HEAD & NECK

Peritonsillar dexamethasone–bupivacaine vs. bupivacaine infiltration for post-tonsillectomy pain relief in children: a randomized, double-blind, controlled study

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Abstract

Objective Post-tonsillectomy pain is one of the most frequent morbidities of tonsillectomy surgery. Currently, there is no standard protocol for post-tonsillectomy pain control. In our study, we aimed to compare the effects of perioperative peritonsillar dexamethasone–bupivacaine and bupivacaine-alone infiltration on pain control in pediatric patients.

Materials and methods This prospective, randomized, double-blind, controlled clinical trial was conducted between February 2018 and May 2018 in a single-center tertiary education and research hospital, otorhinolaryngology/head and neck surgery clinic, under general anesthesia, which included 120 pediatric patients between the ages of 2–12 (mean 5.7 ± 1.8), and who were with ASA (American Society of Anesthesiologists) I–II classification. Patients were randomly divided into three groups as 40 participants in each group. Group 1 consisted of patients who were injected with dexamethasone–bupivacaine into their peritonsillar region, group 2 consisted of patients who were injected with bupivacaine only, and group 3 consisted of patients who were injected with saline only as the control group. FLACC (face, legs, activity, cry, consolability) Scale and Wong-Baker FACES® Pain Rating Scale (WBS) were used for early and late period postoperative pain scoring. Patients with pain score ≥ 4 were treated with paracetamol rescue analgesia. Side effects such as nausea, vomiting and bleeding were recorded. Data of all groups were compared statistically and $p \leq 0.05$ was considered statistically significant.

Results There was no significant difference between the groups in terms of demographic data, duration of operation and duration of anesthesia. The pain scores of group 1 were significantly lower than those of the control group except for postoperative 45th min, 2nd day and 3rd day. The pain scores of the group 1 were significantly lower at all times except for the postoperative 12th and 24th hour, than those of group 2. The pain scores of the group 2 were lower than the control group only at postoperative 7th day, but no significant difference was found at other times. No statistically significant difference was found between the groups in terms of requirement rates for the first 60 min recovery analgesia ($p = 0.686$). No statistical difference was found between the groups in terms of side effects.

Conclusion In our study, preoperative local dexamethasone–bupivacaine infiltration in pediatric patients was shown to be more effective than bupivacaine-only and serum-only infiltration for early and late post-tonsillectomy pain control.

Keywords Tonsillectomy · Pain · Dexamethasone · Bupivacaine · Peritonsillar infiltration · Postoperative pain

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Introduction

Tonsillectomy is a frequently performed operation, and post-tonsillectomy pain is still a serious problem, as it also affects postoperative morbidity [1]. Stimulation of peritonsillar nerves and pharyngeal muscle spasm due to tissue damage during tonsillectomy are the most frequently cited reasons for post-tonsillectomy pain [2, 3].

Effective analgesic therapy with minimal side effects such as nausea, vomiting or respiratory depression is necessary [4]. A variety of agents and methods such as peritonsillar infiltration, multimodal IV and oral medications are used to reduce post-tonsillectomy pain [5–7].

Peritonsillar drug infiltration can be applied for post-tonsillectomy pain control as a preemptive analgesic regimen, which is an effective anesthesia method applied before surgical incision [8].

Steroid administration was also used in pain control; a single dose of IV dexamethasone administration, as well as perioperative peritonsillar steroid injection have been shown to reduce post-tonsillectomy pain, nausea and vomiting [9, 10]. Another contribution of steroids in pain control has been shown in peripheral nerve blocks. The addition of dexamethasone to local anesthetics in peripheral nerve blocks has been shown to increase the analgesic activity [11].

Bupivacaine (Marcaine®) is a long-acting local anesthetic of the amino amide group. It is indicated for infiltration anesthesia, nerve block, epidural and intrathecal anesthesia. It can be used in the surgical area by infiltration or by topical application [12, 13].

In this clinical trial, we aimed to evaluate the effects of dexamethasone–bupivacaine combination and bupivacaine alone on pain control and to compare the results.

