

The Effect of Local Anesthetic Agent Infiltration Around Nephrostomy Tract On Postoperative Pain Control After Percutaneous Nephrolithotomy: A single-centre, randomised, double-blind, placebo-controlled clinical trial

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Purpose: Insufficient alleviation of pain after percutaneous nephrolithotomy causes patient dissatisfaction and generates additional morbidity factors by preventing early mobilization. This study investigated the effects of bupivacaine infiltration with two different doses around the nephrostomy tract after percutaneous nephrolithotomy.

Materials and Methods: Patients who underwent subcostal single entrance percutaneous nephrolithotomy were randomly divided into 3 groups of 20 patients. While the first and second group were planned to receive bupivacaine at rates of 0.5% and 0.25% respectively, the third group was planned to receive a placebo agent to preserve the doubly blinded nature of the study.

Results: A statistically significant difference was found in the number of patients using tramadol. The frequency of analgesic administration was found lower in the two groups that received bupivacaine in comparison to the group that did not, while the time of the first analgesic administration in the group that received high dose bupivacaine was significantly later than the other groups. Although there was no difference between the groups in terms of total amount of analgesic usage, patients who received higher concentrations of bupivacaine were likely to require a lower amount of narcotic agent. The frequency of analgesic administration decreased significantly in patients of both groups that received bupivacaine. Moreover, by administering bupivacaine at a 0.5% rate, fewer patients (50%) required narcotic analgesia and the first time of analgesic administration was found to be significantly later.

Conclusion: Administering bupivacaine at a 0.5% rate around the nephrostomy tract after surgery was demonstrated to be more effective.

Keywords: percutaneous nephrolithotomy; postoperative pain; bupivacaine.

INTRODUCTION

Urinary system stone diseases are the third most frequent reasons of urological complaints following urinary tract infections and prostate pathologies⁽¹⁾. Nephrolithiasis is a highly prevalent disease worldwide with rates in the range of 7-13% in North America, 5-9% in Europe, and 1-5% in Asia⁽²⁾. In terms of urinary system stones, Turkey is considered endemic and the occurrence rate in the population of the ages 18 to 70 is 11.1%⁽³⁾. PNL is an endoscopic method that is used frequently in kidney stone treatment, while its success rate is high, morbidity is low and duration of hospitalization is considerably short in comparison to open surgery⁽⁴⁾. After Rupel and Brown removed the obstructive stone from the nephrostomy path they created surgically, Fernström and Johansson defined the new stone surgery method they named as percutaneous pyelolithotomy in 1976⁽⁵⁾. The advancements in technique and the tools used in operations allowed urologists to remove stones percutaneously with increased success and reduced complications⁽⁶⁾. The alleviation of the pain based on renal entrance dilatation or nephrostomy catheter after PNL may be achieved with various painkillers from simple nonsteroidal anti-inflammatory drugs to narcotic analgesics. Prevalent usage of narcotics for pain control after surgery has brought about issues such as respira-

tory depression. However, in the case of inadequate pain management, in addition to the discomfort of the patients, there is a possibility of additional morbidity factors and increased treatment costs by obstruction of mobility in the short-term⁽⁷⁾. Balanced analgesia administration gained importance in terms of increasing the activity of postoperative pain treatment, and especially, minimizing the side effects of narcotic drugs^(8,9). With this purpose, combined administration of narcotic drugs and nonsteroidal anti-inflammatory drugs or techniques used with local anesthesia, brought about reduction in side effects related to narcotic drugs and increase in quality of analgesia⁽¹⁰⁾. As for all local anaesthetics, the mechanism of action of the bupivacain is based on their ability to reversibly inhibit voltage-gated sodium channels in nervous fibres. This inhibition occurs in a manner that is both time dependent and voltage dependent and results in an increased threshold for activating the action potential, reducing the propagation of the electric impulse along the nerve fibres with complete block of their function. The most rapid onset but the shortest duration of action occurs after intrathecal or subcutaneous administration of local anesthetics. These differences in the onset and duration of anesthesia and analgesia are due in part to the particular anatomy of the area of injection, which will influence the rate of diffusion and

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Table 1. Preoperative signs of the individuals in the groups

