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ORIGINAL RESEARCH

Peritonsillar bupivacaine infiltration reduces emergence delirium after tonsillectomy in children: a randomized, double-blind, controlled study

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Abstract

Background: The study aimed to evaluate the effect of peritonsillar bupivacaine infiltration on the development of postoperative emergence delirium (ED) in pediatric patients undergoing tonsillectomy or adenotonsillectomy. **Methods**: This prospective, randomized, controlled clinical trial included 80 pediatric patients aged 3 to 7 years, classified as American Society of Anesthesiologists (ASA) Physical Status I. Patients were randomly divided into 2 groups of 40 patients each: Group A (peritonsillar bupivacaine injection) and Group B (control). In the recovery unit, delirium was assessed with the Pediatric Emergence Delirium Scale (PAEDS) and pain was assessed with the Face, Legs, Activity, Cry and Consolability (FLACC) scale at baseline and at 5, 10, 20, 30 and 60 minutes after surgery. A PAEDS score of $\geq$10 was considered indicative of postoperative delirium, and 0.5 μg/kg fentanyl was administered intravenously (IV). The FLACC scores $\geq$4 were considered indicative of pain, and 10 mg/kg paracetamol IV was administered as rescue analgesic. **Results**: The rate of rescue analgesic use, rescue fentanyl, and the incidence of delirium were significantly lower in group A compared to group B (p = 0.001, p = 0.001 and p = 0.001, respectively). The 20th, 30th and 60th minute FLACC measurements of group A were found to be significantly lower than those in group B (p = 0.002, p = 0.001 and p = 0.001). No significant differences were observed in PAEDS scores between the groups. The group assignment and PAEDS scores at the 5th minute were found as independent risk factors for the development of ED. In comparison to Group A (infiltration), the risk of delirium was higher in Group B (adjusted Odd Ratio (aOR): 14.533, 95% Confidence Interval (CI): 1.766–119.620). Additionally, a one-unit increase in PAEDS score at the 5th minute was associated with a 2.362-fold increased risk of delirium (95% CI: 1.44–3.87). **Conclusions**: Peritonsillar bupivacaine infiltration significantly reduces the risk of postoperative ED in pediatric patients undergoing tonsillectomy or adenotonsillectomy. **Clinical Trial Registration**: The study was registered with ClinicalTrials.gov as NCT06863714.

Keywords

Emergence delirium; Tonsillectomy; Bupivacaine; Infiltration analgesia; Postoperative pain

1. Introduction

Postoperative emergence delirium (ED) is an important clinical condition characterized by symptoms such as crying, irritability and severe restlessness in patients recovering from anesthesia. ED is more common in children than in adults. Among the various types of surgery, ED is particularly common in Ear, Nose and Throat (ENT) surgery, with reported prevalence rates ranging from 13%–26% [1]. Adenotonsillectomy, a commonly performed ENT procedure, carries a high risk for ED development [2].

ED can lead to self-injury, harm to the surgical site, and may cause parents to question the quality of anesthesia. It is associated with increased postoperative morbidity. Several anesthetic strategies have been proposed in the literature to prevent delirium, including intranasal premedication, deep versus awake removal of the laryngeal mask, and different intravenous anesthetic combinations [3–8]. The application of local anesthetics, such as xylocaine, has been shown to reduce both postoperative pain and ED [9]. Furthermore, it is widely accepted that effective postoperative analgesia can significantly reduce the incidence of ED [10].

Local infiltration of peritonsillar fossa with various local anesthetics, steroids and other agents is an established tech-

nique for relieving the postoperative pain associated with ENT procedures [11]. Bupivacaine, a long-acting local anesthetic, is widely used for local infiltration anesthesia [10]. This technique is considered safe, and several comparative studies have evaluated its efficacy. However, few studies have examined the relationship between effective pain control and postoperative ED development in children undergoing regional anesthesia. Additionally, we could not find any studies in the English literature investigating the effect of local infiltration of peritonsillar fossa on the development of ED in patients who underwent tonsillectomy or adenotonsillectomy.

The aim of this study is, therefore, to evaluate the effect of peritonsillar bupivacaine infiltration on the development of postoperative ED in pediatric patients undergoing tonsillectomy or adenotonsillectomy.

2. Materials and methods

This study was designed as a prospective, randomized, double-blind, controlled clinical trial. Ethical approval was obtained from the local ethics committee of our hospital (27 April 2021; approval reference: 1885), and the study was registered at ClinicalTrials.gov (NCT06863714). After obtaining written informed consent from each patient's legal guardian, 80 pediatric patients aged 3 to 7 years, with American Society of Anesthesiologists (ASA) Physical Status I classification, who underwent tonsillectomy with or without adenoidectomy under general anesthesia at the Otorhinolaryngology-Head and Neck Surgery Clinic of Şişli Hamidiye Etfal Training and Research Hospital between September 2023 and September 2024, were enrolled in the study. This study was conducted in accordance with the Helsinki Declaration.