Materials and methods

Our study was planned as a prospective, randomized, double-blind, controlled clinical trial. Approval was obtained from our hospital's local ethics committee (12-12-2017, No: 907) and registered clinical trials (NCT03443778). After obtaining written informed consent from each patient's legal guardian, 120 pediatric patients (48 female/72 male; mean age 5.7 ± 1.8) operated for tonsillectomy ± adenoidectomy between February 2018 and June 2018 at the Otorhinolaryngology Head and Neck Surgery Clinic of Sisli Hamidiye Etfal Training and Research Hospital under general anesthesia with ASA (American Society of Anesthesiologists) classification physical status I–II, were included in this study. The indications for

tonsillectomy were three attacks per year for chronic and recurrent tonsillitis in three consecutive years, or five attacks in two consecutive years, with symptoms such as fever, snoring, sore throat and the inability to eat a normal diet, history of peritonsillar abscess, and tonsillar hypertrophy leading to obstructive symptoms. Patients with active upper respiratory tract infection, significant cognitive impairment, bupivacaine hypersensitivity, dexamethasone hypersensitivity, patients on chronic systemic steroids, patients with a history of coagulation disorders, chronic pain, chronic use of analgesics, patients who have steroid drug/other drug addiction and with ventilation tube insertions, were excluded from the study.

Solid food was prohibited for 6 h and water for 4 h in all children prior to surgery. Thirty minutes before induction, 0.5 mg/kg midazolam was administered orally. After transfer to the operating room, heart rate, mean arterial pressure (MAP) and oxygen saturation (SpO_2) were continuously monitored. 2 mg/kg propofol, 1–2 µg/kg fentanyl and 0.6 mg/kg rocuronium were used for standard induction of anesthesia. Following tracheal intubation, patients were mechanically ventilated with volume-controlled ventilation (6–8 ml/kg), to adjust to achieve an end-tidal CO_2 level of 32–35 mmHg. Anesthesia was maintained via administration of sevoflurane gas mixture (at 0.75–1.25 minimum alveolar concentration range).

Patients were randomized into three groups by the sealed envelope technique. The study was continued until there was up to 40 cases in each group. Peritonsillar injections were infiltrated superficially at two different points to peritonsillar region, at superior and inferior, with an amount of 2–5 ml. Syringe with a 23G needle was used. 3–5 ml of bupivacaine 0.5% at a dose of 1 mg/kg (max dose 25 mg) combined with dexamethasone 0.5 mg/kg (max dose 8 mg) was applied in two parts for each tonsil before surgery in group 1 ($n = 40$). Bupivacaine 0.5% at a dose of 1 mg/kg (max dose 25 mg) with 3–5 ml saline (0.9% NaCl) was applied separately in two parts for each tonsil before surgery in group 2 ($n = 40$), and 3–5 ml saline (0.9% NaCl) alone was applied in group 3 ($n = 40$) as the control group.

Each patient received a single IV dose of 0.5 mg/kg (max dose 16 mg) dexamethasone sodium phosphate at the time of the surgery.

To achieve the double-blind frame, the parents and the anesthesiologist who collected the data were kept unaware of the patient's assigned group. The first anesthesiologist who prepared the drugs for local infiltration or IV injection was aware of the allocation of the children. However, the second anesthesiologist and the surgeon who recorded the post-surgical pain scores, side effects, and complications were blinded for the study group.

A conventional tonsillectomy with a cold knife was performed in all patients to exclude the confounding effect of

the surgical technique. The tracheal extubation was performed when the child had a regular respiratory pattern and could maintain SpO_2 95% for 5 min with air. The duration of the operation and anesthesia was recorded. After the operation, each child was transferred to the post-anesthesia care unit (PACU), and MAP, heart rate, and SpO_2 were monitored.

