



# Can bupivacaine applied intraoperatively into paravertebral muscle tissues reduce the need for postoperative narcotic analgesics and/or nonsteroids?

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## Abstract

**Aim:** Although the length of hospital stay after lumbar microdiscectomy operations, one of the most common surgical interventions in current neurosurgery practice, is quite short, nausea-vomiting and urinary retention, particularly postoperative pain, may prolong this period. Also, systemic side effects may occur in cases due to pharmacological agents applied for postoperative pain control. This study was conducted to seek answers to whether bupivacaine administered intraoperatively into the paravertebral muscle mass decrease the need for postoperative narcotic analgesics and/or nonsteroidal anti-inflammatory drugs (NSAIDs).

**Materials and Methods:** Lumbar disc hernia patients with a similar history of age, gender, body weight, disc hernia level, preoperative pain score, and preoperative analgesic use were included in the study between 01.06.2020 and 31.06.2021 (n=48). The control group of the study consisted of cases who did not receive paravertebral intramuscular bupivacaine during single-level lumbar microdiscectomy operations under general anesthesia and named as group 1 (n=24). The study group of the study consisted of cases who were administered preoperative paravertebral intramuscular bupivacaine and named group 2 (n=24). After the operation, the assessment of pain with the frequency of need for morphine sulfate or pethidine hydrochloride was performed with the Visual Analogue Scale (VAS). After the obtained data were assessed with a one-way analysis of variance, the relationship between parameters was tested using the Pearson correlation coefficient (r). Alpha significance value was accepted as <0.01.

**Results:** It was found in comparisons between groups that the post-op VAS score (F=47.3; P=0.00), the post-op mobilization time (F=22.8; P=0.00), the post-op NSAIDs need (F=12.7; P=0.00), and the length of stay (F= 12.6; P=0.00) were statistically significant (P<0.01) in the groups using bupivacaine. However, in the cases in group 2, although the mean dose of post-op narcotic drug use decreased from 11.46±16.45 mg to 6.33±2.14 mg, it was reported that this result (F=0.5; P=0.47) was not statistically significant (P>0.01). It was determined that there was a moderate and positive relationship between the use of NSAIDs and the post-op VAS value and between the use of NSAIDs and post-op mobilization. It was determined that the post-op VAS score had a strong correlation above the moderate level with post-op mobilization time (r=0.609) and hospitalization time (r=0.603).

**Conclusion:** In the cases for which pre-op paravertebral intramuscular bupivacaine was applied, although the decrease in the need for narcotic analgesics after the operation is not statistically significant, it was seen that it reduces the need for NSAIDs-featured dexketoprofen trometamol statistically and significantly. These results make us think that preoperative intramuscular bupivacaine administration may be effective in controlling postoperative pain and reducing the need for additional analgesics.

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## Introduction

It is highly important to treat pain, which is defined as an unpleasant sensory and emotional experience that accom-

panies or is within the framework of existing or potential tissue damage. In the last decade, multimodal pain management strategies in neurosurgery practice have gained popularity among the frequently mentioned issues as being critically important [1].

Opioids, nonsteroidal anti-inflammatory drugs (NSAIDs),

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and local anesthetics are mainly preferred in the treatment of pain. However, apart from analgesic drug-drug interaction, many side effects/adverse events such as itching, nausea, vomiting, constipation, and urinary retention can also be observed after the perioperative and/or postoperative use of these drugs [2-5].

Dexketoprofen trometamol is a quick acting NSAIDs for the treatment of painful musculoskeletal conditions. It is also used as a treatment for post-operative pain. Information has been reported in the literature that dexketoprofen trometamol may cause vertigo, dizziness or fatigue, drowsiness, sleep disorders, irritability, headache or body pain, feeling sick, palpitation, and gastrointestinal disorders such as bloating, constipation, or diarrhea, [6] or genotoxicity [7]. Similarly, due to the use of morphine sulfate, it has side effects such as vertigo, headache, nausea, vomiting, and itching [8].