Exclusion criteria included active infection, bleeding or coagulation disorders, neuropsychiatric conditions, hypersensitivity to bupivacaine, a history of peritonsillar abscess, prior head and neck surgery, postoperative delirium, any surgery within the past year, chronic illness, chronic pain, regular analgesic use, or prolonged hospitalization. Additionally, patients who experienced intraoperative complications such as mucosal injury or significant bleeding were also excluded from the study.

The indications for tonsillectomy or adenotonsillectomy included chronic or recurrent tonsillitis, defined according to the widely accepted Paradise criteria as $\geq$7 episodes in a single year, $\geq$5 episodes per year for two consecutive years, or $\geq$3 episodes per year for three consecutive years. Additionally, patients with adenoidal hypertrophy causing obstructive sleep apnea, persistent mouth breathing, or recurrent otitis media with effusion refractory to medical therapy were considered eligible for adenoidectomy.

All patients underwent standard cold dissection tonsillectomy under general anesthesia, using the snare technique. Hemostasis was achieved without the use of monopolar or bipolar diathermy. Adenoidectomy was performed using curettage. All surgical procedures were performed by the same experienced otolaryngologist.

Premedication was not administered before the surgery. The modified Yale Preoperative Anxiety Score was used to assess anxiety levels. Upon arrival in the operation room, continuous monitoring of electrocardiogram, noninvasive arterial blood pressure, and oxygen saturation (SpO_2) were initiated. Anesthesia induction was performed using 8% sevoflurane with a mask. After induction, intravenous vascular access was opened and 1–2 μg/kg fentanyl and 0.6 mg/kg rocuronium were administered. Then subjects were intubated, and mechanical ventilation was applied in volume-controlled mode, tidal volume was 6–8 mL/kg. The end tidal CO_2 volume was monitored and kept at 35–40 mmHg. Sevoflurane was administered in the 0.75–1.25 minimal alveolar concentration (MAC) range for the maintenance of anesthesia. All subjects received a single intravenous dose of 0.5 mg/kg dexamethasone. Patients were placed in the supine position with slight neck extension and a Boyle-Davis mouth gag was used for surgical exposure.

Although the anesthesiologist preparing the study drugs was aware of group assignments, they had no role in drug administration, intraoperative management or postoperative evaluation. The patients, the surgeon performing the procedure, and the anesthesiologist evaluating outcomes in the recovery unit were all blinded to group allocation.

Randomization was performed using a computer-generated sequence prepared by an independent researcher. Group assignments were placed in opaque, sealed and sequentially numbered envelopes. These envelopes were opened immediately before the intervention by an anesthesiologist, who was not involved in the data collection or outcome assessment. Patients were randomly divided into 2 groups of 40 patients each: Group A (peritonsillar bupivacaine injection) and Group B (control group). Peritonsillar infiltration was performed after the induction of general anesthesia and prior to the surgical incision. Using a 23-gauge needle, a volume of 2–5 mL was injected into each tonsil evenly, according to group allocation. In Group A, 0.5% bupivacaine was administered at a dose of 1 mg/kg (maximum 25 mg), while Group B received an equal volume of 0.9% saline. The infiltration was performed superficially, at an approximate depth of 3–5 mm, targeting the submucosal tissue of the superior and inferior peritonsillar fossa, adjacent to the upper and lower poles of the tonsil. All injections were performed by the same surgeon using anatomical landmarks under direct visualization.

At the end of the operation, sevoflurane was discontinued, and neuromuscular blockade was reversed with 0.001 mg/kg atropine and 0.003 mg/kg neostigmine. Subjects with adequate spontaneous respiration and those whose airway reflexes had returned were extubated. The patients were then transferred to the recovery unit, where continuous monitoring was performed.

In the recovery unit, delirium was assessed with the Pediatric Emergence Delirium Scale (PAEDS) and pain was assessed with the Face, Legs, Activity, Cry and Consolability (FLACC Scale) at baseline, and at 5th, 10th, 20th, 30th and 60th minutes postoperatively. A PAEDS score of $\geq$10 was considered indicative of postoperative delirium and 0.5 μg/kg fentanyl IV was administered. FLACC scores $\geq$4 were considered indicative of pain and 10 mg/kg paracetamol IV was administered as a rescue analgesic. Patients with an Aldrete Recovery Score $\geq$9 were transferred to the ward. Any complications observed in the operating room or recovery unit, such as nausea, vomiting, laryngospasm, bronchospasm, desaturation,

bradycardia, and hypotension, were recorded. The time from the beginning to the end of the surgery was defined as the operation time, while the time from the discontinuation of sevoflurane to the transfer to the recovery unit was defined as the recovery time.

Statistical analysis was performed using the SPSS 27.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA) software. Continuous variables were presented as either mean and standard deviation or median, and range depending of the normality of their distribution. Categorical variables were summarized using as frequency and percentage. The Shapiro Wilks test and Box Plot graphics were used to evaluate the normality of the data distribution. For two-group comparisons with normal distribution, the Student's *t*-test was used, while the Mann Whitney-U test was applied for two-group comparisons for variables not following a normal distribution. The Friedman test was used in intra-group evaluations with three or more points. Pearson's Chi-Square test was used for comparisons of categorical data. Multivariable analyses were conducted using logistic regression and results were evaluated at 95% confidence interval, with statistical significance set at $p < 0.05$. Based on an anticipated dropout rate of 20%, an alpha level of 0.05, and a power of 0.80, a sample size of 80 participants (40 per group) was calculated to be sufficient.