Postoperative first 24-h pain (early term pain) scoring was performed using the FLACC (face, leg, activity, cry, consolability) Scale (0 relaxed and comfortable, 1–3 = mild discomfort, 4–6 = moderate pain, 7–10 = severe pain or discomfort or both. A score of 0 is the best, while a score of 10 is the worst) (Table 1). Postoperative 15th, 30th, 45th and 60th min pain scores were monitored in PACU, while postoperative 4th, 8th, 12th and 24th hour pain scores were monitored in the inpatient care unit, and recorded by the clinician in charge.

Wong-Baker FACES® Pain Rating Scale (WBS) (0, no pain; 10, worse pain) was used for late period (postoperative first 7 days) pain and scores were recorded on the tracking cards (Table 2). Postoperative 1st day pain scoring was performed together with the patients and the parents were informed on how to record them. They were told to record on patient tracking cards in the morning hours on postoperative 1st–7th days.

Pain was accepted as both throat and referred pain such as ear and neck pain.

In addition, the data of rescue analgesia for the patients were recorded. A patient whose pain scores were ≥ 4 was treated with IV paracetamol (10 mg/kg maximum daily dose). The children were discharged from the PACU (post-anesthesia care unit) when they could maintain SpO_2 95% with air and if their pain scores were under the pain score of 4. The timing of the first administration of IV paracetamol and average consumption were recorded. Pain scores at the time of the postoperative 4th, 8th, 12th, 24th hour were recorded at the otolaryngology service.

Oral intake was started in patients if no nausea or vomiting was present after 4 h postoperatively. In case of nausea or vomiting, IV metoclopramide (2.5–5 mg/kg) was given. The patients were discharged on the postoperative 1st day. Tracking cards were given to the parents and shown how to fill it in. All patients were prescribed oral paracetamol (10 mg/kg) when discharged.
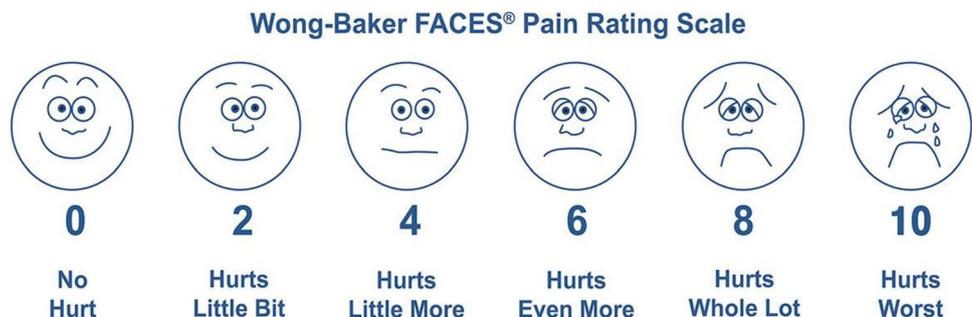
The legal guardians of the patients were also told that if the pain score was 4 ≥, additional oral paracetamol (10 mg/kg, maximum 40 mg/kg/daily dose) should be given to the patient and the data should be written in their cards.

Side effects such as nausea, vomiting and bleeding were recorded. All patients were asked to come to the outpatient clinic on the 7th postoperative day. Oropharyngeal examinations were performed at the control examination. Pain control cards were taken. The data of the groups were analyzed statistically and the data were compared.

Table 1 FLACC Scale

FLACC Scale (face, legs, cry, activity consolability scale)	Score
Face	
0—No particular expression or smile	
1—Occasional grimace or frown, withdrawn, disinterested	
2—Frequent to constant frown, quivering chin, clenched jaw	
Legs	
0—Normal position or relaxed	
1—Uneasy, restless, tense	
2—Kicking or legs drawn up	
Activity	
0—Lying quietly, normal position, moves easily	
1—squirming, shifting back and forth, tense	
2—Arched, rigid, or jerking	
Cry	
0—Not crying (awake or asleep)	
1—Moans or whimpers, occasional complaint	
2—Crying steadily, screams or sobs, frequent complaints	
Consolability	
0—Content, relaxed	
1—Reassured by occasional touching, hugging, or being talked to; distractable	
2—Difficult to console or comfort	
Total score (0–10)	

