Comparison between Peritonsillar Infiltration of Ketamine or Bupivacaine for Post-Tonsillectomy Analgesia

Original Article

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ABSTRACT

Background: Managing post-tonsillectomy pain is crucial for promoting oral intake and hydration while minimizing irritability and discomfort, which can increase the risk of postoperative bleeding.

Objectives: To compare the efficacy of pre-incisional peri-tonsillar infiltration of bupivacaine vs. ketamine in achieving postoperative analgesia following tonsillectomy or adenotonsillectomy.

Methods: Eighty patients aged 3 to 17 years, scheduled for tonsillectomy or adenotonsillectomy, were divided into two equal groups based on the agent used for pre-incisional peritonsillar infiltration to attain postoperative analgesia. In group B, patients received 5ml of bupivacaine 0.5%, while group K received infiltration with ketamine at a dose of 0.5mg/kg.

Results: There was no significant difference between the two groups concerning the modified objective pain scale (MOPS) (*P* value 0.475) or total analgesic consumption during the first 12 hours postoperatively (*P*>0.05). Additionally, no significant difference was noted in the modified Aldrete score between the two groups (*P* value 0.534); however, a significant reduction in the Wilson sedation score was observed in the ketamine group (*P* value 0.006). The occurrence of postoperative complications did not significantly differ between the groups (*P*>0.05).

Conclusion: Pre-incisional peri-tonsillar infiltration of either bupivacaine or ketamine can be safely and effectively used to manage post-tonsillectomy pain, demonstrating nearly equal effects on post-anesthesia recovery time and total postoperative analgesic consumption.

Key Words: Analgesia, bupivacaine, ketamine, tonsillectomy.

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INTRODUCTION

Tonsillectomy is a common one-day surgical procedure that is associated with significant post-operative pain. Tonsillar fossae are highly sensitive because they are well-innervated by the branches of the trigeminal and glossopharyngeal nerves, which are highly represented in the cerebral cortex[1].

Tonsillectomy causes oropharyngeal muscle contraction and irritation of the nerve endings. Intraoperative tissue handling, or the use of electrocautery, causes an inflammatory response, which may aggravate pain[2].

There are several analgesics used to control post-tonsillectomy pain, such as opioids, non-steroid anti-inflammatory drugs (NSAIDs), and local anesthetics. However, opioids decrease upper airway tone and suppress the cough reflex, leading to side effects such as nausea, vomiting, sedation, and respiratory depression. NSAIDs such as ketorolac, ibuprofen, or ketoprofen have been associated with increased postoperative bleeding, and it has been suggested that their use be avoided[3].

Afferent C-fibers around the peritonsillar space mediate the afferent conduction of the stimuli of surgical wounds[4]. This conduction can be blocked by local anesthetics through topical application or infiltration. Peritonsillar infiltration of local anesthetics can decrease pain and the analgesic need in pediatric patients[5,6].

Peritonsillar infiltration of the long-acting amide anesthetic bupivacaine has been used before tonsillectomy and is effective in decreasing early post-operative pain. Also, ketamine is an NMDA receptor antagonist that, when applied by peritonsillar infiltration, produces proper pain relief after tonsillectomy attributed to its modulatory effect on the local release of nociceptive pro-inflammatory

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cytokines during incision and dissection[7]. Therefore, our study aimed to compare the efficacy of regional (pre-incisional peritonsillar) infiltration of bupivacaine and ketamine in the management of postoperative pain after tonsillectomy.

PATIENTS AND METHODS

The local ethical committee approval (Soh_ Med_22_02_07) and informed written consent from the participants' parents were obtained before enrolling the patients in the study. The study was registered in the clinical trial registry under the number NCT05341323.

The study included 80 patients aged between 3 and 17 years old and scheduled to undergo tonsillectomy or adenotonsillectomy with or without ventilation tube application.