3. Results

A total of 80 patients were assessed for eligibility, and after applying the inclusion and exclusion criteria, all were included in the final analysis. The detailed flow of participant selection process is shown in the CONSORT (Consolidated Standards of Reporting Trials) diagram (Fig. 1). Among the patients enrolled in the study, 32 were female and 48 were male. The ages of the subjects participating in the study ranged from 3 to 7 years (the average was 5.54 $\pm$ 1.34 years). There were no significant differences between the groups in terms of gender, age, weight, operation time and recovery time ($p > 0.05$ for all comparisons) (Table 1).

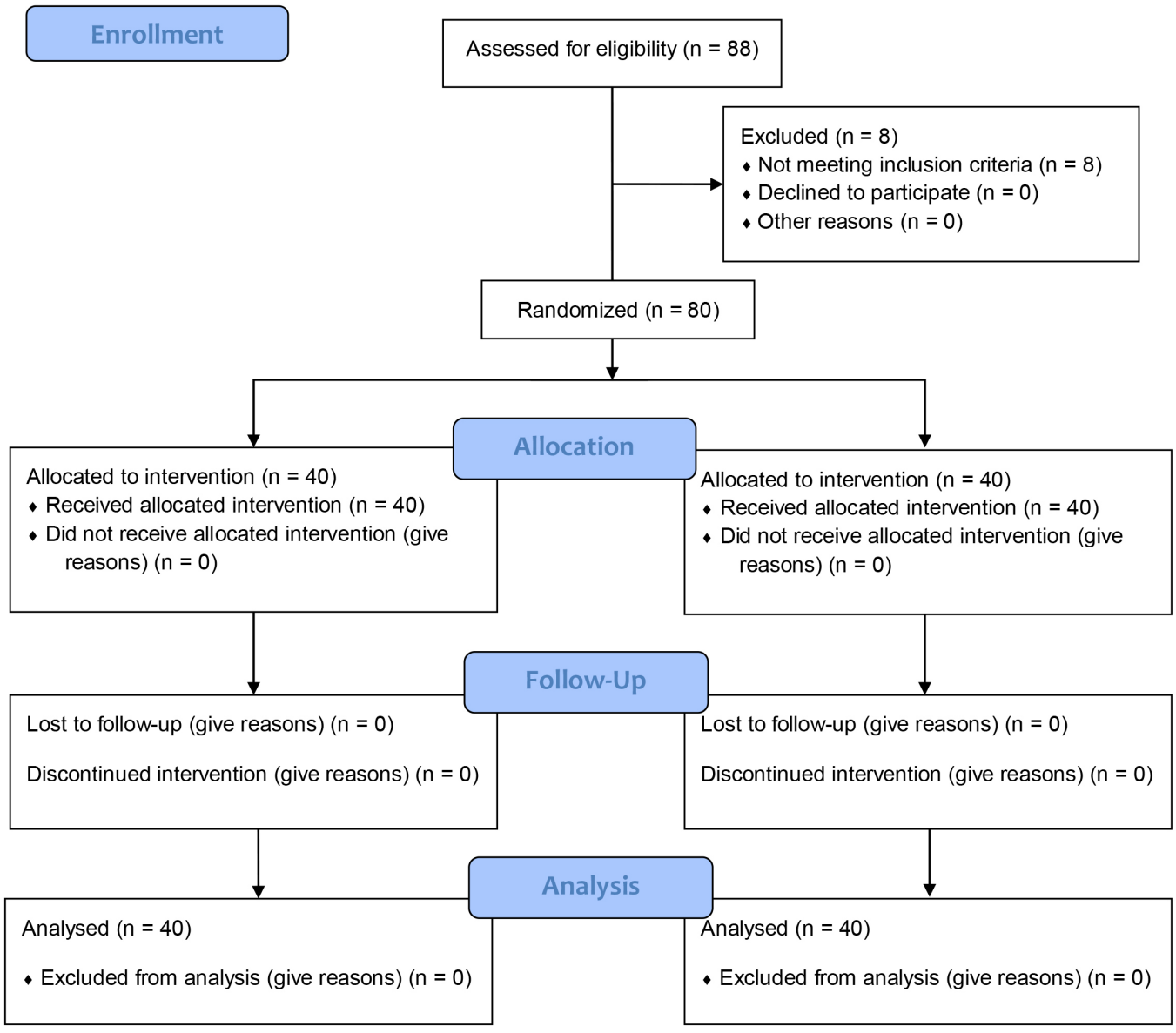

FIGURE 1. CONSORT 2010 flow diagram showing the participant selection process.

TABLE 1. Distribution of descriptive features according to study groups.

