



Local bupivacaine for postoperative pain management in thyroidectomized patients: A prospective and controlled clinical study

Tiroidektomize hastalarda ameliyat sonrası ağrı yönetimi için lokal bupivakain kullanımı: Prospektif ve kontrollü klinik çalışma

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ABSTRACT

Objective: We aimed to evaluate the effect of bupivacaine and to compare the routes of administration of bupivacaine in the management of postoperative incision site pain after thyroidectomy.

Material and Methods: Consecutive patients who were planned for thyroidectomy surgery were randomized into three groups of 30 patients each: Group 1 (control group): standard thyroidectomy surgery without additional intervention; Group 2 (paratracheal infiltration with bupivacaine): following thyroidectomy, 0.25% bupivacaine was applied on the surgical area; Group 3 (subcutaneous infiltration with bupivacaine): following thyroidectomy, 0.25% bupivacaine was injected into the cutaneous, subcutaneous region and fascia of the surgical area. Postoperative pain was evaluated by a visual analog scale (VAS) at 1st, 4th, and 12th hours after thyroidectomy. Total daily requirement for additional analgesia was recorded.

Results: The mean age of 90 patients was 44.37±13.42 years, and the female:male ratio was 62:28. There was no difference between study groups in terms of age, thyroid volume, TSH and T4 levels. VAS score of patients in paratracheal infiltration with bupivacaine group was significantly lower than control group patients at 1st, 4th and 12th hours following thyroidectomy (p=0.030, p=0.033, p=0.039, respectively). The need for analgesics was significantly lower in both paratracheal infiltration and subcutaneous infiltration groups than the control group (86.7%, 83.0%, and 73.3%, respectively, p=0.049).

Conclusions: Intraoperative local bupivacaine application is effective in decreasing postoperative pain in patients with thyroidectomy.

Keywords: Bupivacaine, postoperative pain, thyroidectomy

ÖZ

Amaç: Tiroidektomi sonrası insizyon alanı ağrısının yönetiminde bupivakainin etkinliğinin araştırılmasını ve veriliş yollarının karşılaştırılmasını amaçladık.

Gereç ve Yöntemler: Tiroidektomi planlanan hastalar; Grup 1 (kontrol grubu): ek müdahale olmaksızın standart tiroidektomi uygulananlar; Grup 2 (paratrakeal bupivakain infiltrasyonu): tiroidektomi sonrası cerrahi alana %0,25'lik bupivakain enjeksiyonu uygulananlar; Grup 3 (subkütan bupivakain infiltrasyonu): tiroidektomi sonrası cerrahi alanın kutanöz, subkütan ve fasya tabakalarına %0,25'lik bupivakain enjeksiyonu uygulananlar olacak şekilde 30'ar hastalık üç gruba randomize edildi. Postoperatif ağrı "visual analog scale" (VAS) skorları ile tiroidektomi sonrası 1., 4. ve 12. saatlerde değerlendirildi. Ek analjeziye duyulan toplam günlük ihtiyaç kaydedildi.

Bulgular: Toplam 90 hastanın ortalama yaşı 44,37±13,42 idi ve kadın erkek oranı 62:28 idi. Çalışma grupları arasında yaş, tiroid hacmi, TSH ve sT4 değerleri yönünden fark yoktu. Paratrakeal bupivakain infiltrasyonu grubunda tiroidektomi sonrası 1., 4. ve 12. saat VAS skorları kontrol grubuna göre anlamlı olarak düşüktü (sırasıyla p=0,030, p=0,033, p=0,039). Analjezik ihtiyacı gerek paratrakeal gerek subkütan infiltrasyon grubunda kontrol grubuna göre anlamlı olarak düşüktü (sırasıyla %86,7, %83 ve %73,3 p=0,049).

Sonuç: Tiroidektomi uygulanan hastalarda intraoperatif lokal bupivakain uygulaması postoperatif ağrının azaltılmasında etkilidir.