Table 2 Wong-Baker face pain rating scale

Wong-Baker FACES® Pain Rating Scale

0	2	4	6	8	10
No Hurt	Hurts Little Bit	Hurts Little More	Hurts Even More	Hurts Whole Lot	Hurts Worst

Statistical analysis

The sample size calculation, which used a two-sided design at a significance level of 5% ($a = 0.05$) and a power of 80% ($1 - b = 0.8$), indicated that patients per group would be needed to detect a one-point decrease in FLACC score. To allow for lack of eligibility and attrition, 40 patients per group were enrolled in this study. SPSS 15.0 for Windows program was used for statistical analysis. For descriptive statistics, number and percentage were used for categorical variables, and mean, standard deviation and median were used for numerical variables. As independent variables did not meet the normal distribution condition, more than two independent group comparisons were made with the Kruskal–Wallis test. Subgroup analysis was performed by Mann–Whitney U test and interpreted with Bonferroni correction. The ratios in groups were compared using the Chi-square analysis. Multivariate linear regression analysis according to age, weight, indication for surgery, injection used, and length of operation was also performed. Statistical level of significance (alpha) was accepted as $p < 0.05$.
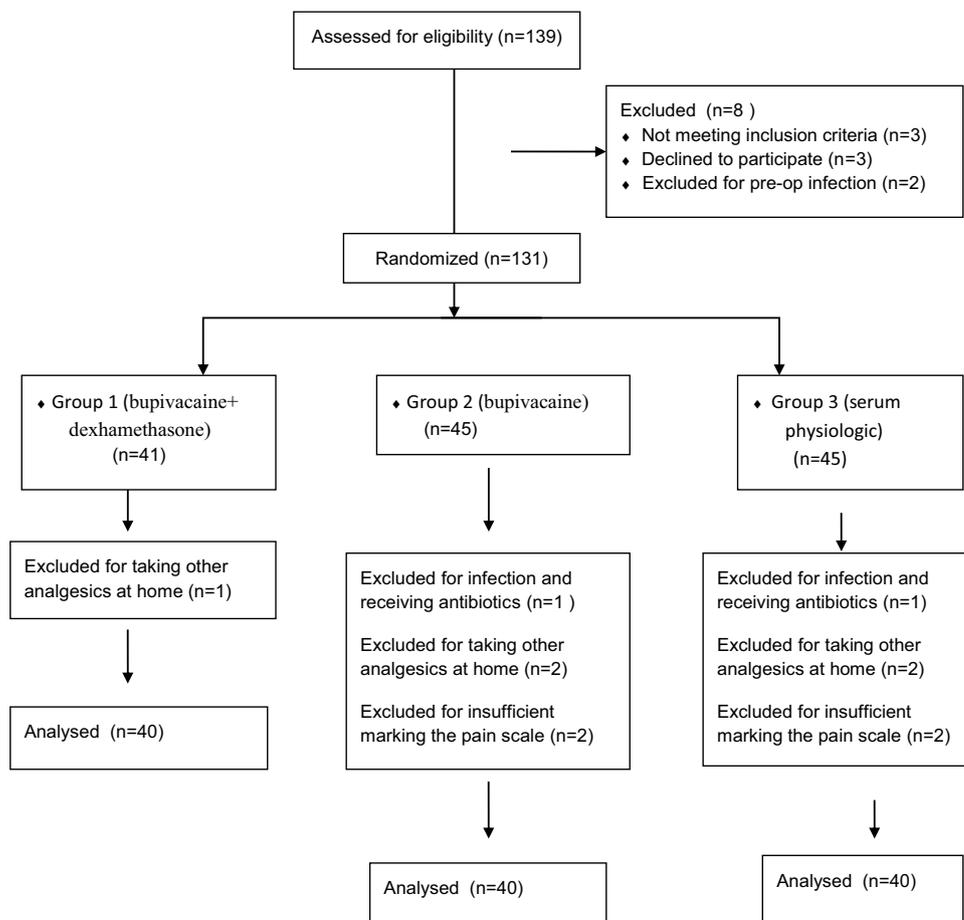
Results

In total, 139 patients were recruited, and 120 were included in this study (Fig. 1). Demographic data, duration of operation and anesthesia duration were shown in Table 3. There were no significant differences among the groups with regard to age, sex, or weight, duration of anesthesia and duration of operation.