	Total	Group A (n = 40)	Group B (n = 40)	*p*
Gender				
Female	32 (40.0)	13 (32.5)	19 (47.5)	0.171[a]
Male	48 (60.0)	27 (67.5)	21 (52.5)	
Age (yr)				
Mean ± SD	5.54 ± 1.34	5.28 ± 1.38	5.80 ± 1.26	0.089[b]
Median (min–max)	6 (3–7)	5 (3–7)	6 (3–7)	
Weight (kg)				
Mean ± SD	20.21 ± 4.27	19.73 ± 4.66	20.70 ± 3.84	0.310[c]
Median (min–max)	20 (12–30)	20 (12–30)	20.5 (15–28)	
Operation time (m)				
Mean ± SD	70.89 ± 22.62	71.85 ± 26.28	69.93 ± 18.54	0.706[c]
Median (min–max)	70 (24–128)	70 (24–128)	71 (35–120)	
Recovery time (m)				
Mean ± SD	5.19 ± 1.37	5.10 ± 1.52	5.28 ± 1.22	0.571[c]
Median (min–max)	5 (1–10)	5 (1–10)	5 (3–9)	
Rescue analgesic				
Absent	51 (63.7)	33 (82.5)	18 (45.0)	0.001[a,**]
Present	29 (36.3)	7 (17.5)	22 (55.0)	
Analgesic duration (m) (n = 29)				
Mean ± SD	218.28 ± 250.08	225.71 ± 278.17	215.91 ± 247.49	0.940[b]
Median (min–max)	20 (5–720)	5 (5–600)	100 (5–720)	
Rescue fentanyl				
Absent	57 (71.3)	35 (87.5)	22 (55.0)	0.001[a,**]
Present	23 (28.7)	5 (12.5)	18 (45.0)	
Delirium				
Absent	57 (71.3)	35 (87.5)	22 (55.0)	0.001[a,**]
Present	23 (28.7)	5 (12.5)	18 (45.0)	
Anxiety scores				
Mean ± SD	7.88 ± 4.18	7.45 ± 4.00	8.30 ± 4.36	0.496[b]
Median (min–max)	7 (4–20)	6 (5–20)	7 (4–19)	

*[a]Pearson's Chi Square Test, [b]Mann-Whitney U Test, [c]Student t-Test, **p < 0.01. n: number; SD: Standard Deviation; min: minimum; max: maximum; m: minute.*

The rate of rescue analgesic use, rescue fentanyl administration, and the incidence of delirium in Group A were significantly lower compared to Group B ($p = 0.001$, $p = 0.001$ and $p = 0.001$, respectively). However, the analgesia duration and anxiety scores did not show a statistically significant difference between the groups ($p > 0.05$ for all comparisons) (Table 1).

In Group A, 29 patients underwent adenotonsillectomy and 11 underwent tonsillectomy alone. In Group B, 27 patients underwent adenotonsillectomy and 13 underwent tonsillectomy alone. There was no statistically significant difference between the two groups regarding the type of surgical procedure performed ($p = 0.807$).

No significant differences were observed in the FLACC measurements at the 5th and 10th postoperative minute between the groups ($p > 0.05$ for all comparisons). The FLACC measurements at the 20th, 30th and 60th postoperative minutes in group A were found to be significantly lower than those in group B ($p = 0.002$, $p = 0.001$ and $p = 0.001$, respectively). The changes in FLACC scores at different measurement points (5 *vs.* 10 min, 5 *vs.* 20 min, 5 *vs.* 30 min, 5 *vs.* 60 min) were not significant between the groups ($p > 0.05$ for all comparisons) (Table 2).

No significant differences were observed in the PAEDS measurements at the 5th and 10th, 20th, 30th and 60th postoperative minute between the groups ($p > 0.05$ for all comparisons). When evaluating the change in PAEDS scores across different time points, the changes from 5th *vs.* 30th min and

TABLE 2. Comparison of FLACC and PAEDS measurements according to groups.