	Group HB n:20	Group LB n:20	Group PA n:20	p
Age Mean ± SD (Min - Max)	51.9 ± 10.5 (33 – 68)	50.7 ± 7.8 (40 – 64)	44.1 ± 13.4 (26 – 75)	0.059
Gender (n)				
Male	11	12	10	0.817
Female	9	8	10	
Body Mass Index Mean ± SD (Min - Max)	29 ± 4.9 (19 – 39.5)	28.5 ± 5.8 (21.3 – 47.2)	28.8 ± 5.1 (21.3 – 40.8)	0.954
Stone burden (mm ²) Mean ± SD (Min - Max)	428 ± 224 (160 – 897)	399 ± 192 (134 – 899)	376 ± 244 (90 – 898)	0.531
Stone Hounsfield Mean ± SD (Min - Max)	1162 ± 366 (340 – 1730)	1115 ± 398 (288 – 1781)	1058 ± 375 (320 – 1532)	0.687
Operation side				
Right	8	12	11	0.420
Left	12	8	9	
Stone opacity				
Opaque	18	20	18	0.343
Non-opaque	2	0	2	
Stone location				
Upper calyx	0	1	0	0.316
Middle calyx	0	3	1	
Lower calyx	7	5	9	
Renal pelvis	13	11	10	

Abbreviations: SD, Standard deviation; Min, Minimum; Max, Maximum; n, number; HU, hounsfield unit.

vascular absorption and, in turn, affect the amount of local anesthetic used for various types of regional anesthesia⁽¹¹⁾. This study aimed to investigate the postoperative pain management effects of two different dosages of bupivacaine, which is a long-acting local anesthetic agent, that we administered after the PNL operation we carried out for kidney stone treatment; the literature was reviewed, and the effectiveness of local anesthetics in similar studies were analyzed.

PATIENTS AND METHODS

Study population

The study included 60 patients over the age of 18 between January 2015 and April 2016 who were given subcostal single percutaneous entry at the urology clinic of Cumhuriyet University Research and Application Hospital with body mass index of 35 kg/m² or lower, with a stone burden of lower than 900 mm², with an operation duration of shorter than 3 hours whose one-sided kidney interventions were planned. The study excluded patients with coagulation disorders, heart, respiration or kidney diseases, bupivacaine allergies, those with supracostal or multiple percutaneous entry, those given bilateral simultaneous PNL, and those who did not agree to participate. This study was conducted with the approval of Cumhuriyet University Clinical Research Ethics Board (decision no: 2015-01/01) and by informing the patients in written and verbal form. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Study design

This was a single-center, prospective, randomized-controlled, and double-blind study. The cases were randomly distributed into 3 groups of 20 people with the method of sealed envelopes. While the first and second group were planned to receive bupivacaine (Marcaine; Zentiva, Kırklareli, Turkey) at rates of 0.5% (100 mg/20 ml) and 0.25% (50 mg/20 ml) respectively, the third group was planned to receive a placebo agent (saline) to preserve the doubly blinded nature of the study. We named the groups as: Group High dose Bupivacaine (HB), Group Low dose Bupivacaine (LB) and Group Placebo Agent (PA).

Anesthesia

Anesthesia was induced (propofol 2–3 mg/kg, fentanyl 1 µg/kg, rocuronium 0.5 mg/kg IV) followed by endotracheal intubation. Controlled ventilation was provided with oxygen, nitrous oxide (50:50), sevoflurane (2% dial setting), 1 L/minute fresh gas flow.

Surgical technique

Renal capsule – skin distances of all patients were measured in their preoperative unenhanced computer tomography. After the PNL operation was carried out under general anesthesia, 20 Fr Malecot-nephrostomy catheters were placed. In the first and second groups; before removing the nephrostomy sheath, infiltration was made using a 25-gauge spinal anesthesia needle in a homogenous way from the renal capsule to the skin for 5 ml in each of the 4 quadrants right near the nephrostomy tract. Attention was paid for the needle to enter in parallel to the nephrostomy tract and perpendicular to the skin, as much as the renal capsule – skin distance. The third group was not given any local anesthetic agents (**Figure 1**).