Anahtar Kelimeler: Bupivakain, postoperatif ağrı, tiroidektomi

INTRODUCTION

Pain in the incision site is a common complaint among patients who undergo thyroidectomy, a widely applied procedure in endocrine surgery (1-3). The postoperative pain following thyroidectomy is due to extensive tissue dissection and tension during the operation (4). Many patients with thyroidectomy suffer from incision site pain especially in the first days after surgery, which delays early discharge and causes a significant burden on both patients and healthcare teams (5-8).

Pain following thyroidectomy is commonly managed with nonsteroidal anti-inflammatory drugs (NSAIDs) or opioid analgesics (9, 10). However, NSAIDs have been reported to be associated with potential adverse events including cardiovascular events, surgical bleeding and renal impairment (11). Opioid analgesics also have side effects such as nausea and vomiting (12).

Local anesthetics have been used in surgery for a long time to reduce postoperative pain and the need for analgesics (13). The use of local anesthetics particularly in abdominal and hernia surgery has been

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known to effectively decrease postoperative pain (14, 15). For this purpose, long-acting local anesthetics are preferred more frequently.

Bupivacaine is a long-acting local anesthetic that effectively reduces postoperative pain (16). In practice, bupivacaine is used for infiltration anesthesia, nerve blocks, epidural, and caudal anesthesia (17). It has a more selective effect on sensory nerve fibers as compared to motor nerve fibers, therefore is preferred for epidural anesthesia in obstetrics (18). However, there are limited studies on the use of local anesthetics in neck surgery. Bupivacaine has been used for preoperative wound infiltration (19), and intraoperative bilateral superficial cervical plexus block in thyroidectomy to prevent postoperative pain (20, 21). However, there is ongoing debate on the effectiveness and the route of application of bupivacaine to control pain following thyroidectomy (17, 19, 20, 22, 23).

Based on the current knowledge, in this study, we aimed to evaluate the effect of bupivacaine and to compare the routes of administration of bupivacaine in the management of postoperative incision site pain after thyroidectomy.

MATERIAL AND METHODS

Patients and Study Design

This was a prospective, three-arm, controlled study performed in Atatürk Training and Research Hospital Department of General Surgery. The study was approved by the Institutional Ethics Committee of the Hospital for Clinical Studies (date, 19/02/2014; no, 21). The study was conducted in accordance with Helsinki Declaration, and written informed consent was obtained from all patients before participation.

Patients who were planned for a total thyroidectomy between February 2013 and October 2013 were randomized into three groups of 30 patients each. Patients who did not want to participate in the study, had undergone previous thyroid surgery, or had undergone thyroid resection in combination with neck dissection were excluded.

Study groups were as follows: Group 1 (control group): standard thyroidectomy surgery following standard anesthesia protocol without additional intervention; Group 2 (paratracheal infiltration): following standard thyroidectomy surgery, Surgicel® (Johnson and Johnson Medical, Arlington, TX, USA) impregnated with 10 mg (4 mL) 0.25% bupivacaine (Marcain 0.5%, 20 mL/flakon, Eczacıbaşı, İstanbul, Turkey) diluted with equal rate of saline was applied on the frontal aspect of the trachea in a way that it expands 1 cm laterally on each side on the surgical area; Group 3 (subcutaneous infiltration): following standard thyroidectomy surgery, local infiltration of the wound was performed by the surgeon at the end of surgery just before wound closure. A 23-gauge needle was inserted along the incision line and 10 mg of 0.25% bupivacaine was applied into the anterior group cervical muscles and subcutaneous tissue in both flaps (top and bottom).

Operation Technique

A 4–7 cm skin incision (depending on the size of the thyroid) was made. Sub-platysmal flaps were elevated, the strap muscles were separated in the midline and reflected laterally. In

none of the patients the strap muscle was transected. The inferior, middle, and superior thyroid vessels were then divided. The same steps were repeated for removal of the contralateral lobe. Finally, the wound was irrigated and closed using interrupted 3-0 polyglactin sutures (Vycril, Ethicon) to approximate the strap muscles and the platysmal layer. The skin was closed subcutaneously. Suction drains were routinely used in all patients. Suction drains were removed at the first postoperative day, and no hematomas or seromas were observed in any patients.