But, the main purpose of using such pharmaceuticals in the treatment of pain is to reduce the length of hospital stay and to minimize the costs arising from the treatment by reducing/eliminating the discomfort of the cases in the postoperative period, contributing to the healing process, reducing the side effects arising from the treatment and/or providing effective pain control. Intraoperative administration of bupivacaine, one of the long-acting local anesthetic agents, into paravertebral muscle kits is one of the ways to achieve this goal. However, while positive results have been reported in the literature comparatively such as the decrease in need for parenteral opioids and the reduced duration of postoperative hospitalization after the administration of perioperative bupivacaine into the muscle, [9] some studies have reported that the administration of intraoperative long-acting local anesthetic agents and combined corticosteroid preparations for lumbar microdiscectomy do not affect the pain that can be observed in the postoperative period or that this issue is not adequately explained [10].

In this retrospective study, it was aimed to find an answer to the question of whether the need for drugs such as narcotic analgesics such as postoperative morphine sulfate or pethidine hydrochloride and/or NSAIDs such as dexketoprofen trometamol could be reduced in lumbar microdiscectomy operations, in the cases where bupivacaine was applied and not applied into intraoperative paravertebral muscle tissues.

## Materials and Methods

### *Ethics permission*

Approval has been obtained from both the hospital management and the local ethics committee of the School of Medicine of Izmir Bakircay University (date: 30.03.2022, number: 555) to conduct this retrospective, cross-sectional study.

### *Inclusion and exclusion criteria of the cases*

The files of the cases, who were diagnosed with lumbar disc hernia after physical examination, neurological examination, electrophysiological examinations, and radiological imaging and not responsive to medical and physical

treatment applications and whose treatment with the surgical intervention was decided, were accessed and evaluated after archive research. The patients who had single-distance lumbar microdiscectomy and/or sequestrectomy were included in the study. The patients who had two or more discectomies with wider incisions, who had instrumentation with discectomy, who had liver and kidney dysfunction, who were allergic to narcotic analgesics such as bupivacaine morphine sulfate or pethidine hydrochloride, and/or pharmaceuticals such as NSAIDs and dexketoprofen trometamol were excluded from the study.

The sample size was determined using "G\*Power (3.1.9.4 version) [11, 12]. Reaching the required number of files according to the sample calculation was determined as the primary endpoint of the study.

### *Visual Analog Scale (VAS)*

When the archive files were examined, it was found that VAS was used to determine pain levels. The validity and reliability study of this scale, with "0= no pain" and "10=unbearable pain" on the pain scale, was based on the study of Price et al. [13].

### *Study design*

The lumbar disc herniation cases with similar age, sex, body weight, disc herniation level, preoperative pain score, and preoperative analgesic use history between 01.06.2020 – 31.06.2021 were included in the study (n=48). The control group of the study consisted of cases who did not receive paravertebral intramuscular bupivacaine during single-level lumbar microdiscectomy operations under general anesthesia and named as group 1 (n=24). The study group of the study consisted of cases who were administered preoperative paravertebral intramuscular bupivacaine and named group 2 (n=24). After the operation, the assessment of pain with the frequency of need for morphine sulfate or pethidine hydrochloride was performed using the VAS.

### *Statistical analysis*

Minitab 22.0 version software was used to assess the obtained data. Estimated power was 0.80, alpha (margin of error): 0.05, effect size was 0.4. Accordingly, the sample size was determined as 40 for the statistical test. All files (48 files) were included in the study, as the number of files remaining after assessing all the files according to the exclusion criteria. Intergroup comparisons of the data studied at the 95% confidence interval were assessed with a one-way analysis of variance (ANOVA). Then, the Pearson correlation (r) test was used to determine whether there is a linear relationship between two numerical measurements and, if so, to determine the direction and severity of this relationship. Alpha significance value was accepted as <0.01.

## Results

The findings of the data obtained as a result of the statistical assessments of the archival data were presented in the tables (Table 1, and Table 2).

**Table 1.** Findings of intergroup comparison of descriptive statistics.

Variable	Groups	N	Mean± StDev	Min	Max	SE Mean
Pre-op VAS	Group 1	24	8.58±0.50	8.00	9.00	0.10
	Group 2	24	8.58±0.83	7.00	10.00	0.17
Post-op VAS	Group 1	24	2.92±0.58	2.00	4.00	0.12
	Group 2	24	1.63±0.71	1.00	3.00	0.15
Post-op mobilization time (hours)	Group 1	24	9.50±2.45	6.00	12.00	0.50
	Group 2	24	6.33±2.14	4.00	12.00	0.44
Post-op narcotic analgesic requirement (mg)	Group 1	24	11.46±16.45	0.00	50.00	3.36
	Group 2	24	7.29±2.70	0.00	100.00	4.63
Post-op NSAIDs requirement (mg)	Group 1	24	64.58±12.59	50.00	75.00	2.57
	Group 2	24	51.04±13.75	25.00	75.00	2.81
Hospitalization (days)	Group 1	24	2.88±0.74	2.00	5.00	0.15
	Group 2	24	2.25±0.44	2.00	3.00	0.09

VAS: Visual Analogue Scale; NSAIDs: nonsteroidal anti-inflammatory drugs.