Table 2. Perioperative signs of the individuals in the groups

	Group HB	Group LB	Group PA	p
Operation time Mean ± SD (Min - Max)	63.6 ± 24.6 (35 – 120)	61.4 ± 17.8 (30 – 90)	74.8 ± 35.4 (30 – 165)	0.251
Fluoroscopy time (second)	253.1 ± 157.5 (89 – 792)	251.8 ± 127.2 (92 – 580)	290.0 ± 195.6 (45 – 900)	0.702
Creatinine change (mg/dL)	0 ± 0.2 (-0.3 – 0.3)	0 ± 0.2 (-0.3 – 0.4)	0 ± 0.2 (-0.5 – 0.2)	0.291
Hemoglobin change (g/dL)	-1.1 ± 1.0 (-4.0 – 0)	-1.4 ± 0.9 (-3.1 – 0.6)	-1.4 ± 1.3 (-5.3 – 0.1)	0.487
Nephrostomy removal time (day)	3.0 ± 0.5 (2.0 – 4.0)	3.3 ± 0.5 (3.0 – 4.0)	3.3 ± 0.6 (3.0 – 5.0)	0.126
Hospitalization time (day)	3.6 ± 0.8 (3.0 – 6.0)	3.9 ± 0.9 (3.0 – 7.0)	4.2 ± 1.1 (3.0 – 6.0)	0.090

Abbreviations: SD, Standard deviation; Min, Minimum; Max, Maximum.

Table 3. VAS and DVAS values of the groups

	Group HB	Group LB	Group PA	p
VAS2 Mean ± SD (Min - Max)	3.3 ± 3.0 (0 - 9)	4.5 ± 2.9 (0 - 10)	6.5 ± 2.8 (0 - 10)	0.004*
VAS4 Mean ± SD (Min - Max)	3.1 ± 3.0 (0 - 9)	3.2 ± 2.7 (0 - 10)	3.9 ± 2.3 (0 - 7)	0.567
VAS6 Mean ± SD (Min - Max)	2.6 ± 2.5 (0 - 7)	2.8 ± 2.2 (0 - 8)	3.8 ± 3.0 (0 - 10)	0.327
VAS8 Mean ± SD (Min - Max)	2.0 ± 1.7 (0 - 6)	2.2 ± 2.3 (0 - 9)	2.7 ± 2.6 (0 - 9)	0.810
VAS12 Mean ± SD (Min - Max)	1.1 ± 1.0 (0 - 3)	1.7 ± 2.0 (0 - 8)	1.3 ± 1.3 (0 - 4)	0.795
VAS24 Mean ± SD (Min - Max)	0.7 ± 0.7 (0 - 2)	1.0 ± 1.2 (0 - 4)	0.8 ± 1.2 (0 - 3)	0.626
DVAS2 Mean ± SD (Min - Max)	3.9 ± 3.1 (0 - 9)	5.0 ± 2.9 (0 - 10)	7.3 ± 2.8 (0 - 10)	0.002*
DVAS4 Mean ± SD (Min - Max)	3.8 ± 3.3 (0 - 10)	3.9 ± 2.8 (0 - 10)	5.0 ± 2.4 (0 - 9)	0.273
DVAS6 Mean ± SD (Min - Max)	3.3 ± 2.8 (0 - 8)	3.9 ± 2.3 (0 - 9)	4.7 ± 3.0 (1 - 10)	0.261
DVAS8 Mean ± SD (Min - Max)	2.7 ± 1.9 (0 - 7)	3.1 ± 2.5 (0 - 10)	3.7 ± 2.5 (0 - 10)	0.437
DVAS12 Mean ± SD (Min - Max)	1.8 ± 1.0 (0 - 4)	2.4 ± 2.1 (0 - 9)	2.4 ± 1.3 (0 - 5)	0.430
DVAS24 Mean ± SD (Min - Max)	1.2 ± 1.1 (0 - 3)	1.6 ± 1.4 (0 - 4)	1.3 ± 1.6 (0 - 4)	0.679

Abbreviations: VASx, Visual Analogue Scale score at time “x”; DVASx, Dynamic Visual Analogue Scale score at time “x”; SD, Standard deviation; Min, Minimum; Max, Maximum; * $p < 0,05$, significant.

Outcome assessment

Postoperative pain levels at rest were assessed using the Visual Analogue Scale (VAS), and dynamic VAS (DVAS) was used to assess the level of pain during coughing and deep breathing. The patients were asked to evaluate their pain with VAS and DVAS under the supervision of our clinical nurses who were blind to the study. On a need-basis, the suitable analgesic was given to the patient in the following way: if the greater of the VAS or DVAS scores is higher than 4 (≥ 5), 1mg/kg tramadol (Contramal; Abdi İbrahim, Istanbul, Turkey), and if it is lower than 5, 50 mg diklofenac (Dikloron; Deva, Tekirdağ, Turkey) were given. The maximum dosage was determined as 400 mg/day for tramadol and 150 mg/day for diclofenac.