FLACC Scale		Group A (n = 40)	Group B (n = 40)	*p*
5th m				
	Mean ± SD	3.00 ± 2.12	3.80 ± 2.42	0.120[c]
	Median (min–max)	3 (0–8)	4 (0–9)	
10th m				
	Mean ± SD	2.68 ± 1.69	3.05 ± 1.84	0.259[b]
	Median (min–max)	2 (0–8)	3 (0–7)	
20th m				
	Mean ± SD	1.25 ± 1.24	2.28 ± 1.57	0.002[c,]**
	Median (min–max)	1 (0–4)	2 (0–7)	
30th m				
	Mean ± SD	0.68 ± 1.00	1.83 ± 1.48	0.001[c,]**
	Median (min–max)	0 (0–3)	2 (0–7)	
60th m				
	Mean ± SD	0.43 ± 0.78	1.28 ± 1.22	
	Median (min–max)	0 (0–3)	2 (0–4)	0.001[c,]**
	p^d	0.001**	0.001**	
ChangeΔ				
5th *vs.* 10th m	Mean ± SD	−0.33 ± 1.40	−0.75 ± 1.53	0.558[b]
	p^{dd}	1.000	1.000	
5th *vs.* 20th m	Mean ± SD	−1.75 ± 2.02	−1.53 ± 2.25	0.582[b]
	p^{dd}	0.001**	0.003**	
5th *vs.* 30th m	Mean ± SD	−2.33 ± 2.00	−1.98 ± 2.49	0.696[b]
	p^{dd}	0.001**	0.001**	
5th *vs.* 60th m	Mean ± SD	−2.58 ± 1.96	−2.53 ± 2.66	0.888[b]
	p^{dd}	0.001**	0.001**	
PAEDS Scale		Group A (n = 40)	Group B (n = 40)	*p*
5th m				
	Mean ± SD	7.20 ± 4.10	7.75 ± 4.76	0.581[c]
	Median (min–max)	7.5 (0–20)	8.5 (0–20)	
10th m				
	Mean ± SD	5.80 ± 3.57	7.05 ± 4.15	0.153[c]
	Median (min–max)	5 (0–18)	7 (0–15)	
20th m				
	Mean ± SD	3.50 ± 3.08	4.85 ± 3.41	0.069[b]
	Median (min–max)	3 (0–12)	4.5 (0–12)	
30th m				
	Mean ± SD	2.28 ± 3.02	3.25 ± 2.93	0.147[c]
	Median (min–max)	0 (0–10)	3 (0–10)	
60th m				
	Mean ± SD	1.50 ± 2.14	2.40 ± 2.55	
	Median (min–max)	0 (0–6)	1 (0–8)	0.091[c]
	p^d	0.001**	0.001**	

TABLE 2. Continued.

FLACC Scale		Group A (n = 40)	Group B (n = 40)	*p*
ChangeΔ				
5th *vs.* 10th m	Mean ± SD	−1.40 ± 2.04	−0.70 ± 4.03	0.031[b,*]
	p^{dd}	0.771	1.000	
5th *vs.* 20th m	Mean ± SD	−3.70 ± 2.78	−2.90 ± 3.61	0.047[b,*]
	p^{dd}	0.001**	0.007**	
5th *vs.* 30th m	Mean ± SD	−4.93 ± 3.38	−4.50 ± 4.31	0.351[b]
	p^{dd}	0.001**	0.001**	
5th *vs.* 60th m	Mean ± SD	−5.70 ± 3.44	−5.35 ± 4.17	0.492[b]
	p^{dd}	0.001**	0.001**	

*[b]Mann-Whitney U Test, [c]Student t-Test, [d]Friedman Test, [dd]Dunn Bonferroni Test. *p < 0.05, **p < 0.01. n: number; SD: Standard Deviation; min: minimum; max: maximum; m: minute; FLACC: Face, Legs, Activity, Cry and Consolability; PAEDS: Pediatric Anesthesia Emergence Delirium Scale.*

5th *vs.* 60th min were not significant between the groups ($p > 0.05$ for all comparisons). The change of PAEDS scores for 5 *vs.* 10 min and 5 *vs.* 20 min were significantly greater in Group A than Group B ($p = 0.031$ and $p = 0.047$ respectively) (Table 2).

No statistically significant differences were found for gender, age, weight, operation time, recovery time and anxiety scores in relation to the presence of delirium ($p > 0.05$ for all comparisons). The rate of rescue analgesic use, and the rate of rescue fentanyl administration were significantly higher in subjects with delirium compared to those without delirium ($p = 0.017$ and $p = 0.001$, respectively). The duration of analgesia in subjects with delirium was significantly shorter than in those without delirium ($p = 0.002$; $p < 0.01$) (Table 3).

The FLACC measurements at the 5th, 10th, 20th, 30th and 60th postoperative minutes were significantly higher in subjects with delirium than those without delirium ($p = 0.001$ for all comparisons). When evaluating the change in FLACC scores at different time points, the change from 5 *vs.* 10 min was not significant between the groups ($p = 0.158$). The change of FLACC scores from 5 to 20 minutes, 5 to 30 minutes, and 5 to 60 minutes was significantly higher in subjects with delirium than in those without delirium ($p = 0.017$, $p = 0.001$, and $p = 0.002$, respectively). However, the change from 5 to 10 minutes was not statistically significant ($p = 0.158$) (Table 4).

The 5th, 10th, 20th, 30th and 60th postoperative minute PAEDS measurements of the subjects with delirium were found to be significantly higher than those without delirium ($p = 0.001$ for all comparisons). When evaluating the change in PAEDS scores according to different measurement points, the changes from 5 *vs.* 10 min and 5 *vs.* 20 min were not significant between the groups ($p > 0.05$ for all comparisons). The changes of PAEDS scores for 5 *vs.* 30 min and 5 *vs.* 60 min were significantly higher in subjects with delirium than in subjects without delirium ($p = 0.001$ for both comparisons) (Table 4).

