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MISCELLANEOUS

Topical bupivacaine compared to bupivacaine infiltration for post-tonsillectomy pain relief in children: a prospective randomized controlled clinical study

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Abstract The objective of this study is to compare the topical administration of bupivacaine hydrochloride, saline and bupivacaine hydrochloride infiltration on post-tonsillectomy pain in children. Sixty children undergoing tonsillectomy were enrolled in the study. Patients were randomized into three groups using sealed envelopes. Group 1 ($n = 20$) received topical 0.5 % bupivacaine hydrochloride, group 2 ($n = 20$) received topical 0.9 % NaCl (saline), and group 3 ($n = 20$) received 0.5 % bupivacaine hydrochloride infiltrated around each tonsil. Pain was evaluated using McGrath's face scale. Pain scores in topical bupivacaine hydrochloride group was significantly lesser than the topical saline group at 5th, 13th, 17th and 21st hours, until the 6th day ($p < 0.017$). Moreover, pain scores of topical bupivacaine hydrochloride group was superior to bupivacaine hydrochloride infiltration group at 5th, 13th, 17th hours and 2nd, 3rd, 4th and 5th day ($p < 0.017$). There were significantly lesser morbidities in topical bupivacaine hydrochloride than saline group in 1st and 4th day ($p < 0.017$). Topical administration of bupivacaine hydrochloride proved to provide more efficient pain control than bupivacaine hydrochloride infiltration.

Keywords Tonsillectomy · Pain · Bupivacaine · Topical · Infiltration

Introduction

Tonsillectomy is one of the most commonly performed surgical procedures in pediatric patients. Post-operative morbidity from tonsillectomy is mainly caused by pain, which results in poor oral intake in children and leads to dehydration which may cause serious complications. Many attempts to reduce the post-tonsillectomy pain with perioperative administration of local anesthetics are present in the literature. However, the efficiency of the method of anesthetic administration was not researched in any of these studies.

Bupivacaine is a local anesthetic drug belonging to the amino amide group. It is indicated for local anesthesia including infiltration, nerve block, epidural, and intrathecal anesthesia. It can be used either by infiltration of topically for local anesthesia on surgical field [1–6]. The aim of the present study was to document the efficiency of topical use or infiltration of bupivacaine hydrochloride by comparing to the saline for the relief of post-tonsillectomy pain.

Material and methods

Sixty children aged 3–15 years, undergoing tonsillectomy were enrolled in the study. The design of this study has been approved by the ethical committee of study center. After informed consent was obtained from the parents, patients admitted for tonsillectomy were randomized into three groups using sealed envelopes. Indications for tonsillectomy included tonsillar hypertrophy with obstructive symptoms and recurrent tonsillitis. Criteria for exclusion were underlying chronic disease or bleeding disorder or another synchronous procedure in addition to tonsillectomy. Group 1 ($n = 20$, mean age 6.1 ± 3.7) received topical 0.5 % bupivacaine hydrochloride (standard USP), group 2 ($n = 20$, mean age 6.7 ± 3.6) received topical 0.9 % NaCl (saline), and group 3 ($n = 20$, mean age 5.9 ± 2.4) received 0.5 % bupivacaine hydrochloride infiltrated around each tonsil.

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In group 1–2, topical bupivacaine hydrochloride and saline were applied to tonsillar fossae just after the excision of each tonsil. In group 3, prior to tonsillectomy bupivacaine hydrochloride was infiltrated into the peritonsillar fossae at the lower pole, the upper pole and between the two (3 ml per tonsil) with the use of an aspiration injection technique. A straight 23-G needle was used for infiltration. The injections were superficial and ballooned out the submucosal tissues of the tonsillar pillar. The infiltrate was free of adrenaline. All patients underwent tonsillectomy using a standardized general anesthesia protocol by endotracheal intubation; for premedication 0.5 mg/kg midazolam was applied rectally between the ages of 3 and 6, and 0.1 mg/kg midazolam was applied intravenously between the ages of 6 and 15. Following anesthesia induction with intravenous propofol (3 mg/kg) and 2 mg/kg succinyl-choline, maintenance was achieved with nitrous oxide (50 %) in oxygen and sevoflurane. Children also received an acetaminophen suppository (25–30 mg/kg), intravenous dexamethasone, 1 mg/kg (maximum dose, 25 mg); and fentanyl citrate (1 μg/kg).