**Table 2.** Data of groups compared with one-way analysis of variance.

Variable	One-way ANOVA					Model Summary		
	Adj SS	Adj MS	F	P*	S	R-sq (%)	R-sq(adj) (%)	R-sq(pred) (%)
Pre-op VAS	0.00	0.00	0.00	1.00	0.69	0.00	0.00	0.00
Post-op VAS	20.0	20.02	47.3	0.00	0.65	50.71	49.64	46.33
Post-op mobilization time (hours)	120	120.33	22.8	0.00	2.29	33.09	31.63	27.14
Post-op narcotic analgesic requirement (mg)	208	208.30	0.5	0.47	19.82	1.14	0.00	0.00
Post-op NSAIDs requirement (mg)	2201	2200.50	12.7	0.00	13.18	21.58	19.88	14.62
Hospitalization (days)	4.69	4.69	12.6	0.00	0.61	21.49	19.78	14.51

\*P<0.01 was accepted as a statistical significance indicator. VAS: Visual Analogue Scale; NSAIDs: nonsteroidal anti-inflammatory drugs.

There was a weak and inverse relationship between age and post-op VAS scores, need for narcotic drug use, and length of stay, while there was a very weak but positive correlation between age and pre-op VAS scores, post-op mobilization time, and need for NSAIDs use. While there was a weak positive correlation between narcotic use and post-op VAS, a moderate positive correlation was observed between narcotic drug use and post-op mobilization times. It was reported that there was a moderate positive correlation between the use of NSAIDs and post-op VAS value and between the use of NSAIDs and post-op mobilization. It was observed that the correlation of post-op VAS with post-op mobilization time (r=0.609) and hospitalization time (r=0.603) was strong (Table 3).

The findings regarding the Pearson correlation coefficient demonstrating whether there is a linear relationship between two numerical measurements and, if so, the direction and the severity of this relationship (Figure 1).

**Discussion**

Lumbar disc herniation is one of the most common causes of low back and leg pain, and in most cases, the symptoms are relieved with medical treatment and physical therapy

without the need for any surgical intervention. Surgical treatment protocols are recommended for the patients with recurrent clinical findings, neurological deficits, and progression in their neurological deficits during their follow-up [14].

Postoperative pain continues to be an inevitable problem in neurosurgery practice in almost all branches [15]. Thanks to postoperative pain control, early recovery after surgery and shorter hospital stay are provided. In the prevention of post-surgical pain, it is important to detect and prevent the mechanisms that cause pain before it occurs.

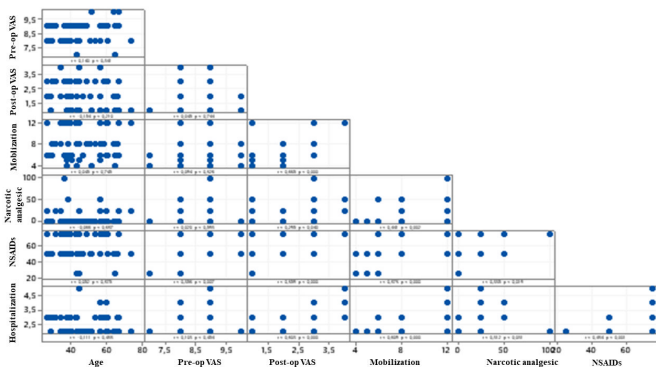
Various mechanisms and trauma can cause post-surgical pain. Invasive spine surgery causes intense pain. If post-operative pain management is inadequate, chronic pain and failed back surgery syndrome may occur [16].