Early pain scores were found to be lower in group 1 than the control group except for the 45th min and found to be lower than group 2 except in the 12th and 24th hour (Fig. 2, Table 4). Late pain scores were found to be lower in group 1 than the control group except on the 4th day and after and were found to be lower than group 2 at 2nd, 3rd, 4th, 5th, 6th, 7th days (Fig. 3, Table 4). Subgroup analyses are also shown in Table 5.

The pain scores of the group 2 were lower than the control group only at postoperative 7th day, but no significant difference was found at other times.

According to pain VAS score at postoperative 7th day, when the multivariate linear regression analysis was performed for age, weight, indication for surgery and length of

Fig. 1 Flow diagram describing patient recruitment

Assessed for eligibility (n=139)

Excluded (n=8)
♦ Not meeting inclusion criteria (n=3)
♦ Declined to participate (n=3)
♦ Excluded for pre-op infection (n=2)

Randomized (n=131)

♦ Group 1 (bupivacaine+ dexhamethasone) (n=41)

♦ Group 2 (bupivacaine) (n=45)

♦ Group 3 (serum physiologic) (n=45)

Excluded for taking other analgesics at home (n=1)

Excluded for infection and receiving antibiotics (n=1)

Excluded for taking other analgesics at home (n=2)

Excluded for insufficient marking the pain scale (n=2)

Excluded for infection and receiving antibiotics (n=1)

Excluded for taking other analgesics at home (n=2)

Excluded for insufficient marking the pain scale (n=2)

Analysed (n=40)

Analysed (n=40)

Analysed (n=40)

Table 3 Demographic data, operation time, operation types, anesthesia time

	Group 1		Group 2		Group 3		p
	Mean ± SD	Min–Max	Mean ± SD	Min–Max	Mean ± SD	Min–Max	
Age (year)	5.8 ± 1.9	3–10	5.9 ± 2.0	3–10	5.4 ± 1.8	3–10	0.588
Gender, n (%)							
Male	23 (57.5)		25 (62.5)		24 (60.0)		0.901
Female	17 (42.5)		15 (37.5)		16 (40.0)		
ASA, n (%)							
I	36 (90.0)		36 (90.0)		38 (95.0)		0.767
II	4 (10.0)		4 (10.0)		2 (5.0)		
Height (cm)	111.4 ± 15.3	79–135	109.5 ± 13.9	79–132	105.4 ± 12.6	86–135	0.063
Weight (kg)	23.4 ± 7.4	14–40	24.7 ± 8.4	15–40	23.8 ± 7.2	13–50	0.751
Anesthesia time (min)	63.8 ± 15.7	35–95	63.8 ± 13.2	40–95	62.5 ± 10.7	45–95	0.820
Operation time	55.9 ± 14.4	25–80	56.1 ± 11.8	35–80	54.1 ± 10.7	35–80	0.686
Operation type, n (%)							0.750
Tonsillectomy	29 (72.5)		27 (67.5)		30 (75.0)		
Adenotonsillectomy	11 (27.5)		13 (32.5)		10 (25.0)		