All of the operations were performed by the same otolaryngologist. The patients were positioned supine in Rose position and the neck was extended with a shoulder-roll placed under the shoulders; the tonsillectomy was performed using bipolar forceps. Each of the tonsillar fossae was tightly packed with a swab soaked 2–3 min with 5 ml bupivacaine hydrochloride in group 1 and 5 ml saline in group 2. All cases were encouraged to feed orally at 3rd hour post-operatively with cold tonsil diet. A questionnaire including age, weight, sex and information regarding the patients' post-operative morbidity was filled in. Post-operative morbidities (nausea, vomiting, otalgia, and trismus) were filled in by the parents. These morbidities were scored as absent or present (positive or negative) for each day by the parents during the first week after the operation. We computed the total numbers of positive scores according to the days and groups.

Pain scores at 1st, 5th, 13th, 17th and 21st hour, and 1st, 2nd, 3rd, 4th, 5th and 6th day post-operatively were recorded by the parents using McGrath's face scale [7].

All patients were administered post-operatively the same oral acetaminophen pediatric suspension (10–20 ml/kg) and antibiotic suspension (sulbactam-ampicillin, 40 mg/kg) twice daily for a week.

Statistical analyses were performed with SPSS for Windows (version 16.0; SPSS Inc, Chicago, IL, USA). The Chi-square test (χ^2 test) was used when sex, intraoperative morbidity and tonsillectomy indication of the groups were compared with one another statistically. Normality of the distributions was analyzed with Shapiro–Wilk's test. Kruskall–Wallis test and Mann–Whitney *U* test were used to analyze pain scores, age, bleeding volume of the groups where distribution was not normal. A *p* value lesser than 0.05 was accepted as significance threshold. In identifying the groups responsible for significance, Bonferroni correction was used. So a *p* value of less than 0.017 was determined as the level of statistical significance.

Table 1 Demographic data of the groups

	Group 1 ($n = 20$)	Group 2 ($n = 20$)	Group 3 ($n = 20$)	*p* value
Age (years)	6.1 ± 3.7	6.7 ± 3.6	5.9 ± 2.4	$p > 0.05$
Weight (kg)	27.6 ± 8.3	28.3 ± 10.9	29.7 ± 9.8	$p > 0.05$
Gender	10 F, 10 M	10 F, 10 M	10 F, 10 M	$p > 0.05$

Results

There were no differences in mean age, body mass index, sex distribution, tonsillectomy indication and intraoperative bleeding volume between the three groups ($p > 0.05$) (Table 1). The post-operative pain scores at 1 h were similar among the groups ($p > 0.05$). Pain scores in topical bupivacaine hydrochloride group were significantly lesser than the topical saline group at 5th, 13th, 17th and 21st hour, until the 6th day ($p < 0.017$). Moreover, pain scores of topical bupivacaine hydrochloride group were superior to bupivacaine hydrochloride infiltration group at 5th, 13th, 17th hour and 2nd, 3rd, 4th and 5th day ($p < 0.017$). Pain scores of bupivacaine hydrochloride infiltration were lesser than saline group at 17th, 21st hour and 1st, 2nd, 3rd, 4th, 5th and 6th day ($p < 0.017$) whereas, there was no significant difference at other times (Table 2).

The morbidity scores of the all groups were summarized in Table 3. In this table, the numbers show the sum of positive morbidities in corresponding days and groups (in rows and columns). Regarding the post-operative morbidity (nausea, vomiting, otalgia, and trismus), there were significantly lesser morbidities in topical bupivacaine hydrochloride than saline group in 1st and 4th day ($p < 0.017$). Also there were significantly lesser morbidities in topical bupivacaine hydrochloride than bupivacaine hydrochloride infiltration group in 2nd, 3rd and 4th day ($p < 0.017$). Topical saline and bupivacaine infiltration groups were not found to be different regarding morbidities ($p > 0.017$). In 5th and 6th day all groups were found to be similar for morbidities ($p > 0.05$) (Table 3).

No major complications such as airway obstruction, hemorrhage, dehydration, or local anesthetic toxicity developed.

Discussion

It has been suggested that injection of a local anesthetic agent may decrease pain by blocking the sensory pathways

Table 2 Pain scores of topical bupivacaine, topical saline and bupivacaine infiltration groups according to post-operative time