Patients with a history of peritonsillar abscess or tonsillar malignancy, patients who had a history of allergy to bupivacaine or ketamine, those with coagulopathy, endocrine, neuropsychiatric, or cardiopulmonary dysfunction, children with increased intracranial pressure (ICP), a history of seizures, patients under chronic analgesic treatment, and those who received any analgesic drug during the last 24h before surgery were excluded.

Anesthetic technique was standardized in all the patients after they had fasted for 6 hours before surgery, and it included induction with either IV propofol 2mg/kg plus fentanyl 1µg/kg or sevoflurane inhalation (increased every 3 breaths in 0.5% concentrations till a concentration of 7%) plus fentanyl 1µg/kg depending on the age of the patient or the presence of an IV line already inserted before coming to the operative room or not.

Endotracheal intubation was facilitated using IV 0.5mg/kg atracurium, and anesthesia was maintained using isoflurane 1–2% inhalation under controlled mechanical ventilation that maintained an end-tidal carbon dioxide ($EtCO_2$) around 30–35mmHg.

All the patients received IV atropine 0.02mg/kg, dexamethasone 0.15mg/kg, and either IV amoxicillin 25mg/kg (maximum of 1gm) or clindamycin 10mg/kg (maximum of 600mg/kg) if they are penicillin-allergic. No additional opioids or NSAIDs were administered intraoperatively. All the patients were monitored intraoperatively using pulse oximetry, blood pressure, capnography, and ECG.

Surgery was performed by a single otolaryngology fellow using the same surgical technique (sharp dissection with 20 W bipolar cautery for hemostasis).

The patients were randomly allocated into two groups (group B and group K) according to the agent used for pre-incisional peritonsillar infiltration. Randomization was done by using computer-generated number lists, and the allocation was concealed using closed opaque envelopes.

Group B received 5ml of bupivacaine 0.5% infiltration, while group K received ketamine 0.5mg/kg infiltration. An anesthetist who was not sharing in the study prepared the 10ml syringes containing the appropriate study infiltration drug diluted in normal saline to achieve a 10ml volume.

Following the application of sterile drapes, a Boyle-Davis gag was inserted by the surgeon, and the pre-incisional infiltration solution was injected by the surgeon on each side submucosally in approximately equal amounts at three places: the upper pole of the tonsil and the lower end of the anterior and posterior pillars. Injection into the correct tissue plane was confirmed by swelling up of the mucosa to form a watery bleb around the tonsil. The surgical incision started 5min after the infiltration.

At the end of the surgery, the inhalation agent was discontinued, and the neuromuscular blocker was reversed by neostigmine 0.05mg and atropine 0.02mg/kg. The tracheal tube was removed in the lateral position after proper suctioning of the airway secretions and/or bleeding, and then oxygen was administered through a face mask to the patient, and then the patients were transferred to the recovery room.

In the recovery room, the heart rate and oxygen saturation were monitored for 2 hours; the post-anesthesia sedation level was assessed using the Wilson sedation scale at 30min, 1h, and 2h after surgery (Table 1), and the post-anesthesia recovery level was assessed using the modified Aldrete score at the same previous time intervals where the patients were to be discharged to the ward after obtaining an Aldrete score equal to or greater than 9 (Table 2).

The postoperative pain was assessed using the Modified Objective Pain Scale (MOPS) (Table 3) at a 60-minute interval in the recovery room, and when the patients were discharged to the ward, the postoperative pain was assessed at 2-hour intervals till discharge (12 hours). Patients with a score of 4 or more were given oral diclofenac sodium at a dosage of 1mg/kg as a rescue analgesic, and the total analgesic consumption during the first 12 hours postoperatively was recorded. On discharge, paracetamol (15mg/kg) orally on an 8-hour basis interval was prescribed to the patients.

Laryngeal or bronchospasm, nausea and vomiting, fever, and dysphagia for solids or liquids; primary bleeding; hallucinations; and sleep disturbance were observed after the surgery in the hospital and then through a telephone follow-up for 24 hours postoperatively.

