and powerful analgesic effects [5, 7]. Morphine is a pure agonist of phenanthrene, an opium alkaloid, and exhibits its effects on the central nervous system [10, 24]. Morphine can be used iv, im or orally, and also topically. In one double-blinded crossover pilot study, 10 mg morphine was administered topically to patients with a painful sacral base. Following 2-day cleansing, patients were compared with a control group, and significantly lower VAS scores were determined in the morphine group [25]. Similarly, we assessed the postoperative analgesic effect of morphine injection into the incision area in cases of lumbar disc herniectomy and observed a superior analgesic effect to those in the other groups (tramadol, dexketoprofen, and bupivacaine). There was significant reduction in other four groups according to Group C about the postoperative analgesic consumption. Especially, as patients in the group M consumed 240 mg paracetamol and 0 (zero) mg tramadol, in group C was consumed 1541.7 mg paracetamol and 124.0 mg tramadol (Table 3). Additionally, no local or systemic drug-related side-effects were observed in any of the four drugs we used.

The limitation of our study is to be a single center study firstly. And patients with VAS scores and analgesic consumption of the patients were not grouped according to their age.

Conclusion

Our study shows that morphine as an infiltrative agent in the incision area, is superior to dexketoprofen at 15th min postoperative pain control, that at 1st h it is superior to both dexketoprofen and tramadol, that at 6th h it is superior to bupivacaine as well as the other two drugs, and that patient satisfaction at the end of 24th h was better in the morphine group compared to in the dexketoprofen and bupivacaine groups. We conclude thatall four drugs can be reliably used, but that morphine provides more effective analgesia.

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