Assessment of Postoperative Pain

Postoperative pain of the patients was evaluated by a visual analog scale (VAS) at 1, 4, and 12 hours after thyroidectomy by an investigator blinded to study groups. VAS is scored on a scale of 0 to 10 (0=no pain, 10=worst pain imaginable). For patients with a VAS score over 5, additional analgesia was provided with intramuscular 75 mg/amp diclofenac sodium. The total daily requirement for additional analgesia was recorded.

Calculation of Thyroid Gland Volume

Ellipsoid formula with correction factor, which is the most commonly used two-dimensional ultrasonographic mathematical method to estimate thyroid gland volume was used for calculation (24–26). This formula refers to width × depth × length × 0.524 for each lobe. For this calculation, both thyroid lobes were scanned with ultrasonography (Sonoline Ultrasonography Equipment, Siemens, Munich, Germany) individually in the transverse and longitudinal planes. Estimated error rate of this formula is approximately 15%.

Statistical Analysis

Study data were summarized using descriptive statistics (e.g., mean, median, standard deviation, range, frequency, percentage). Kolmogorov-Smirnov test was used to test whether continuous variables were distributed normally or not. Data of the three study groups were compared with analysis of variance (ANOVA) test, and secondary comparisons between two groups were performed with post-hoc Tukey test. For the comparison of data at different time points, repeated measured ANOVA test was applied. For comparison of categorical variables, chi-square and Fisher's exact tests were used. Statistical analysis was performed using Statistical Package for the Social Sciences version 16.0 (SPSS Inc; Chicago, IL, USA). Statistical significance was set to $p < 0.05$.

RESULTS

Clinical and Demographic Characteristics of Study Patients

The mean age of 90 patients included in the study was 44.37 ± 13.42 years (range 18–67 years), and the female:male ratio was 62:28 (females, 68.9%; males, 31.1%). The indication for thyroidectomy was a significantly large nodule ($n=26$, 28.9%), toxic goiter ($n=20$, 22.2%), malignancy ($n=14$, 15.6%), suspicion of malignancy ($n=8$, 8.9%), atypia of undetermined significance ($n=8$, 8.9%), insufficient thyroid fine needle aspiration biopsy ($n=6$, 6.7%), follicular lesion of undetermined significance ($n=4$, 4.4%), and difficulty in swallowing ($n=4$, 4.4%).

The mean thyroid volume calculated by the ellipsoid volume formula was 37.16 ± 23.59 cm³. There was no difference between study groups in terms of age, thyroid volume, TSH and

T4 levels ($p>0.05$). T3 level was significantly lower in the control group than subcutaneous bupivacaine infiltration group ($p=0.006$) (Table 1). Considering TSH, T4 and T3 levels together, study groups were not different in terms of hyperthyroidism that may interfere with the duration of surgery, amount of intraoperative bleeding, and postoperative pain by increasing vascularization in the surgical area. In each group, one patient developed transient hypocalcemia, no additional complication was observed.

VAS Score

VAS score of all study patients decreased significantly after the thyroidectomy operation at all time points ($p<0.001$ for all groups) (Table 2). VAS score of patients in the paratracheal infiltration with bupivacaine was significantly lower than control group patients at 1, 4, and 12 hours following the thyroidectomy operation ($p=0.030$, $p=0.033$, $p=0.039$, respectively) (Table 2).

Analgesic Requirement

Of all study patients ($n=90$), 72 (66.7%) required analgesics in addition to bupivacaine application. The need for analgesics was significantly lower in both the paratracheal infiltration and subcutaneous infiltration groups as compared to the control group (86.7%, 83.0%, and 73.3%, respectively, $p=0.049$) (Table 3).