Table 1: Wilson sedation scale[8]:

Parameter	Score
Fully awake, orientated	1
Drowsy	2
Opens eyes with a verbal command	3
Opens eyes with mild physical stimulation	4
Does not respond to mild physical stimulation	5

Table 2: The modified Aldrete post-anesthesia recovery scale[9]:

Activity:	
Unable to move limbs voluntarily or on command	0
Able to move 2 limbs voluntarily or on command	1
Able to move 4 limbs voluntarily or on command	2
Respiration:	
Apnea	0
Dyspnea or limited breathing	1
Able to breathe deeply and cough freely	2
Circulation:	
±50% pre-operative value	0
±20-49% pre-operative value	1
±20% pre-operative value	2
Consciousness:	
Not responding	0
Arousable on calling	1
Fully awake	2
Oxygen saturation:	
<90% even with oxygen supply	0
>90% with oxygen supply	1
>92% on air	2

the other 40 received preincisional ketamine infiltration. The two groups did not show a significant difference in terms of age, sex, or the type of surgery performed, as indicated in (Table 4).

There was no significant difference between bupivacaine and ketamine groups as regards post-anesthesia recovery Aldrete score (P 0.534) with Bupivacaine (Range) Mean±SD (7-9) 8.35±0.65 while Ketamine (7-9) 8.45±0.66.

Table 4: Demographic data of the two groups:

	Group B	Group K	*P*. value
Age (Years):			
Range	3-17	3-15	0.449
Mean±SD	7.63±3.96	7.00±3.35	
sex: *n*(%)			
Male	23(57.5%)	22(55%)	0.500
Female	17(42.5%)	18(45%)	
Type of surgery *n*(%)			
Tonsillectomy	15(37.5%)	24(60%)	
Adenotonsillectomy	22(55%)	13(32.5%)	0.111
Adenotonsillectomy and bilateral grommets ventilation tubes	3(7.5%)	3(7.5%)	

Data expressed as mean±SD and *n*(%); *: *P* value was considered significant if <0.05. Age (Years).

Table 3: The Modified Objective Pain Scale (MOPS)[10]

Parameter	Crying	Movement	Agitation	Posture	verbal
0	Not crying	None	Asleep or calm	No special posture	asleep/no complaint
1	Crying but responds to loving care	Restless	Mild	Flexing Legs and thighs	complains/cannot localize
2	Cry, not respond to loving care	Thrashing	Hysterical	Holding injury (Surgical) site	complains/can localize

Sample size calculation and statistical analysis

We aimed for a study power of 0.8 with an alpha error of 0.5. Sample size calculation based on the Modified Objective Pain Scale (MOPS). We considered a 25% reduction in MOPS to be clinically significant, assuming a standard deviation of 15%. Forty participants per group were calculated to be sufficient for this study.

Statistical analysis was performed using SPSS version 15. Data were reported as mean (±SD) or number (%). Categorical variables were compared using the chi-squared test, while continuous variables were analyzed using the independent t-test or Mann-Whitney test. A *P*-value less than 0.05 was considered statistically significant.

RESULTS

In this study involving 80 patients aged 3 to 17 years scheduled for tonsillectomy or adenotonsillectomy, 40 patients received preincisional bupivacaine infiltration, and

There was no significant difference in post-anesthesia recovery, as indicated by the Aldrete score, between the bupivacaine and ketamine groups. The mean Aldrete score for bupivacaine was 8.35±0.65, and for ketamine, it was 8.45±0.66 (*P*= 0.534).

There was a significant reduction in Wilson sedation score (*P* value 0.006) in the ketamine {(Range) Mean±SD: (1-3) 1.68±0.61} than in the bupivacaine groups {(Range) Mean±SD: (1-4) 2.12±0.79}.

There was no significant difference between the bupivacaine and ketamine groups as regards the modified objective pain score (MOPS) (*P* 0.475), as Bupivacaine (Range) Mean±SD (1-9) 2.95±1.97. While ketamine (1-9) 2.65±1.76.

There was no significant difference between the bupivacaine group and the ketamine group as regards postoperative complications (*P*>0.05), as shown in Table (5).