In addition to the patients' sociodemographic information, localization of their stones, stone load, operation time, fluoroscopy duration, preoperative hemoglobin and creatinine values, and VAS and DVAS scores in the 2nd, 4th, 6th, 8th, 12th and 24th hours were recorded. Time of the first analgesic use, analgesic requirement, amount of analgesics administered, and concomitant analgesic doses were also recorded. Postoperative complications were assessed according to the Modified Clavien Classification.

The data obtained in our study were coded into the SPSS 22.00 software, and in the analysis of the data; when normal distribution assumptions were satisfied (Kolmogorov-Smirnov), for difference analyses, F Test was used in variables with more than two groups and independent samples t-test was used for variables with two groups; when normal distribution assumptions were not satisfied, Kruskal-Wallis Test was used in variables with more than two groups and Mann-Whitney Test was used in variables with two groups. In the difference analyses of categorical variables, the Chi-Squared test of association was used. The statistical analyses were interpreted in a 95% confidence interval.

RESULTS

No significant differences were found in terms of age, BMI, stone size and placement among the 3 groups consisting of sixty patients including thirty-three men and twenty-seven women. **Table 1** shows the distribution and demographic data of the groups. The mean durations of operation for the groups were 63.6, 61.4 and 74.8 minutes respectively, while the mean fluoroscopy durations were calculated respectively as 253.1, 251.8 and 290 seconds. No significant differences were found among the groups in terms of operation and fluoroscopy



Figure 1. Bupivacaine infiltration near the nephrostomy tract, into 4 quadrants (A: Marking 4 quadrants around the renal capsule; B, C, D, E: 5ml bupivacaine infiltration into the quadrants; F: fixation of nephroureterostomy to the skin with no. 1 silk suture)

Table 4. Analgesic implementation frequency and first analgesic implementation time (min) of the groups

	Group HB	Group LB	Group PA	p
Analgesic implementation frequency Mean ± SD (Min - Max)	1.40 ± 0.82 (0 - 3)	1.60 ± 1.05 (0 - 4)	2.35 ± 0.88 (1 - 5)	0.002*
First analgesic implementation time (min) Mean ± SD (Min - Max)	86 ± 98 (25 - 360)	44 ± 21 (20 - 100)	40 ± 18 (15 - 100)	0.033*

durations ($P > .05$). While no difference was observed among the groups in preoperative and postoperative hemoglobin and serum creatinine values, removal of nephrostomy catheters and hospital discharge times were found similar. The perioperative data of the patients are summarized in **Table 2**.

When the pain levels of the patients were analyzed using VAS and DVAS in the 2nd, 4th, 6th, 8th, 12th and 24th hours, significant differences were found only in the values measured in the 2nd hour, and no significant difference was found in values measured at other times (**Table 3**).

The mean usage of diclofenac in case the greater of the VAS and DVAS scores was < 5 was found as 42.1, 37.5 and 35.0 mg respectively in the groups HB, LB and PA. In case the greater of the VAS or DVAS scores was ≥ 5 , the mean tramadol usage was found 52.4, 83.6 and 100.6 mg in the groups. No significant difference was found between the diclofenac and tramadol usage amounts in the groups (respectively $p = .543$, $p = .066$).

However, a statistically significant difference was found in the numbers of patients using tramadol among the groups ($p = .029$). While 17 patients in Group PA and 16 in Group LB needed analgesics to require tramadol, only 10 patients were given tramadol in Group HB. In terms of analgesic implementation frequency and the time of applying the first analgesics, there was a significant difference (respectively $p = .002$, $p = .033$). In the subgroup analysis in terms of analgesic implementation frequency while differences were found between the Groups HB and PA ($p1-3 = .002$) and the Groups LB and PA ($p2-3 = .009$), no difference was found between the Groups HB and LB ($p1-2 = .640$). In terms of the first time of analgesic implementation, there were differences between the Groups HB and PA ($p1-3 = .009$) and the Groups HB and LB ($p1-2 = .047$), but not between the Groups LB and PA ($p2-3 = .557$) (**Table 4**). Comparison of postoperative complications in terms of the Modified Clavien Classification between the groups did not indicate any significant difference ($p > 0.05$).