DISCUSSION

The elimination or reduction of postoperative pain following thyroidectomy enhances patients' quality of life and allows patients to quickly return to normal daily activities. For the management of postoperative pain following thyroidectomy, NSAIDs and/or opioid analgesics are used commonly in practice. To decrease the postoperative pain and reduce the need for analgesics following thyroidectomy surgery, preoperative oral controlled-release analgesia with opioids and alternative regional techniques such as incisional local anesthesia, intraoperative bilateral superficial and/or deep cervical plexus block, local wound infiltration with local analgesia have also been suggested recently (20, 21, 23, 27-29). Performing thyroidectomy under local or regional anesthesia rather than general anesthesia has also been suggested to control postoperative pain (30).

In the present study, we evaluated whether bupivacaine is effective in postoperative pain control in thyroidectomy surgery, and compared the two administration ways of bupivacaine: paratracheal infiltration and subcutaneous infiltration. Bupivacaine is a local anesthetic with minimum effect on motor nerve conduction (16). Since postoperative pain following thyroid sur-

Table 1. Clinical and demographic characteristics of study patients

	Total (n=90)	Control (n=30)	Paratracheal infiltration of bupivacaine (n=30)	Subcutaneous infiltration of bupivacaine (n=30)	p
Age	44.37±13.42	47.1±12.79	45.37±13.88	44.38±13.43	0.159
Thyroid volume (cm ³)	37.16±23.59	30.07±17.61	40.71±24.61	37.17±23.6	0.130
TSH (U/mL)	1.03±1.00	1.2±1.1	0.74±0.66	1.04±1.01	0.137
T3 (pg/mL)	3.50±1.87	2.74±0.64	3.59±2.05	3.51±1.88	0.009 ^a
T4 (ng/dL)	2.15±5.31	1.44±0.88	1.45±0.65	2.16±5.32	0.197

TSH: Thyroid stimulating hormone; T3: triiodothyronine; T4: thyroxine

^a $p=0.163$ for Control vs. paratracheal infiltration; $p=0.006$ for Control vs. subcutaneous infiltration; $p=0.400$ for Paratracheal infiltration vs. subcutaneous infiltration groups.

Table 2. VAS scores (mean±standard deviation) of study groups at 1, 4, and 12 hours after the thyroidectomy operation

VAS scoring time	Control (n=30)	Paratracheal infiltration of bupivacaine (n=30)	Subcutaneous infiltration of bupivacaine (n=30)	p
1 st hour	6.64±1.76	5.37±2.42	5.4±1.36	0.026 ^a
4 th hour	4.14±2.12	2.93±1.60	3.33±1.71	0.038 ^b
12 th hour	1.94±0.95	1.6±0.9	1.78±0.63	0.048 ^c
p	0.001	0.001	0.001	

VAS Score: Visual Analog Scale Score

^a $p=0.030$ for Control vs. paratracheal infiltration; $p=0.882$ for Control vs. subcutaneous infiltration; $p=0.092$ for Paratracheal infiltration vs. subcutaneous infiltration groups.

^b $p=0.033$ for Control vs. paratracheal infiltration; $p=0.210$ for Control vs. subcutaneous infiltration; $p=0.672$ for Paratracheal infiltration vs. subcutaneous infiltration groups.

^c $p=0.039$ for Control vs. paratracheal infiltration; $p=0.272$ for Control vs. subcutaneous infiltration; $p=0.622$ for paratracheal infiltration vs. subcutaneous infiltration.

Table 3. Patients who required analgesia in study groups

	Control (n=30)	Paratracheal infiltration of bupivacaine (n=30)	Subcutaneous infiltration of bupivacaine (n=30)	p
Requirement for analgesics	26 (86.7%)	25 (83.0%)	20 (73.3%)	0.049 ^a
No requirement for analgesics	4 (13.3%)	5 (17.0%)	10 (26.7%)	

^a $p=0.037$ for Control vs. paratracheal infiltration; $p=0.020$ for Control vs. subcutaneous infiltration; $p=0.0791$ for paratracheal infiltration vs. subcutaneous infiltration groups.