Table 5: Comparison between the two groups as regards post-operative complications.

Post-operative complications	Group B	Group K	*P* value
	(Range) Mean±SD		
Laryngeal or bronchospasm	0(0)	1(2.5)	0.256
Fever	1(2.5)	5(12.5)	
Nausea and Vomiting	1(2.5)	1(2.5)	
Dysphagia	5(12.5)	2(5)	
1ry post-tonsillectomy bleeding	0(0)	1(2.5)	
hallucinations or sleep disturbance	0(0)	0(0)	

*: Data expressed as *n*(%); *: *P* value was considered significant if <0.05.

There was no significant difference (*P* 0.301) between the bupivacaine group (3.38±3.24) and the ketamine group (2.68±2.74) as regards the total analgesic consumption during the first 12 hours postoperatively (Table 6).

Table 6: Comparison between the two groups as regards the total analgesic consumption during the 1st 12 hours postoperatively.

	Bupivacaine	Ketamine	*P* value
	(Range) Mean±SD		
Analgesia intake Diclofenac Na (mg)	(0-12) 3.38±3.24	(0-12) 2.68±2.74	0.301

Data expressed as mean±SD; *: *P* value was considered significant if <0.05.

DISCUSSION

Tonsillectomy is one of the most common surgical procedures performed by otolaryngologists, which is usually uncomplicated[11].

There are great concerns about decreasing post-tonsillectomy problems, including pain, bleeding, laryngospasm, nausea, and vomiting, particularly to avoid pulmonary aspiration. Management of post-tonsillectomy pain is very important to prevent complications such as secondary bleeding and infection, shorten the length of hospitalization, and speed up the patient's return to normal activities[12]. Therefore, our study aimed to compare the efficacy of regional (pre-incisional peritonsillar) infiltration of bupivacaine versus ketamine in the management of postoperative pain after tonsillectomy.

In our study, both the bupivacaine and ketamine groups showed no significant difference in the MOPS, indicating that both drugs provided effective postoperative analgesia, with no notable difference in the post-anesthesia Aldrete recovery score.

In agreement with these results, Khavidaki *et al*., (2018) conducted a double-blind clinical trial on 60 patients undergoing tonsillectomy, divided into two groups. In the first group, 2cc of ketamine (0.5mg/kg) solution was injected into the peritonsillar space; in the second group, a similar administration was performed but with normal saline. At the end of the study, they showed that pain intensity experienced in the ketamine-treated group was significantly lower than that for the placebo group[13].

Also, Asyari *et al*., (2020) conducted research on 24 patients, 12 without local infiltration of ketamine as a control group and 12 with local infiltration of ketamine in the peritonsillar pillar. The pain was assessed 2 hours and 24 hours post-extubation with a Visual Analog Scale (VAS), and they found that the pain scale of patients given ketamine infiltration in the peritonsillar pillar had a lower mean VAS than that of patients without infiltration either 2 hours or 24 hours postoperatively[14].

The previous findings may be explained by the fact that ketamine has a strong analgesic effect. This drug has central and peripheral effects. If ketamine is given by local infiltration, it will cause higher tissue concentration compared to systemic administration and has a low affinity and slow absorption into the blood circulation[15]. Local infiltration of ketamine inhibits the peripheral channel of sodium, calcium, and potassium in the peripheral nerve (tonsillar nerve). Besides, by giving it locally, the function of ketamine as a glutamate N-methyl-d-aspartate (NMDA) receptor blocker will also reduce pain, as the glutamate receptors are also found at the nerve endings, and the inflammatory response, and the tissue damage will cause an increase in glutamate release at the primary afferent nerve end[16].

In agreement with our findings, Javaherforooshzadeh *et al*., (2021) conducted a double-blind clinical trial with 96 patients undergoing tonsillectomy, divided into bupivacaine (48 patients) and placebo (48 patients) groups. The visual analog score was measured in the recovery period at 0, 1, 2, 4, 8, 12, and 24 h after surgery, and they showed significantly lower VAS in the recovery period in the bupivacaine group than in the placebo group. Also, they concluded that preoperative local injection of 0.5% bupivacaine for tonsillectomy reduces the postoperative recovery period[17].