Iatrogenic damage to the tissues after surgery reduces the pain threshold by activating the nociceptors of inflammatory substances. As a result, it causes peripheral sensitization by increasing signal transmission and central sensitization by increasing the excitability of neurons in the medulla spinalis. Increased central sensitization and hyperexcitability increase the severity of postoperative

**Table 3.** In intergroup comparisons, the presentation of the data of the Pearson correlation coefficient.

	Age	Pre-op VAS	Post-op VAS	Post-op mobilization	Narcotic analgesic	NSAIDs
Pre-op VAS	0.140					
Post-op VAS	-0.184	0.048				
Post-op mobilization (hours)	0.048	0.094	0.668			
Narcotic analgesic (mg)	-0.066	0.020	0.298	0.441		
NSAIDs (mg)	0.082	0.386	0.589	0.575	0.338	
Hospitalization (days)	-0.111	0.103	0.603	0.609	0.312	0.454

VAS: Visual Analogue Scale; NSAIDs: nonsteroidal anti-inflammatory drugs.



**Figure 1.** Findings of the Pearson correlation coefficient demonstrating whether there is a linear relationship between two numerical measurements, and if so, the direction and the severity of the relationship.

pain [17]. Narcotic analgesics and NSAIDs are frequently used to provide analgesia in the postoperative period. Narcotic analgesics have highly harmful side effects [18].

Despite recent research demonstrating the adverse effects and addiction potential of narcotics, opioids have remained as the main element of management in providing analgesia following spine surgeries. However, hyperalgesia, tolerance, and the side effects such as subsequent dependence limit the frequent use of opioids after surgery [19]. Not only opioid group analgesics but also non-opioidergic analgesics such as gabapentinoids and NSAIDs have many adverse events/side effects and their abuse is increasingly reported in the literature [20]. Posterior spinal fusion surgery is very painful and often significant amounts of opioids are required for adequate perioperative analgesia [21]. Due to the negative side-effect profiles of drugs and their addictive potential, scientists administer different drug mixtures or drugs in the perioperative period for postoperative analgesia.

The management of severe postoperative back and low back pain following spinal surgical procedures continues to be a challenge. Research is ongoing to find simple, efficient, and safe perioperative analgesia with low side effects [22].

Therefore, it was planned to research whether bupivacaine administered intraoperatively into the paravertebral mus-

cle mass reduces the need for postoperative narcotic analgesic drugs and/or NSAIDs.

It has been reported in a study on Zynrelef® (prolonged-release or extended-release bupivacaine/meloxicam), a synergistic fixed-dose combination of bupivacaine included in the local anesthetic group and meloxicam included in the NSAIDs group, that pain control is much better than normal applications [23]. It has been emphasized that it reduces the need for opioids after surgery and that this prolonged-release form of bupivacaine/meloxicam is a promising non-opioid treatment option for the management of postoperative pain [23].

It was reported in a study on three cases of adolescent idiopathic scoliosis who had intercostal liposomal bupivacaine [24] that the optimal anesthetic technique, including the preferred management of postoperative pain, is unknown. It was determined that paravertebral anesthetic agent use administered during lumbar disc surgery was effective in postoperative pain control in this study in accordance with the literature.

In the study of Yesiltas et al. [22] in which they randomly divided 56 consecutive adult patients, having posterior spinal instrumentation and fusion for spondylolisthesis, into two groups, the study (erector spinae plane block) group (n = 28) received intraoperative freehand bilateral ESPB with a 20-mL mixture solution of 0.25% bupivacaine and 1.0% lidocaine equally divided into all operating levels. In the control group (n = 28), 20 mL physiological saline was injected. Postoperatively, they ordered 1 g paracetamol thrice/day, besides patient-controlled analgesia pumps with morphine [22]. They performed a postoperative evaluation with a VAS, morphine consumption, ESPB-related adverse effects, and postoperative length of hospital stay (PLOS) [22]. Morphine consumption was significantly higher in the controls within the first postoperative 24-hour 44.75 ± 12.3 mg versus 33.75 ± 6.81 mg in the ESPB participants (P < 0.001). Except for postoperative 24th-hour VAS (P = 0.127), all postoperative VAS scores recorded at all time-points were significantly higher in the controls (P < 0.05). In control individuals, the first analgesic demand time was shorter, and PLOS was longer (P < 0.001). Patient satisfaction was significantly higher in the ESPB group. They observed no significant difference regarding postoperative complications [22].