Table 5. Studies on activity of a local anesthetic agent in similarity to our study

Author Year	Anesthetic Dose	VAS / DVAS Times	Groups: Applications	(n)	Analgesic agent	Outcomes	Effect	Result
Ugras 2007 (13)	R 0.02 %	2, 6, 24	1: 30 ml R 2: 30 ml S	16 18	Metamizole	VAS 6 / PEF 2, 6 FAT TAA AAF	:(+) :(+) :(+) :(+)	(+)
Haleblian 2007 (14)	B 0.25 %	2, 4, 24, 48	1: 1.5 mg/kg B 2: 60 ml S	10 12	Narkotic	VAS TAA	:(-) :(-)	(+/-)
Jonnavithula 2009 (15)	B 0.25 %	2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24 / Same	1: 20 ml B 2: none	20 20	Tramadol	VAS FAT TAA AAF	:(+) :(+) :(+) :(+)	(+)
Parikh 2011 (16)	B 0.25 %	0, 0.5, 1, 1.5, 2, 4, 6, 8, 12, 16, 20, 24 / Same	1: 20 ml B 2: 20 ml S	30 30	Tramadol	FAT TAA AAF	:(+) :(+) :(+)	(+)
Parikh 2013 (17)	R 0.25 %	0, 0.5, 1, 1.5, 2, 4, 6, 8, 12, 16, 20, 24 / Same	1: 10 ml R 2: 10 ml S	30 30	Tramadol	VAS FAT TAA AAF	:(+) :(+) :(+) :(+)	(+)
Tüzel 2014 (18)	L 0.25 %	2, 4, 6, 8, 12, 24	1: 75 mg/30 ml L 2: 30 ml S	23 23	Meperidine	VAS FAT TAA AM	:(-) :(+) :(-) :(-)	(-)
Gokten 2011 (20)	L 0.25 %	6, 24	1: (SP) 20 ml S+P 2: (LP) 20 ml L+P 3: (LS) 20 ml L+S	20 20 20	Meperidine	VAS AAF MOB TAA	:(LP+) :(LP+) :(LP+) :(LP+)	Levobupivacain + parasetamol (+)
Parikh 2013 (21)	R 0.25 %	0.5, 1, 1.5, 2, 4, 6, 8, 12, 16, 20, 24 / Same	1: (R) 20 ml R + 0.5 ml distile water 2: (Rm) 20 ml R + 0.5 ml (5 mg) m	30 30	Tramadol	VAS/DVAS FAT AAF TAA	:(Rm+) :(Rm+) :(Rm+) :(Rm+)	Ropivacain + morphine (+)
Nirmala 2015 (22)	B 0.25 %	4, 8, 12, 16, 20, 24	1: (B) 20 ml B 2: (Bb) 20 ml B + 100 µg b	20 20	Tramadol	VAS/DVAS AAF TAA	:(Bb+) :(Bb+) :(Bb-)	Bupivacaine + buprenorphine (+)

Abbreviations: B, Bupivacaine; R, Ropivacaine; L, Levobupivacaine; S, Salin; P, Parasetamol; m, morphine; b, buprenorphine; TAA, Total analgesic amount; AAF, Analgesic administration frequency; FAT, First analgesic administration time; MOB, mobilization; AM, Ambulation time; PEF, Peak expiratory flow; (+), Effective; (-), Not effective; (+/-), Partially effective