Fig. 2 Early pain scale (FLACC) of the groups
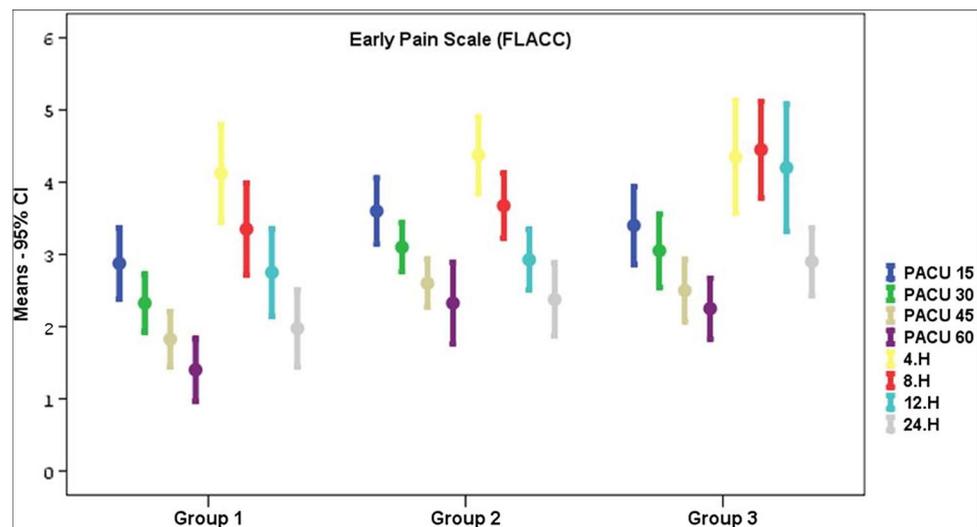
operation, none of these independent variables were found to influence the late pain scores (Table 6).

There was no statistically significant difference between the groups in terms of the need for recovery analgesia in the first 60 min after surgery ($p = 0.686$). Also there was no statistically significant difference in terms of the recovery analgesia taken at home. The recommended routine paracetamol administration was enough for the patients generally.

Regarding the side effects, no difference was found between the groups. No postoperative tonsil hemorrhage which required intervention was seen in any of them. Six patients revisited the hospital for insufficient oral intake and dehydration, and three patients were hospitalized for pain management. There was no statistically significant difference between the groups.

Discussion

Postoperative pain control is very important to decrease the morbidity of tonsillectomy. Pain in the early period starts with muscle spasm and nerve irritation and continues on 2nd–7th days, therefore it is important to treat inflammation. Long-acting pain control is also effective in reducing morbidity. It has been reported in the literature that dehydration that develops in patients increases the duration of hospital stay [14, 15]. Restriction of oral intake, especially in pediatric patients, may lead to dehydration and increased morbidity.

The management of post-tonsillectomy pain is still controversial. A combination of different medicines and

Table 4 Postoperative pain scores of the groups

	Group 1		Group 2		Group 3		p
	Mean ± SD	Median	Mean ± SD	Median	Mean ± SD	Median	
PACU 15th min	2.88 ± 1.54	3	3.60 ± 1.43	4	3.40 ± 1.68	3	0.076
95 CI%	2.38–3.37		3.14–4.06		2.86–3.94		
PACU 30th min	2.33 ± 1.25	2	3.10 ± 1.06	3	3.05 ± 1.58	3	0.012
95 CI%	1.93–2.72		2.76–3.44		2.54–3.56		
PACU 45th min	1.83 ± 1.20	2	2.60 ± 1.03	3	2.50 ± 1.34	2	0.020
95 CI%	1.44–2.21		2.27–2.93		2.07–2.93		
PACU 60th min	1.40 ± 1.35	1	2.33 ± 1.76	2.5	2.25 ± 1.32	2	0.006
95 CI%	0.97–1.83		1.76–2.89		1.83–2.67		
4th h	4.13 ± 2.11	4	4.38 ± 1.64	4.5	4.35 ± 2.42	4	0.641
95 CI%	3.45–4.80		3.85–4.90		3.57–5.13		
8th h	3.35 ± 1.99	4	3.68 ± 1.40	4	4.45 ± 2.09	4	0.074
95 CI%	2.71–3.99		3.23–4.12		3.78–5.12		
12th h	2.75 ± 1.89	2	2.93 ± 1.31	2	4.20 ± 2.75	4	0.020
95 CI%	2.15–3.35		2.51–3.34		3.32–5.08		
24th h	1.98 ± 1.67	2	2.38 ± 1.58	2	2.90 ± 1.46	3	0.023
95 CI%	1.44–2.51		1.87–2.88		2.43–3.37		
2nd day	3.03 ± 1.80	3	4.25 ± 1.68	4	3.75 ± 2.22	4	0.016
95 CI%	2.45–3.60		3.71–4.79		3.04–4.46		
3rd day	2.60 ± 1.61	2	3.73 ± 1.57	4	3.20 ± 2.11	3	0.008
95 CI%	2.08–3.12		3.22–4.23		2.52–3.88		
4th day	2.28 ± 1.48	2	3.38 ± 1.23	3	3.05 ± 1.85	2	0.003
95 CI%	1.80–2.75		2.98–3.77		2.46–3.64		
5th day	1.80 ± 1.32	2	2.78 ± 0.83	3	3.25 ± 1.81	3.5	< 0.001
95 CI%	1.38–2.22		2.51–3.04		2.67–3.83		
6th day	1.30 ± 1.07	1	2.18 ± 0.81	2	2.80 ± 1.80	2	< 0.001
95 CI%	0.96–1.64		1.92–2.43		2.22–3.38		
7th day	0.78 ± 1.00	0	1.68 ± 0.89	2	2.60 ± 1.79	2	< 0.001
95 CI%	0.46–1.09		1.39–1.96		2.03–3.17		