A univariable analysis was performed to evaluate the effects of variables on delirium. We included the variables with a significance level below 0.200 in the multivariable logistic regression analysis. Accordingly, risk factors such as group (infiltration/control), operation time, rescue analgesic, 5th minute PAEDS score, and 5th minute FLACC score were evaluated with multivariable logistic regression. The multivariable model was found to be significant (Chi Square = 62.901; $p = 0.001$), with an explanatory coefficient of 93.8%. The effects of the group ($p < 0.01$) and 5th minute PAEDS measurement ($p < 0.01$) remained significant in the model, while the effects of other variables were not found to be significant. When those who underwent infiltration (group A) were used as a reference, the risk of delirium in the control group (Group B) was higher (aOR 14.533 times, 95% CI: 1.766–119.620). For 5th minute PAEDS measurements, a one-unit increase in scores was associated with a 2.362-fold higher risk of delirium (95% CI: 1.441–3.872). Group assignment and 5th minute PAEDS measurement were identified as independent risk factors for the development of ED (Table 5).

4. Discussion

The present study, conducted on 80 subjects, indicated that preoperative peritonsillar bupivacaine infiltration reduces both postoperative pain and development of ED by effectively managing postoperative pain. Several previous studies have evaluated the role of local anesthesia in reducing the risk of ED development [12–14]. However, to our knowledge, no study in the in English literature has specifically examined the effect of local infiltration of peritonsillar fossa on the development of ED in patients undergoing tonsillectomy/adenotonsillectomy operations. These findings could also provide valuable insights for other local infiltration techniques. Moreover, in the postoperative period, particularly in pediatric patients, pain should be effectively managed to eliminate it as a confounding factor. Once pain is adequately controlled, ED can be assessed independently and more accurately.

ED is a critical concern that every anesthesiologist should carefully address in the recovery room. ED can lead to disruption of the surgical site, increased postoperative complications, extended Post-Anesthesia Care Unit (PACU) stay and overall

TABLE 3. Comparison of descriptive features according to the presence of delirium.

	Delirium presence		*p*
	Absent (n = 57)	Present (n = 23)	
Gender			
Female	24 (42.1)	8 (34.8)	0.545[a]
Male	33 (57.9)	15 (65.2)	
Age (yr)			
Mean ± SD	5.56 ± 1.34	5.48 ± 1.38	0.759[b]
Median (min–max)	6 (3–7)	6 (3–7)	
Weight (kg)			
Mean ± SD	20.19 ± 4.42	20.26 ± 3.97	0.949[c]
Median (min–max)	20 (12–30)	20 (15–28)	
Operation time (m)			
Mean ± SD	73.07 ± 23.51	65.48 ± 19.67	0.176[c]
Median (min–max)	72 (24–128)	65 (35–100)	
Recovery time (m)			
Mean ± SD	5.04 ± 1.41	5.57 ± 1.20	0.118[c]
Median (min–max)	5 (1–10)	5 (4–9)	
Rescue analgesic			
Absent	41 (71.9)	10 (43.5)	0.017[a,*]
Present	16 (28.1)	13 (56.5)	
Analgesic duration (m)			
Mean ± SD	338.75 ± 249.81	70.00 ± 157.31	0.002[b,**]
Median (min–max)	420 (5–720)	5 (5–480)	
Rescue fentanyl			
Absent	56 (98.2)	1 (4.3)	0.001[a,**]
Present	1 (1.8)	22 (95.7)	
Anxiety scores			
Mean ± SD	7.53 ± 3.75	8.74 ± 5.07	0.472[b]
Median (min–max)	7 (4–20)	7 (5–20)	

*[a]Pearson's Chi Square Test, [b]Mann-Whitney U Test, [c]Student t-Test, *p < 0.05, **p < 0.01. n: number; SD: Standard Deviation; min: minimum; max: maximum; m: minute.*

TABLE 4. Comparison of FLACC and PAEDS scales according to the presence of delirium.

FLACC scale	Delirium presence		*p*
	Absent (n = 57)	Present (n = 23)	
5th m			
Mean ± SD	2.63 ± 1.75	5.30 ± 2.42	0.001[c,**]
Median (min–max)	3 (0–7)	6 (0–9)	
10th m			
Mean ± SD	2.32 ± 1.40	4.22 ± 1.86	0.001[b,**]
Median (min–max)	2 (0–6)	4 (0–8)	
20th m			
Mean ± SD	1.26 ± 1.17	3.00 ± 1.51	0.001[c,**]
Median (min–max)	1 (0–4)	3 (0–7)	

TABLE 4. Continued.