DISCUSSION

Postoperative pain is an outcome of the inflammation that occurs as a result of tissue damage, and management of this pain is a critical component of the operation⁽¹²⁾. While narcotic analgesics are one of the main options for postoperative pain management, their usage for analgesia is limited after major surgical interventions due to their adverse effects. Thus, narcotic analgesics that are accepted as a standard option in treatment of acute postoperative pain are now being replaced by the method of multimodal analgesia. With the help of this approach, synergic effects are obtained by the usage of different drugs that influence the central and peripheral nervous systems. Additionally, lower amounts of side effects may be achieved in comparison to analgesia using a single agent⁽¹³⁾. Since Ugras et al.'s⁽¹⁴⁾ first analgesic application with ropivacaine in the percutaneous tract to our time, similar studies have been conducted with different local anesthetics. Most of these studies investigated the activity of a single molecule⁽¹⁴⁻¹⁹⁾. Parikh et al. compared the activities of bupivacaine and ropivacaine in 2014⁽²⁰⁾. In addition to these, there are also studies that measured the activities of local anesthetic substances in combination of added molecules (such as paracetamol, morphine, buprenorphine)⁽²¹⁻²³⁾. A large part of the studies that involved administration of local anesthetic agents into the nephrostomy tract used the local anesthetic with long-lasting effects bupivacaine and its 0.25% concentration. While this molecule's positive effects by administration into the percutaneous entrance pathway are known in general, its 0.5% form was not administered into the nephrostomy tract, and there is a dearth of data on which concentration is effective or if so, which is more effective.

The studies in the literature investigating the activity of a local anesthetic agent are summarized in Table 5. In a study where 0.02% ropivacaine was applied to the nephrostomy tract and the skin and methimazole was used as a recovery analgesic on 34 patients, in the group given local anesthesia, the VAS values and total analgesic amounts were lower in the 6th hour, the first time of analgesia was later, and analgesia application frequency was lower. It was also asserted that parenteral methimazole administration in combination with ropivacaine application to the surgical area decreased postoperative pain and the amount of analgesics used, and additionally, it improved respiration by increasing peak expiratory flow⁽¹⁴⁾. In another study, in a series of 22 patients where bupivacaine was applied to the postoperative nephrostomy tract, the VAS values and total analgesic amounts did not differ in comparison to the control group, but there was a tendency found in the patients in the local anesthetic group in terms of lowered usage of narcotic anesthetics⁽¹⁵⁾. In similar studies where 0.25% bupivacaine was administered to the nephrostomy tract in which recovery analgesia was achieved with 1 mg/kg intravenous tramadol; in patients with bupivacaine administration, VAS scores were lower, first analgesia time was later, total analgesics amount and analgesia frequency were lower^(16,17). Similar results were reached with 0.25% ropivacaine applied to the nephrostomy tract in combination with ultrasound⁽¹⁸⁾. In another study with 46 patients investigating the activity of levobupivacaine where recovery analgesia was achieved with meperidine; the time of first analgesia was found to be later in comparison to the control group, no signif-

icant difference was found between the group in terms of VAS scores, total analgesic amounts and ambulation time⁽¹⁹⁾.

Among the 6 studies where local anesthetic agents were applied singly and analyzed for activity, 3 used bupivacaine, 2 used ropivacaine and 1 used levobupivacaine, while bupivacaine was always used in a concentration of 0.25%. The 2nd hour VAS and DVAS scores of the first group with 0.5% bupivacaine concentration and the second group with 0.25% bupivacaine concentration in our study were found significantly lower than those in the third group with no intervention. On the other hand, no significant differences were found among the groups in terms of VAS and DVAS scores measured after the 2nd hour. In addition to studies that showed local anesthetic substance infiltration into the PNL tract did not affect VAS scores^(15,19), there are also those that reported significant decreases in VAS scores (16,18). In Ugras et al.'s study, only the VAS in the 6th hour was found significantly lower⁽¹⁴⁾. In this study, the VAS and DVAS scores were mostly lower in the groups given bupivacaine, but the difference was statistically significant only in the VAS scores measured in the 2nd hour. In most studies where a single local anesthetic substance is infiltrated into the nephrostomy tract, data were presented towards lowered total analgesics requirement^(14,16-18). In two similar studies, no significant change was found in the total analgesic amounts used in the postoperative period as a result of local anesthetic infiltration^(15,17). The difference among the groups in our study was found insignificant in terms of the amounts of diclofenac and tramadol used. What is noteworthy here is that diclofenac usage decreased and tramadol usage increased along the way from Group HB to Group PA. The patients given 0.5% bupivacaine infiltration required almost half of the tramadol given to the patients to whom no infiltration was given. Additionally, there was a tendency for lower tramadol requirement for patients given the higher concentration of bupivacaine. Another interesting issue in our study was that the difference among the groups in terms of the patients who required tramadol was found to be statistically significant. By giving bupivacaine in a concentration of 0.5%, fewer patients (17 versus 10 patients) needed narcotic analgesics.