Post-op Time	Group 1	Group 2	Group 3	3 Groups	*p*		
					G1–G2	G1–G3	G2–G3
1 h	0.61 ± 0.08	0.65 ± 0.08	0.64 ± 0.08	0.213	–	–	–
5 h	0.42 ± 0.22	0.58 ± 0.12	0.57 ± 0.14	**0.014**	**0.014**	**0,013**	0.818
13 h	0.39 ± 0.17	0.64 ± 0.16	0.58 ± 0.13	**<0.001**	**<0.001**	**0.002**	0.177
17 h	0.37 ± 0.16	0.67 ± 0.16	0.50 ± 0.10	**<0.001**	**<0.001**	**0.007**	**0.001**
21 h	0.34 ± 0.19	0.66 ± 0.13	0.47 ± 0.19	**<0.001**	**<0.001**	0.046	**0.002**
1st day	0.30 ± 0.17	0.65 ± 0.14	0.42 ± 0.21	**<0.001**	**<0.001**	0.096	**0.001**
2nd day	0.24 ± 0.16	0.52 ± 0.20	0.38 ± 0.14	**<0.001**	**<0.001**	**0.002**	**0.007**
3rd day	0.21 ± 0.17	0.57 ± 0.25	0.35 ± 0.13	**<0.001**	**<0.001**	**0.001**	**0.01**
4th day	0.15 ± 0.17	0.40 ± 0.27	0.26 ± 0.20	**0.008**	**0.008**	**0.001**	**0.011**
5th day	0.20 ± 0.17	0.47 ± 0.27	0.37 ± 0.18	**0.004**	**0.002**	**0.016**	**0.202**
6th day	0.17 ± 0.26	0.47 ± 0.28	0.29 ± 0.14	**0.01**	**0.006**	0.056	**0.013**

Bold values are statistically significant

Post-op post-operative, *G* group, *h* hour

Table 3 Cumulative number of post-operative morbidities by group according to days

Days	Group 1	Group 2	Group 3	*p* value	G1–G2	G1–G3	G2–G3
0	4	6	10	0.122	–	–	–
1	4	12	10	0.031	**0.011**	0.05	0.602
2	4	10	12	0.031	0.05	**0.011**	0.602
3	6	10	14	0.043	0.202	**0.012**	0.289
4	4	12	12	**0.015**	**0.011**	**0.011**	1
5	8	6	10	0.435	–	–	–
6	4	4	10	0.057	–	–	–

Bold values are statistically significant

G group

and thus preventing the nociceptive impulses [8]. There are numerous studies in which a local anesthetic has been applied to the tonsillar fossae in tonsillectomy. The local anesthetic is usually applied by infiltration. The efficacy of bupivacaine infiltration in post-tonsillectomy pain has been extensively studied. Bupivacaine is very safe in benefiting the analgesia without increasing the risk of complications [2, 9–11]. However, some investigators have been unable to confirm these results [8, 12–14]. Preincisional infiltration of 2 % ropivacaine was found to be effective against both early and late post-operative pain in adult patients [15]. Giannoni et al. [16] compared ropivacaine 1 %, clonidine containing ropivacaine 1 % and normal saline infiltrations in pediatric patients undergoing tonsillectomy operations and they found that pain scores and additional analgesic consumption were significantly lower with ropivacaine and clonidine added ropivaciane solutions than with normal saline solutions at the first post-operative day. In contrast, Unal et al. [17] suggested that peritonsillar bupivacaine infiltration was insufficient to control post-operative pain, however, it was found to be more effective than ropivacaine (0.2 %) for reducing post-operative analgesic requirement.

The infiltration technique carries the risk of accidental intravascular injection which can lead to cardiac arrest [18] and convulsion [19]. Injection was also reported to cause severe upper airway obstruction [20], facial nerve paralysis [21], vocal cord paralysis [22] and brainstem stroke [23]. However, we did not encounter any complication related to infiltration.

The topical use of bupivacaine in pediatric tonsillectomy cases for post-operative analgesia is limited. Kadar et al. [24] showed whereas, Violaris et al. [25] could not show the effectiveness of topical bupivacaine in tonsillectomy patients using an intra-individual study design. Hung et al. [3] investigated the effectiveness of topical bupivacaine in reducing post-operative pain in pediatric day-case tonsillectomy and found that the pain scores were significantly lower in the bupivacaine group compared to the control group. Ozmen et al. [26] found the pain scores significantly lower in the topical bupivacaine group compared to the topical saline and lidocaine group during pediatric tonsillectomy. Considering the VAS pain scale can be confusing to use for children who were unwilling or unable to verbalize [16] some preferred Cheops, a valid and reliable method of assessing pain in children. But Cheops was designed for use in the immediate post-operative period and became imprecise after hospital discharge [27]. Therefore, we preferred to use McGrath's face scale.