gery is related to increased excitability of the dorsal horn neurons, blocking superficial branches of the cervical plexus was proposed in order to prevent postoperative pain. Local injection of bupivacaine may provide blockage of superficial branches of the cervical plexus. Bilateral superficial cervical plexus block with bupivacaine has been shown to significantly reduce pain intensity in the postoperative period after thyroid surgery, but did not provide optimal pain relief alone (31). We found that paratracheal infiltration with bupivacaine is effective in decreasing postoperative pain as assessed by VAS score. On the other hand, the need for analgesia with diclofenac sodium, an NSAID, was lowest in subcutaneous infiltration with bupivacaine group. In previous studies on the effect of bupivacaine on the control of postoperative pain, various dose intervals and routes were implemented with conflicting results. Sardar et al. (23) applied bilateral superficial cervical plexus block with 0.25% bupivacaine intraoperatively to decrease pain after thyroid surgery, but did not find decrease in postoperative analgesic requirement. In a prospective controlled study, Ayman et al. (19) compared preoperative incision site infiltration of bupivacaine 0.5% and ropivacaine 0.75% to decrease postoperative pain in total thyroidectomy, and concluded that wound infiltration with local analgesia had limited efficacy in decreasing postoperative pain in the short period up to 4 hours after surgery, and ropivacaine was more effective than bupivacaine in this manner. In contrast, Herbrand et al. (32) found that bilateral superficial cervical plexus block with ropivacaine did not prevent postoperative pain after total thyroidectomy. However, Karthikeyan et al. (20) reported that intraoperative bilateral superficial cervical plexus block with bupivacaine was effective in reducing postoperative pain and analgesic requirements in thyroidectomy. In a study comparing preoperative oral controlled release morphine, postoperative sublingual buprenorphine and intraoperative wound infiltration with 0.25% bupivacaine, sublingual buprenorphine was found to provide better analgesia after thyroidectomy than the other interventions (22). Gozal et al. (27) reported that bupivacaine 0.5% wound infiltration at the end of surgery reduced postoperative pain and opioid demand. In a recent study by Ryu et al. (33), spraying 0.25% levobupivacaine on the dissection area after robotic thyroidectomy reduced postoperative pain and patient-controlled analgesia consumption without adverse events. We determined that VAS score of patients with paratracheal infiltration of bupivacaine was significantly lower at 1, 4 and 12 hours following thyroidectomy, which indicates that paratracheal infiltration with bupivacaine is effective in decreasing postoperative pain in both the short and long term. The need for analgesics decreased in both paratracheal infiltration and subcutaneous infiltration groups. We think that our overall findings suggest the efficacy of bupivacaine by paratracheal infiltration in the management of postoperative pain following thyroidectomy; however, further studies are required to determine the most appropriate route of administration. Since total thyroidectomy was applied on all patients, we do not think that the difference between preoperative T3 values of the groups is a factor that may affect postoperative pain. We believe this to be pure coincidence (34).

Our findings along with previous reports indicate that bupivacaine application may be promising for control of postoperative pain following thyroidectomy. Recently, the advent of a liposomal formulation of bupivacaine has provided more favorable pharmacokinetics that reduces the risk of amide-relat-

ed toxicity and provides long-lasting postoperative analgesia (13, 18, 35, 36). Potential risks and benefits of liposomal bupivacaine, a very recently approved formulation of bupivacaine, need to be elucidated for postoperative pain control (36, 37). It is obvious that bupivacaine is used in high doses for motor and sensory blockade in both spinal anesthesia and peripheral nerve block. However, there were no signs of motor blockage in any of our operations (38).

In spite of our findings in favor of the analgesic efficacy of bupivacaine, the main limitation of our study is the small sample size precludes us from reaching a definite conclusion. Further studies with a larger sample size and those comparing different application routes are required to conclude on the efficacy of and the most efficient application route of bupivacaine for postoperative pain control.

In addition, the absence of data on operation durations, the volume of pathologic specimens, and comparison with the ultrasonographic volume measurements may be considered as other limitations of our study.

CONCLUSION

Intraoperative local bupivacaine application is effective in decreasing postoperative pain in patients undergoing thyroidectomy. Effective pain management following thyroidectomy should be implemented in order to increase the quality of postoperative care, to reduce both opioid consumption and subsequent dose-related complications.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Yıldırım Beyazıt University School of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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