There are data suggesting that the first analgesic agent is administered in a later postoperative period with local anesthetic substance infiltration into the percutaneous tract (14,16-19). In this study, when bupivacaine was given in the concentration of 0.5%, the first analgesic administration time was found to be significantly later. However, when bupivacaine was given in the dosage of 0.25%, while this time was later than the control group (as in the dosage of 0.5%), the difference was not statistically significant.

In a study that compared the administration of 0.25% bupivacaine and 0.25% ropivacaine into the nephrostomy tract with the guidance of ultrasonography, it was found that the VAS scores in the 6th and 8th hours were significantly lower and the times of first analgesia were significantly later in the group given ropivacaine. While the total amount of analgesics and analgesia frequency were lower in the group given ropivacaine, the difference between this group and the group given bupivacaine was not found statistically significant⁽²⁰⁾. In addition to the infiltration of a local anesthetic agent

into the percutaneous tract, studies where these are combined with different molecules also reported in general that VAS and DVAS scores were lower, the first time of analgesia was later, and the total analgesics amount and analgesia frequency were lower⁽²¹⁻²³⁾.

There are also studies demonstrating that intercostal or paravertebral blockage with bupivacaine and thoracic paravertebral blockage with levobupivacaine applied for pain management after PNL increased patient satisfaction, decreased usage of narcotic analgesics, and achieved good perioperative analgesia with minimal side effects⁽²⁴⁻²⁶⁾.

The limitation of our study was that we included patients with single punctures with a single nephrostomy tube, thus being unable to evaluate the efficacy of our study when more than one puncture was involved. Moreover, other long-acting agents with different doses would be likely to provide further benefit and should be evaluated.

CONCLUSIONS

Our study reached the conclusion that bupivacaine, which is a local anesthetic agent with long-lasting effects, decreased the pain scores only in the second postoperative hour. While no significant difference was found among the groups in terms of the total amount of analgesics used, there was a tendency to need lower amounts of narcotic analgesia in patients provided with the higher concentration of bupivacaine. The analgesic administration frequency was reduced significantly in both dosages of bupivacaine. Moreover, with the 0.5% concentration of bupivacaine, fewer patients (50%) needed narcotic analgesia, and their first time of analgesia was found to be significantly later. In conclusion, administering bupivacaine at a 0.5% rate around the nephrostomy tract immediately after surgery was demonstrated to be more effective than lower dose bupivacaine.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

REFERENCES

- Smith LH. The medical aspects of urolithiasis: an overview. *J Urol.* 1989 Mar;141(3 Pt 2):707-10.
- Sorokin I, Mamoulakis C, Miyazawa K, Rodgers A, Talati J, Lotan Y. Epidemiology of stone disease across the world. *World J Urol.* 2017 Feb 17.
- Musulmanoglu AY, Binbay M, Yuruk E, et al. Updated epidemiologic study of urolithiasis in Turkey. I: Changing characteristics of urolithiasis. *Urol Res*, ;39:309-14, 2011.
- Wein AJ, Kavoussi LR, Novick AC, et al. Chapter 47: Percutaneous Approaches to the Upper Urinary Tract Collecting System, *Campbell-Walsh Urology.* Elsevier Saunders, Philadelphia, 10th edition, 1324-56, 2012.
- Fernström I ve Johanson B. Percutaneous pyelolithotomy: A new extraction technique. *Scand J Urol Nephrol*, 1976; 10:257-259.
- Lingeman JE, Newmark JR, Wong MYC. Classification and management of staghorn calculi, Smith AD (ed.) *Controversies in Endourology.* WB Saunders, Philadelphia, p:136-144, 1995.
- White PF, Rawal S, Latham P, et al. Use of a continuous local anesthetic infusion for pain management after median sternotomy. *Anesthesiology*, 2003; 99: 918–23.
- Kehlet H ve Dahl JB. The value of multimodal or balanced analgesia in postoperative pain treatment. *Anesthesia Analgesia*, 1993; 77:1048–56.
- Kehlet H. Controlling acute pain–role of preemptive analgesia, peripheral treatment and balanced analgesia and effects on outcome. *Pain 1999—an updated review*, M Mitchell. IASP Pres, Seattle, 1999; 459–62.
- Pinzur M, Gupta P, Pluth T. Continuous postoperative infusion of a regional anesthetic after amputation of the lower extremity: a randomized clinical trial. *J Bone Joint Surg Am*, 1996; 78:1501–5.
- Miller, R. D. (2015). *Local anesthetics.* In *Miller's anesthesia* (8th ed.). Philadelphia, PA: Churchill Livingstone/Elsevier. pp. 1028–54.
- Barden J, Derry S, McQuay HJ, Moore RA. Single dose oral ketoprofen and dexketoprofen for acute postoperative pain in adults. *Cochrane Database Syst Rev*, 2009; 7:CD007355.
- Buvanendran A ve Kroin JS. Multimodal analgesia for controlling acute postoperative pain. *Curr Opin Anaesthesiol*, 2009; 22:588–93.
- Ugras MY, Toprak HI, Gunen H, Yucel A, Gunes A. Instillation of skin, nephrostomy tract, and renal puncture site with ropivacaine decreases pain and improves ventilatory function after percutaneous nephrolithotomy. *J Endourol*, 2007; 21:499-503.
- Haleblian GE, Sur RL, Albala DM, Preminger GM. Subcutaneous bupivacaine infiltration and postoperative pain perception after percutaneous nephrolithotomy. *J Urol*, 2007;178(3 Pt 1):925-8.
- Jonnavithula N, Pisapati MV, Durga P, Krishnamurthy V, Chilumu R, Reddy B. Efficacy of peritubal local anesthetic infiltration in alleviating postoperative pain in percutaneous nephrolithotomy. *J Endourol*, 2009;23:857-60.
- Parikh GP, Shah VR, Modi MP, Chauhan NC. The analgesic efficacy of peritubal infiltration of 0.25% bupivacaine in percutaneous nephrolithotomy - A prospective randomized study. *J Anaesthesiol Clin Pharmacol*, 2011;27:481-4.