Mirzai et al. [10] administered 20 ml of 0.9% saline to the

subcutaneous tissue and paravertebral muscle tissue of 22 patients at the end of the operation in their study, in which they performed unilevel and unilateral lumbar discectomy, and classified this group as group 1. They administered 20 ml of 0.25% bupivacaine and 40 mg of methylprednisolone to the subcutaneous and paravertebral muscle tissues of the other cases and named it group 2. At the end of their study, they suggested that perioperatively administered bupivacaine together with methylprednisolone was an effective method for postoperative pain control and reduced opioid use [10].

Cherian et al. [25] reported that parenteral narcotic administration is the main element of pain management to relieve postoperative pain in patients undergoing lumbar laminectomy. In their study, they emphasized that adverse events such as respiratory depression and nausea may be experienced in the cases for which narcotic analgesic drugs are administered [25]. It was concluded that all the 21 placebo recipients required analgesics in the first 9 hours postoperatively, compared to only 11 of 24 patients who received bupivacaine ( $P < 0.001$ ). In addition to all these, they emphasized that bupivacaine is a safe and effective method for local wound infiltration, relief of postoperative pain, and reduction of narcotic use in the patients undergoing lumbar laminectomy [25].

Perera et al. [26] found in their systematic review and meta-analysis involving 11 publications and 438 patients that postoperative intramuscular local anesthetic infiltration reduced postoperative analgesic requirements and the duration until the first analgesic demands in the patient's lumbar spine surgery.

In this study, it was found in accordance with the literature that the administration of preoperative paravertebral intramuscular bupivacaine significantly reduced the need for postoperative analgesics in the patients who underwent single-level lumbar microdiscectomy. Samoladas et al. [27] reported that postoperative pain management following lumbar discectomy was important and that different pharmacological agents containing a wide range of agents were used in postoperative pain protocols worldwide in daily practice. In their study, they randomly divided sixty patients who had lumbar discectomy into two groups [27]. They named the patients that they treated with 3 mg betamethasone acetate and 18 mg ropivacaine as group A and the patients with normal saline as group B [27]. They reported that infiltration was performed immediately after discectomy and decompression and just before the incision was closed. They stated that they followed a standard intravenous acetaminophen administration and physiotherapy protocol after the surgery and that additional analgesia was administered with tramadol in postoperative pain-resistant cases despite only acetaminophen [27]. They reported that no case in Group A needed more narcotic analgesic drugs in addition to acetaminophen analgesia, while 12 cases in the placebo group (group B) needed tramadol treatment in more posology ( $P < 0.01$ ). They emphasized that the administration of betamethasone and ropivacaine was effective but the duration of action was short [27].

However, it is also known in the literature that this effect is controversial in the local area block for postoperative analgesia, although the synergistic effect of bupivacaine

and clonidine administration is well known in peripheral nerve blocks [28].

In our study, post-op VAS score, post-op mobilization time, post-op NSAIDs Requirement, and length of hospital stay were found to be statistically significantly reduced in the patients in group 2 who had unilateral lumbar microdiscectomy and preoperative paravertebral bupivacaine injection compared to those who didn't have any paravertebral intramuscular injection ( $P < 0.01$ ). However, although the need for post-op narcotic drug use was found to be less in the patients in group 2, this result was reported to be statistically insignificant ( $P > 0.01$ ). Also, it was determined that there was a moderate and positive relationship between the use of NSAIDs and the post-op VAS value, and between the use of NSAIDs and post-op mobilization.

As for limitations, in a retrospective study, some file data may be missing, especially from follow-up. In addition, the research was conducted in a single center.

## Conclusion

In current neurosurgery practice, postoperative pain after lumbar disc surgeries is one of the important problems that clinicians work hard to solve. Problems such as the side effects, prolonged hospitalization, postoperative mobilization, and delayed return to work-life that can be observed due to the pharmacological agents administered to provide analgesia and/or control the pain have increased the importance of pain control. For this purpose, it is suggested that intramuscular local anesthetic applications to be applied peri-operatively, especially during lumbar disc surgeries, may be an effective method for pain control in the postoperative period. However, to make this evident, prospective, placebo-controlled, and randomized studies including different races and involving more cases are needed.

## Ethics approval

Approval has been obtained from both the hospital management and the local ethics committee of the School of Medicine of Izmir Bakircay University (date: 30.03.2022, number: 555) to conduct this retrospective, cross-sectional study.

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