FLACC scale		Delirium presence		*p*
		Absent (n = 57)	Present (n = 23)	
30th m				
Mean ± SD		0.86 ± 1.16	2.22 ± 1.44	0.001[c,**]
Median (min–max)		0 (0–3)	2 (0–7)	
60th m				
Mean ± SD		0.54 ± 0.91	1.61 ± 1.20	
Median (min–max)		0 (0–3)	2 (0–4)	0.001[c,**]
p^d		0.001**	0.001**	
ChangeΔ				
5th *vs.* 10th m	Mean ± SD	−0.32 ± 1.14	−1.09 ± 2.02	0.158[b]
	p^{dd}	1.000	1.000	
5th *vs.* 20th m	Mean ± SD	−1.37 ± 1.73	−2.30 ± 2.84	0.017[b,*]
	p^{dd}	0.001**	0.028*	
5th *vs.* 30th m	Mean ± SD	−1.77 ± 1.82	−3.09 ± 2.91	0.001[b,**]
	p^{dd}	0.001**	0.001**	
5th *vs.* 60th m	Mean ± SD	−2.09 ± 1.87	−3.70 ± 2.91	0.002[b,**]
	p^{dd}	0.001**	0.001**	
PAEDS scale				
5th m	Mean ± SD	5.56 ± 2.87	12.22 ± 4.03	0.001[c,**]
	Median (min–max)	5 (0–10)	12 (0–20)	
10th m	Mean ± SD	4.61 ± 2.40	10.91 ± 3.20	0.001[c,**]
	Median (min–max)	5 (0–9)	11 (2–18)	
20th m	Mean ± SD	2.84 ± 2.43	7.48 ± 2.83	0.001[b,**]
	Median (min–max)	3 (0–9)	8 (2–12)	
30th m	Mean ± SD	1.84 ± 2.37	5.04 ± 3.21	0.001[c,**]
	Median (min–max)	0 (0–9)	5 (0–10)	
60th m	Mean ± SD	1.25 ± 1.98	3.70 ± 2.44	
	Median (min–max)	0 (0–8)	5 (0–7)	0.001[c,**]
	p^d	0.001**	0.001**	
ChangeΔ				
5th *vs.* 10th m	Mean ± SD	−0.95 ± 1.74	−1.30 ± 5.37	0.568[b]
	p^{dd}	1.000	1.000	
5th *vs.* 20th m	Mean ± SD	−2.72 ± 2.30	−4.74 ± 4.57	0.052[b]
	p^{dd}	0.001**	0.013*	
5th *vs.* 30th m	Mean ± SD	−3.72 ± 2.93	−7.17 ± 4.75	0.001[b,**]
	p^{dd}	0.001**	0.001**	
5th *vs.* 60th m	Mean ± SD	−4.32 ± 2.88	−8.52 ± 4.20	0.001[b,**]
	p^{dd}	0.001**	0.001**	

*[b]Mann-Whitney U Test, [c]Student t-Test, [d]Friedman Test, [dd]Dunn Bonferroni Test, **p < 0.01, *p < 0.05. n: number; SD: Standard Deviation; min: minimum; max: maximum; m: minute; FLACC: Face, Legs, Activity, Cry and Consolability; PAEDS: Pediatric Anesthesia Emergence Delirium Scale.*

TABLE 5. Multivariable Logistic regression analysis of risk factors for delirium.

	p	aOR	95% CI	
			Lower	Upper
Group B	0.013*	14.533	1.766	119.62
Rescue analgesic (none)	0.899	1.130	0.172	7.432
5th minute PAEDS score	0.001*	2.362	1.441	3.872
5th minute FLACC score	0.909	0.974	0.618	1.535
Operation time	0.263	0.970	0.921	1.023

**p < 0.05, FLACC: Face, Legs, Activity, Cry and Consolability; PAEDS: Pediatric Anesthesia Emergence Delirium Scale; aOR: Adjusted Odds Ratio; CI: Confidence Interval.*

hospital stay, and reduced patients' or parenteral satisfaction [3]. These factors can negatively affect the patient's wellbeing and hinder the recovery period. Several risk factors contribute to the development of ED, including preoperative anxiety, lack of premedication, the use of volatile anesthetic drugs and anticholinergics, and waking up in an unfamiliar environment. To prevent recovery agitation, it is essential to identify children at risk, administer appropriate adjuvant drugs, ensure effective postoperative pain control, and allow parents to accompany their children in the recovery room. These strategies are currently the primary measures in preventing the occurrence of ED.

For the development of ED, various factors such as age, type of surgery, patient or parenteral anxiety, pre-existing patient behaviors, and interactions with health-care providers have been proposed as contributors [2]. Among these, younger age and tonsillectomy operations have been reported as dominant factors that increase the risk of ED [2]. While several strategies have been suggested to decrease the risk of ED, no definitive strategy is universally accepted. Our study, which focuses on children undergoing tonsillectomy or adenotonsillectomy, provides a well-designed group to analyze the effect of local anesthetic infiltration on the risk of postoperative ED development.

Although the baseline characteristics (age, gender, weight, operation time and preoperative anxiety scores) were similar between the groups, a high ED rate was observed in our study (28.7%). We conducted our study in a pediatric population that underwent adenotonsillectomy surgery, both of which are well-established risk factors for the development of ED. Additionally, no premedication was used for the subjects in our study, anesthesia induction was performed using volatile anesthetic agents, and anticholinergic drugs were administrated. The combination of these factors, all known to increase the risk of ED, may help explain the high ED rate observed in our study.