This may be because bupivacaine prevents pain by blocking afferent nerve endings through the inhibition of voltage-gated Na+ channels, reducing peripheral nociceptive excitation. Bupivacaine also reduces inflammatory activity by inhibiting Ca^{2+} ion signaling and the release of interleukin 1β in astrocytes and by interacting with 5 hydroxytryptamine, opioid, and glutamate receptors. These effects also reduce the need for intravenous opiates, resulting in a more rapid recovery[17].

Our study did not observe any major postoperative complications, and there was no significant difference between the bupivacaine and ketamine groups.

In line with our results, Pirzadeh *et al*., (2012) found that there were no postoperative cases of apnea or laryngospasm in the ketamine group, while patients in the control group who received a peritonsillar injection of normal saline experienced more vomiting in the recovery room, but the difference was not significant[18].

Our study found no significant difference in total analgesic consumption between the bupivacaine and ketamine groups in the first 12 hours postoperatively.

This goes in accordance with a study reported by Erhan *et al*., in which 0.5mg/kg ketamine was used, and the CHEOPS and Wilson sedation scales were assessed and showed that ketamine reduces pain and the need for analgesia and increases the time to the first request for analgesia, without significant changes in heart rate or nausea and vomiting[19].

Also, Inanoglu *et al*., enrolled 90 children undergoing tonsillectomy and divided them into three groups. Group I received intravenous and peritonsillar saline, group II received intravenous saline and peritonsillar bupivacaine, and group III received intravenous 0.5mg/kg ketamine and peritonsillar 0.25% bupivacaine (3-5ml per tonsil). Intravenous ketamine and peritonsillar infiltration with bupivacaine were safe and effective as part of a multimodal regimen in reducing post-tonsillectomy pain. Patients in group III also had significantly lower pain scores than group II at all time intervals except at the 15th minute, but analgesic requirements and the time to first analgesia were also significantly better in the ketamine group[20].

Additionally, a hundred patients with a mean age of 10.5 years undergoing adenotonsillectomy were divided into four groups: Group K1 received ketamine (0.5mg/kg) peritonsillar infiltration, Group M1 received meperidine (1mg/kg) peritonsillar infiltration, and groups K2 and M2 received a combination of ketamine (0.5mg/kg) or meperidine (1mg/kg) with bupivacaine (5mg/ml). Peritonsillar injection of a combination of bupivacaine and ketamine provided efficient postoperative analgesia after adenotonsillectomy and achieved higher parents' satisfaction with the outcome of surgery[21].

While previous studies focused on ketamine or bupivacaine alone or in combination, our study uniquely compares the effects of ketamine and bupivacaine on post-tonsillectomy analgesia.

CONCLUSION

Pre-incisional peri-tonsillar infiltration of either bupivacaine or ketamine may be a safe and effective option to manage post-tonsillectomy pain, with nearly equal effects on post-anesthesia recovery time and total postoperative analgesic consumption.

CONFLICT OF INTERESTS

There are no conflicts of interest.

REFERENCES

1. M.C. White, J.A. Nolan, (2005). An evaluation of pain and postoperative nausea and vomiting following the introduction of guidelines for tonsillectomy, Pediatr. Anaesth. 15, 683–688.

2. Lauder G, Emmott A. (2014). Confronting the challenges of effective pain management in children following tonsillectomy. Int J Pediatr Otorhinolaryngol. 78:1813-27.

3. Jensen DR. (2021). Pharmacologic management of post-tonsillectomy pain in children. World J Otorhinolaryngol Head Neck Surg. May 29;7(3):186-193. Doi: 10.1016/j.wjorl.2021.03.004. PMID: 34430826; PMCID: PMC8356107.