We did not encounter any study analyzing the efficacy of administration method of bupivacaine in the literature. This report is the first controlled prospective study in literature by comparing the effect of topical bupivacaine and

bupivacaine infiltration on post-tonsillectomy pain relief. Our study demonstrated that packing swabs soaked with 0.5 % bupivacaine hydrochloride into the each peritonsillar fossae intraoperatively improved throat pain compared to 0.5 % bupivacaine hydrochloride infiltration and topical saline application. The superiority of topical bupivacaine to bupivacaine hydrochloride infiltration on pain relief was a surprising result. More studies are needed to document the accuracy and biochemical mechanism of this model. But one explanation could be, since the tonsillar fossae and nerve endings are open after tonsillectomy, topical application of bupivacaine into the fossae may provide easy and better reaching of bupivacaine to its targets.

Second result of this study was concerning the nausea, vomiting, otalgia, and trismus, there were significantly lesser morbidities in topical bupivacaine hydrochloride than bupivacaine hydrochloride infiltration and topical saline group. We think, lesser morbidities in topical bupivacaine hydrochloride group are related to throat pain relief. Early post-operative throat pain relief in this group gave the chance of sufficient oral intake on time. Although we did not have any statistical data, our observations show that 'As the oral intake starts earlier, the throat pain decreases early and vice versa; as the oral intake delays, pain continues and the patient rejects oral feeding.' This 'vicious circle' should be interrupted at early post-operative period to avoid morbidities, dehydration, long hospital stay and high dose of analgesic use. The positive scores of each morbidities itself were small in groups and we could not reach statistically comparable number of each morbidity between groups. Instead of this, we compared the sum of all the morbidities as same in the study of Ozmen AO et al. [26]. In future, a study with high numbers of cases in groups will document any significant differences for morbidity one by one.

Since any major complication was not encountered in any groups, we could not compare the complication rates between groups. Also we did not encounter any systemic side effect of bupivacaine hydrochloride in two groups. On the other hand, bupivacaine infiltration carries more systemic risks than topical bupivacaine. This study had the limitation of being small number of groups, which could not reflect the real systemic side effect and complication rate. Further studies with large number of groups are needed to document systemic risks of bupivacaine infiltration over topical bupivacaine.

As a result, topical bupivacaine proved to provide more efficient pain control than both saline and bupivacaine infiltration without any complication. Thus, we concluded that topical bupivacaine hydrochloride appeared to be a safe and easy medication for post-operative pain control in pediatric cases. The superior effect on post-operative pain of topical bupivacaine to infiltration technique and saline may change the routines on pain relief in children who have been tonsillectomised.

Conclusion

Throat pain is one of the most common causes of morbidity after tonsillectomy, which may result poor oral intake, dehydration, long hospital stay and high dose of analgesic use. Although bupivacaine hydrochloride infiltration to peritonsiller area has been shown to decrease post-tonsillectomy throat pain, this manipulation carries some systemic risks. Our study showed that, topical application of the packing swabs soaked with 0.5 % bupivacaine hydrochloride to tonsillar fossae intraoperatively is an effective, easy and safe method for post-operative pain relief.

Conflict of interest None.

References

1. Park AH, Pappas AL, Fluder E, Creech S, Lugo AR, Hotaling A (2004) Effect of perioperative administration of ropivacaine with epinephrine on postoperative pediatric adenotonsillectomy recovery. Arch Otolaryngol Head Neck Surg 130:459–464
2. Jebeles JA, Reilly JS, Gutierrez JF, Bradley EL Jr, Kissin I (1990) The effect of pre-incisional infiltration of tonsils with bupivacaine on the pain following tonsillectomy under general anesthesia. Pain 47:305–308
3. Hung T, Moore-Gillon V, Hern J, Hinton A, Patel N (2002) Topical bupivacaine in paediatric day-case tonsillectomy: a prospective randomized controlled trial. J Laryngol Otol 116:33–36
4. Yilmaz S, Demiraran Y, Akkan N, Yaman H, Iskender A, Güçlü E et al (2009) The effects of topical levobupivacaine on morbidity in pediatric tonsillectomy patients. Int J Pediatr Otorhinolaryngol 73:1208–1210
5. Oghan F, Harputluoglu U, Guclu E, Kocaman B, Ozturk O (2008) Does topical ropivacaine reduce the post-tonsillectomy morbidity in pediatric patients. Int J Pediatr Otorhinolaryngol 72:361–365
6. Karaaslan K, Yilmaz F, Gulcu N, Sarpkaya A, Colak C, Kocoglu H (2008) The effects of levobupivacaine versus levobupivacaine plus magnesium infiltration on postoperative analgesia and laryngospasm in pediatric tonsillectomy patients. Int J Pediatr Otorhinolaryngol 72:675–681
7. McGrath PA, deVeber LL, Hearn MT (1985) Multidimensional pain assessment in children. In: Fields HL, Dubner R, Cervero F (eds) Advances in pain research and therapy, vol 9. Raven Press, New York, pp 387–393
8. Molliex S, Haond P, Baylot D (1996) Effect of pre- vs. postoperative tonsillar infiltration with local anesthetics on postoperative pain after tonsillectomy. Acta Anaesthesiol Scand 40:1210–1211
9. Sun J, Wub X, Meng Y, Jin L (2010) Bupivacaine versus normal saline for relief of post-adenotonsillectomy pain in children: a meta-analysis. Int J Pediatr Otorhinolaryngol 74:369–373
10. Kountakis SE (2002) Effectiveness of perioperative bupivacaine infiltration in tonsillectomy patients. Am J Otolaryngol 23:76–80
11. Jebeles JA, Reilly JS, Gutierrez JF, Bradley EL Jr, Kissin I (1993) Tonsillectomy and adenoidectomy pain reduction by local bupivacaine infiltration in children. Int J Pediatr Otolaryngol 25:149–154
12. Schoem SR, Watkins GL, Kuhn JJ, Thompson DH (1993) Control of early post-operative pain with bupivacaine in pediatric tonsillectomy. Ear Nose Throat J 72:560–563
13. Broadman LM, Patel RI, Feldman BA, Sellman GL, Milmoe G, Camilon F (1989) The effects of peritonsillar infiltration on the