Delirium and rescue fentanyl use was less common in the group that received peritonsillar bupivacaine infiltration compared to the control group. Although PAEDS scores were not statistically different in the two groups, higher scores were measured in the control group. PAEDS scores decreased more in the infiltration group at the 10th and 20th postoperative minutes compared to the 5th minute. Although the duration of analgesia in the infiltration group was similar to the control group, rescue analgesic use and postoperative FLACC scores after the 10th minute were found to be lower.

Among the possible factors that contribute to the development of ED, pain is a major one. However, pain is not solely responsible for ED since it has also been observed after anesthesia is applied in procedures such as magnetic resonance imaging where no pain is observed, and this has led to questioning the relationship between pain and delirium. Postoperative pain is a common condition in tonsillectomy [3]. Tonsillectomy pain, believed to result from peritonsillar nerve stimulation and pharyngeal muscle spasm, is a frequent and important condition that requires specific management. Postoperative pain is associated with increased morbidity, and several anesthetic and analgesic regimens are available to mitigate it [1]. While there is some overlap between the features of postoperative pain and ED, they are different conditions with unique implications.

In the postoperative period, pain and ED often occur together but can also be defined as separate events. Distinguishing them can be particularly challenging, especially in children. In ED, the lack of eye contact and environmental awareness are prominent, whereas in pain, abnormal facial expressions, crying and inability to be comforted are more evident [15, 16]. The FLACC and PAEDS scales were used to differentiate postoperative pain from ED. We used both assessments to evaluate the presence of ED [2].

We defined pain and ED as separate events and developed distinct rescue treatment strategies for both conditions. Delirium was diagnosed when the PAEDS score was 10 and above. In total 23 patients were diagnosed with ED and fentanyl was administered to these subjects as a rescue treatment. The presence of pain was accepted if FLACC scores were 4 and above, and paracetamol was administered as a rescue analgesic to the 29 patients with pain. In patients who developed delirium, FLACC scores were high at all measurement points, analgesia durations were short and rescue analgesic needs were found to be high. The PAEDS scores were also found to be high at all measurement points in patients who developed delirium. In our study, the 5th minute PAEDS score was found as an independent risk factor for delirium. ED can be seen in the first 20 minutes of the postoperative period. The inability to make eye contact and lack of environmental awareness are more common in the early postoperative period which defines parameters for ED, and are among the important parameters of PAEDS score.

Recent studies have highlighted the use of propofol and

Total Intravenous Anesthesia (TIVA) instead of sevoflurane, as well as the substitution of sugammadex for fentanyl-like narcotics, to prevent delirium after adenotonsillectomy. Additionally, agents such as dexmedetomidine, alpha 2 adrenergic agonists like clonidine, ketamine, magnesium, and anticholinergics have also been suggested as strategies to prevent delirium. However, the effect of peritonsillar local anesthetic infiltration, which has been shown to provide effective analgesia after adenotonsillectomy, on the development of postoperative delirium had not yet been evaluated.

This study has some limitations that should be acknowledged. First, we did not assess the exact time of onset and duration of postoperative delirium. The absence of this information may hinder a more precise characterization of delirium episodes and their progression, potentially limiting our ability to identify time-specific risk factors. Second, the length of hospital stay was not recorded, which could be an important outcome variable related to both pain and delirium. Patients with prolonged pain or severe ED might require extended postoperative monitoring or care, and the absence of this data prevents evaluation of potential associations. Lastly, intraoperative opioid consumption was not assessed, which might have influenced postoperative pain and delirium scores. Future studies with longer follow-up and more comprehensive perioperative data collection, including duration and timing of delirium, hospital stay, and intraoperative medication use, are warranted to better understand the multifactorial nature of ED.

There are a limited number of studies evaluating the effects of local anesthetic infiltration and regional anesthesia on the development of ED in pediatric patients. One such study demonstrated that an infraorbital nerve block provides effective postoperative analgesia in pediatric patients undergoing cleft lip in surgery. The block reduces the development of ED and shortens the duration of ED [14]. However, it has been reported that scalp block application in nevus surgery and ilioinguinal/iliohypogastric nerve block application in inguinal hernia surgery reduce pain but do not reduce the incidence of ED [12, 13]. These results, which differ from our study, can be explained by the fact that the surgical group selected was low-risk surgery in terms of ED.

5. Conclusions

Peritonsillar bupivacaine infiltration is a practical and effective technique for reducing ED and postoperative pain in pediatric tonsillectomy, and its use may contribute to safer recovery, decreased need for rescue medications, and overall improvement in the quality of perioperative pediatric anesthesia care.

AVAILABILITY OF DATA AND MATERIALS

The data used to support the findings of this study are available from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

HST, PS, MA, BT—study conception and design. MA, LK, BT, ASÇ, SO—data collection. HST, PS, LK—analysis and interpretation of results. HST, BT, ASÇ, SO—draft manuscript preparation. HST, PS, ASÇ, SO—critical revision of the article. MA, LK, BT—other (study supervision, funding, materials, *etc.*). All authors reviewed the results and approved the final version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Clinical Trials Ethical Commite of Sisli Etfal Research and Training Hospital (27 April 2021; approval reference: 1885). Written informed consent were obtained from all patient's parents/legal guardians.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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