4. Souza LR, Oliveira MVM, Basile JR, *et al*. (2015). Anatomical and physiopathological aspects of oral cavity and oropharynx components related to oropharyngeal dysphagia. In: Speyer R, Bogaardt H, editors. Seminars in dysphagia. InTech. pp 10–11.

5. Unal Y, Pampel K, Korkmaz S, *et al*. (2007). Comparison of bupivacaine and ropivacaine on postoperative pain after tonsillectomy in pediatric patients. Int J Pediatr Otorhinolaryngol. 71:83-7.

6. Akoglu E, AkkurtBc, Inanoglu K, *et al*. (2006). Ropivacaine compared to bupivacaine for post-tonsillectomy pain relief in children: a randomized controlled study. Int J PediatrOtorhinolaryngol. 70:1169-73.

7. Honarmand A, Reza M. (2008). The preventive analgesic effect of pre-incisional peritonsillar infiltration of two doses of ketamine for postoperative pain relief in children following adenotonsillectomy. Pediatric Anesthesia. 18:508-514.

8. Wilson E, David A, MacKenzie N, Grant IS. (1990). Sedation during spinal anesthesia: comparison of propofol and midazolam. British Journal of Anesthesia. Jan 1;64(1):48-52.

9. Aldrete JA. (1995). The post-anesthesia recovery score was revisited. J Clin Anesth. 7(1):8991.

10. Carl L. von Baeyer, Lara J. Spagrud. (2007). A systematic review of observational (behavioral) measures of pain for children and adolescents aged 3 to 18 years, Pain. 127 (1): 140-150.

11. Al-ani, R.M. (2012). Post-tonsillectomy bleeding: Incidence and risk factors. Running title: PTB: Incidence and risk factors. Iraqi J. Comm. Med. 3 (1): 261-264.

12. Hultcrantz E. LinderA.Markström. A. (2005). Long-term effects of intracapsular partial tonsillectomy (tonsillotomy) compared with full tonsillectomy. Int J PediatrOtorhinolaryngol. 69: 463-469.

13. Khavidaki GD, Keykha A, Beirami F, *et al*. (2018). The effect of using preoperative ketamine injection on post-tonsillectomy pain intensity in children. Biomed Res Ther, 5(2): 2013-2021. DOI: 10.15419/bmrat.v5i02.416.

14. Asyari A, Novialdi, Morina E, *et al*. (2020). The effect of local ketamine infiltration on post-tonsillectomy pain scale. 50(1):39-45.

15. Sawynok J. (2014). Topical and peripheral ketamine as an analgesic. Anesth Analg. 119(1):170-8.

16. Schmid RL, Sandler AN, Katz J. (1999). Use and efficacy of low-dose ketamine in the management of acute postoperative pain: a review of current techniques and outcomes. Pain. 82:111-25.

17. Javaherforooshzadeh F, Gousheh M, Akhondzadeh R, *et al*. (2021). Effect of Local Injection of Bupivacaine for Pain Management After Tonsillectomy: A Randomized Clinical Trial. J Compr Ped. 12(3): e109328. Doi: 10.5812/compreped.109328.

18. Pirzadeh A, Mohammadi MA, Allaf-Akbari S, *et al*. (2012). The Effect of Ketamine on Posttonsillectomy Pain in Children: A Clinical Trial. Iranian Journal of Otorhinolaryngology. 24(1):23-28.

19. Erhan L, Goksu H, Alpay C, *et al*. (2007). Ketamine in post-tonsillectomy pain. Int J PediatrOtorhinolaryngol. 71:735-9.

20. Inanoglu K, OzbakisAkkurt BC, *et al*. (2009). Intravenous ketamine and local bupivacaine infiltration are effective as part of a multimodal regime for reducing post-tonsillectomy pain. Med Sci Monit. 15:CR539-543.

21. El Sonbaty MI, Abo el Dahab H, Mostafa A, Abo Shanab O. (2011). Preemptive peritonsillar ketamine infiltration: postoperative analgesic efficacy versus meperidine. Middle East J Anaesthesiol. 21:43-51.109, 86, 90, 93.