reduction of intraoperative blood loss and post-tonsillectomy pain in children. Laryngoscope 99:578–581
14. Orntoft S, Longreen A, Moiniche S, Dhal JB (1994) A comparison of pre- and post-operative tonsillar infiltration with bupivacaine on pain after tonsillectomy: a preemptive effect? Anaesthesia 49:151–154
15. Arikan OK, Ozcan S, Kazkayasi M, Akpinar S, Koc C (2006) Preincisional infiltration of tonsils with ropivacaine in post-tonsillectomy pain relief: double-blind, randomized, placebo-controlled intraindividual study. J Otolaryngol 35:167–172
16. Giannoni C, White S, Enneking FK, Morey T (2001) Ropivacaine with or without clonidine improves pediatric tonsillectomy pain. Arch Otolaryngol Head Neck Surg 127:1265–1270
17. Unal Y, Pampal K, Korkmaz S, Arslan M, Zengin A, Kurtipek O (2007) Comparison of bupivacaine and ropivacaine on post-operative pain after tonsillectomy in paediatric patients. Int J Pediatr Otorhinolaryngol 71:83–87
18. Marwick PC, Levin AI, Coetzee AR (2009) Recurrence of cardiotoxicity after lipid rescue from bupivacaine-induced cardiac arrest. Anesth Analg 108:1344–1346
19. Gunter JB (2002) Benefit and risks of local anesthetics in infants and children. Paediatr Drugs 4:649–672
20. Bean-Lijewski JD (1998) Glossopharyngeal nerve block for pain relief after pediatric tonsillectomy: retrospective analysis and two cases of life-threatening upper airway obstruction from an interrupted trial. Anesth Analg 86:678
21. Shlizerman L, Ashkenazi D (2005) Peripheral facial nerve paralysis after peritonsillar infiltration of bupivacaine: a case report. Am J Otolaryngol 26:406–407
22. Weksler N, Nash M, Rozentsveig V, Schwartz JA, Schily M, Gurman GM (2001) Vocal cord paralysis as a consequence of peritonsillar infiltration with bupivacaine. Acta Anaesthesiol Scand 45:1042–1044
23. Alsarraf R, Sie KC (2000) Brain stem stroke associated with bupivacaine injection for adenotonsillectomy. Otolaryngol Head Neck Surg 122:572–573
24. Kadar AA, Obaid MA (2003) Effect on post-operative pain after local application of bupivacaine in the tonsillar fossa; a prospective single blind controlled trial. J Pak Med Assoc 53:422–426
25. Violaris NS, Tuffin JR (1989) Can post-tonsillectomy pain be reduced by topical bupivacaine? Double blind controlled trial. J Laryngol Otol 103:592–593
26. Ozmen AO, Ozmen S (2011) Topical bupivacaine compared to lidocaine with epinephrine for post-tonsillectomy pain relief in children: a randomized controlled study. Int J Pediatr Otorhinolaryngol 75(1):77–80
27. Beyer JE, McGrath PJ, Berde CB (1990) Discordance between self report and behavioral pain measures in 3–7 year old children following surgery. J Pain Symptom Manage 5:350–356