18. Parikh GP, Shah VR, Vora KS, Parikh BK, Modi MP, Panchal A. Ultrasound guided peritubal infiltration of 0.25% ropivacaine for postoperative pain relief in percutaneous nephrolithotomy. *Middle East J Anaesthesiol*, 2013;22:149-54.
19. Tüzel E, Kızıltepe G, Akdoğan B. The effect of local anesthetic infiltration around nephrostomy tract on postoperative pain control after percutaneous nephrolithotomy. *Urolithiasis*, 2014; 42:353-8.
20. Parikh GP, Shah VR, Vora KS, Parikh BK, Modi MP, Kumari P. Ultrasound guided peritubal infiltration of 0.25% Bupivacaine versus 0.25% Ropivacaine for postoperative pain relief after percutaneous nephrolithotomy: A prospective double blind randomized study. *Indian J Anaesth*, 2014; 58:293-7.
21. Gokten OE, Kilicarslan H, Dogan HS, Turker G, Kordan Y. Efficacy of levobupivacaine infiltration to nephrostomy tract in combination with intravenous paracetamol on postoperative analgesia in percutaneous nephrolithotomy patients. *J Endourol*, 2011; 25:35-9.
22. Parikh GP, Shah VR, Vora KS, Modi MP, Mehta T, Sonde S. Analgesic efficacy of peritubal infiltration of ropivacaine versus ropivacaine and morphine in percutaneous nephrolithotomy under ultrasonic guidance. *Saudi J Anaesth*, 2013; 7:118-21.
23. Nirmala J, Kumar A, Devraj R, Vidyasagar S, Ramachandraiah G, Murthy PV. Role of buprenorphine in prolonging the duration of postoperative analgesia in percutaneous nephrolithotomy: Comparison between bupivacaine versus bupivacaine and buprenorphine combination. *Indian J Urol*, 2015 ;31:132-5.
24. Honey RJ, Ghiculete D, Ray AA, Pace KT. A randomized, double-blinded, placebo-controlled trial of intercostal nerve block after percutaneous nephrolithotomy. *J Endourol*, 2013; 27:415-9.
25. Ak K, Gursoy S, Duger C, et al. Thoracic paravertebral block for postoperative pain management in percutaneous nephrolithotomy patients: a randomized controlled clinical trial. *Med Princ Pract*, 2013; 22:229-33.
26. Borle AP, Chhabra A, Subramaniam R, et al. Analgesic efficacy of paravertebral bupivacaine during percutaneous nephrolithotomy: an observer blinded, randomized controlled trial. *J Endourol*, 2014; 28:1085-90.