PACU Postoperative Anesthesia Care Unit, *CI* confidence interval

Fig. 3 Late pain scale (WBS) of the groups
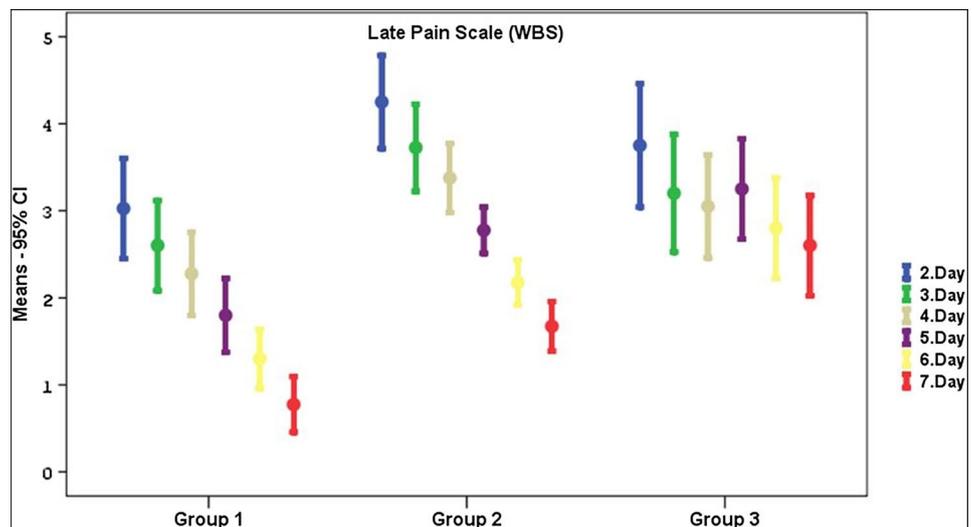
Table 5 Pain score comparison between groups

	Group 1 vs. group 2	Group 1 vs. group 3	Group 3 vs. group 2
	p	p	p
PACU 15 min	0.022	0.221	0.321
PACU 30 min	0.003	0.041	0.701
PACU 45 min	0.005	0.059	0.526
PACU 60 min	0.012	0.003	0.875
12 h	0.312	0.007	0.074
24 h	0.202	0.008	0.098
2 day	0.003	0.148	0.202
3 day	0.002	0.293	0.054
4 day	0.001	0.043	0.247
5 day	< 0.001	< 0.001	0.183
6 day	< 0.001	< 0.001	0.146
7 day	< 0.001	< 0.001	0.012

Table 6 Multivariate linear regression analysis according to pain score on postoperative 7th day

	B	Beta	p
Consent	3.715		
Age	− 0.072	− 0.090	0.574
Weight	0.017	0.088	0.582
Indication for surgery	0.023	0.092	0.341
Length of operation	− 0.005	− 0.038	0.641

techniques is used to reduce pain [16]. Although IV opioids have been used to reduce pain in an acute period, they were not preferred because of their side effects and short-term effects [17]. Additionally, local mucosal flaps or intracapsular tonsillectomy are also some of the suggested surgical tonsillectomy methods used to reduce tonsillectomy pain [18, 19].

Peritonsillar infiltration of local anesthetic agents have been shown to reduce post-tonsillectomy pain by preventing nociceptive impulses and make analgesic effect [3, 20]. Topical agents, oral rinses and sprays have been used to reduce post-tonsillectomy pain, but local anesthetic infiltration of the incision is one of the most effective analgesic methods [21]. Increased postoperative analgesia time was observed after peritonsillar infiltration of lidocaine, ropivacaine, levobupivacaine. However, in another study, peritonsillar adrenaline administration to levobupivacaine showed no statistically significant difference for post-tonsillectomy pain relief comparing to when only levobupivacaine was applied [5, 10, 14, 22].

Peritonsillar bupivacaine infiltration has been shown to be safe and effective in reducing post-tonsillectomy pain in several studies [23–25].

On the other hand, dexamethasone is a synthetic glucocorticoid drug with potent anti-inflammatory effects. The mechanism of action of corticosteroids is decreasing the local inflammation by blocking the chemical mediators of inflammation. Dexamethasone is currently recommended for routine prophylaxis against postoperative nausea and vomiting after tonsillectomy procedures [26, 27]. In the literature, dexamethasone has been shown to decrease the postoperative analgesic requirement after neuraxial blocks and peripheral nerve blocks [28–31]. Adding dexamethasone to local anesthetic can effectively inhibit inflammation caused by surgery and reduce pain [32]. It has been suggested that the perineural administration of dexamethasone may prevent the bupivacaine-induced reversible neurotoxicity and short-term rebound hyperalgesia while guarding against demyelination and Schwann cell degeneration. Therefore, it demonstrates the anti-nociceptive and anti-neurotoxic effects after the resolution of block [33].

Based on studies showing that dexamethasone increases the effect and duration of local anesthetics, we conducted this study to evaluate the effects of infiltration of dexamethasone–bupivacaine combination and bupivacaine alone on peritonsillar region on postoperative tonsillectomy pain. As the control group, the data of the group in which the serum infiltrated the peritonsillar region were used.

There was no statistically significant difference in pain scores in the bupivacaine-only group compared to the control group, except for the postoperative 7th day. However, we found that peritonsillary infiltration of dexamethasone–bupivacaine combination was more effective on early and late post-tonsillectomy pain than both bupivacaine-only and control groups. The pain relief at early period due to the local anesthetic infiltration to the surgical region was an expected outcome. However, the results for the late-term pain relief could be attributed to the early pain relief that improves early and sufficient oral intake for the pediatric patients. Another underlying mechanism could be the anti-inflammatory effect of the corticosteroid at the surgical region leading to late-term pain relief.

When postoperative complications seen after tonsillectomy such as nausea, vomiting and tonsil hemorrhage were investigated, no significant difference was found between the groups. None of our patients had post-tonsillectomy hemorrhage which may require intervention and surgical hemorrhage control. We thought that the most important reason for the unsignificant difference in patients in terms of side effects such as nausea and vomiting could be related to all the patients that were given IV dexamethasone.

There were some limitations in the study, one of which is that the infiltration technique is an invasive procedure. Peritonsillar bupivacaine infiltration has been shown to be effective in relieving post-tonsillectomy pain, but it carries the risk of serous systemic side effects such as intravascular

or intra-arterial injection, hemorrhage, airway obstruction, allergy, vocal cord paralysis, mucosal sloughing, cardiac arrest and convulsion that could be lethal [34, 35]. These risks should be kept in mind even though there was no systemic side effect in our cases.

Conclusion

In conclusion, in our prospective, randomized, double-blinded and controlled study conducted on 120 pediatric cases, perioperative local dexamethasone–bupivacaine infiltration has been shown to be more effective than bupivacaine alone and serum infiltration only in early and late post-tonsillectomy pain control.

Compliance with ethical standards

Conflict of interest There is no conflict of interest.

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