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Original Article

Comparative Analgesic Efficacy of Varying Concentrations of Oxybuprocaine Hydrochloride Gargle Following Adult Tonsillectomy: A Pilot Randomized Controlled Study

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ABSTRACT

Background: Adult tonsillectomy is associated with severe postoperative pain, often leading to readmission. This pilot study evaluates the feasibility, safety, and dose-response relationship of three concentrations of Oxybuprocaine hydrochloride gargle as an analgesic adjunct. **Materials and Methods:** Sixty healthy adults (18-60 years) were randomized into four groups (n=15 per group): Control (saline), Group A (0.3% Oxybuprocaine), Group B (0.15%), and Group C (0.06%). Patients gargled 10-15 mL for 30 sec thrice daily for three postoperative days. Pain was measured using a Visual Analogue Scale (VAS) before and 10 min after administration. **Results:** Groups A and B showed significantly higher VAS reduction compared to control (p<0.001). Group A provided the strongest relief (2.71±1.17 reduction) but had a 53.3% adverse reaction rate. Group B (1.08±0.71 reduction) provided the optimal therapeutic window with a 33.3% reaction rate. **Conclusion:** 0.15% oxybuprocaine gargle is a safe and effective adjunct for managing adult post-tonsillectomy pain.

Keywords: Tonsillectomy, Postoperative pain, Oxybuprocaine hydrochloride, Topical anesthetic, Visual Analog Scale (VAS), Dose-response, Coblation, Breakthrough pain, Multimodal analgesia, Gargle therapy, Safety profile, Randomized pilot study.

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INTRODUCTION

Tonsillectomy remains one of the most frequently performed surgical procedures in otorhinolaryngology, with over 600,000 cases annually in the United States alone (Afman *et al.*, 2006). Despite its ubiquity, the procedure is associated with intense postoperative pain that is often reported as more severe than major abdominal or orthopedic surgeries (Gerbershagen *et al.*, 2013). This pain typically peaks between postoperative days three and five, frequently leading to poor oral intake, dehydration, and unplanned readmissions (Geißler *et al.*, 2025; Roskvist *et al.*, 2024).

The pathophysiology of post-tonsillectomy pain involves mechanical trauma to the pharyngeal constrictor muscles and the exposure of raw nerve endings in the tonsillar fossa. This triggers the release of inflammatory mediators that sensitize peripheral nociceptors (Guntinas-Lichius *et al.*, 2023). While systemic multimodal analgesia-including paracetamol, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), and intraoperative steroids-is the current standard, it often fails to adequately control breakthrough pain during swallowing (Aldamluji *et al.*, 2021; Geißler *et al.*, 2019). Studies indicate that up to 26% of adult patients contact healthcare providers due to insufficient home pain management (Roskvist *et al.*, 2024).

Topical anesthetics offer a non-invasive, localized alternative to manage breakthrough symptoms. Oxybuprocaine hydrochloride (benoxinate) is an ester-type anesthetic known for its rapid onset and high mucosal permeability. While its efficacy has been explored in pediatric populations using gel (Xiaoning *et al.*, 2023) dose-response evaluation. This study aims to identify the optimal concentration of oxybuprocaine gargle that balances analgesic efficacy with local side effects like oral numbness.

MATERIALS AND METHODS

Ethical Approval

This prospective, randomized pilot study received approval from the Institutional Ethics Committee (No. PJ - Department - 2022 - 155) and adhered to the Declaration of Helsinki. All participants provided written informed consent.

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Participants

Sixty adult patients scheduled for bilateral tonsillectomy were recruited. Inclusion criteria included: (1) ASA grade I-II; (2) Age 18-60 years; and (3) No history of chronic pain syndromes or neurocognitive deficits (Wong Chung *et al.*, 2018). Patients with a history of recurrent peritonsillar abscess or allergies to local anesthetics were excluded (Caixeta *et al.*, 2020).

Surgical Procedure

All procedures were performed under general anesthesia using low-temperature plasma (Coblation) technology. Coblation is associated with reduced thermal damage to surrounding tissues and lower primary hemorrhage rates compared to electrocautery.

Intervention and Randomization

Patients were randomized (1:1:1:1) into four groups (n=15 each):

1. **Control:** 0.9% NaCl (Saline).
2. **Group A:** 0.3% Oxybuprocaine hydrochloride solution.
3. **Group B:** 0.15% Oxybuprocaine hydrochloride solution.
4. **Group C:** 0.06% Oxybuprocaine hydrochloride solution.

Patients gargled 10-15 mL of the assigned solution for 30 sec, three times daily from postoperative day 1 to 3.

Outcome Measures

The primary endpoint was pain reduction, calculated as the difference between pre-gargling VAS scores and scores 10 min post-administration. Secondary outcomes included the incidence of adverse reactions such as tongue numbness, nausea, or bleeding.

Sample Size Justification

As a pilot feasibility study, the sample size of 15 patients per arm was chosen to provide preliminary estimates of variability and effect size. This aligns with statistical "rules of thumb" for exploratory clinical trials, which suggest 12-15 participants per group are sufficient to power future definitive trials (Whitehead *et al.*, 2016).

RESULTS

Sixty patients completed the study. There were no significant differences in age, sex, smoking status, or operation time across the four groups (p>0.05). The mean age was 34.50±11.00 years, with a baseline surgical time of 29.20±9.95 min (Table 1).

Analgesic Efficacy

VAS reduction was significantly higher in Group A (2.71±1.17) and Group B (1.08±0.71) compared to the Control group (0.06±0.12, p<0.001). Group C (0.50±0.44) showed a minor trend toward relief but did not reach statistical significance compared to the control (p=0.101). Pairwise comparison showed Group A provided significantly greater relief than all other groups (p<0.05) (Table 2).

Safety Profile

Adverse reactions were reported by 26.7% of the total cohort, all of which were mild and self-limiting. The incidence followed a clear dose-response curve: 53.3% in Group A, 33.3% in Group B, and 20.0% in Group C (p=0.005). The most common symptoms were transient tongue numbness and mild nausea. No serious complications, such as secondary hemorrhage or systemic anesthetic toxicity, were observed (Table 3).

DISCUSSION

Managing post-tonsillectomy pain remains a significant challenge, with standard multimodal care often falling short during the critical 72-hr period after discharge (Alm *et al.*, 2021). The analgesic effect is likely mediated by the rapid blockade of sodium channels in the exposed nerve endings of the tonsillar bed. Unlike systemic opioids, which act centrally, topical anesthetics target the circulus tonsillaris plexus directly, dampening the primary source of nociception. Previous studies have indicated that topical lidocaine spray can reduce pain until the third postoperative day, but oxybuprocaine's higher mucosal permeability may provide a more robust effect in the denuded surgical site. Our results demonstrate that topical oxybuprocaine gargle provides immediate, clinically meaningful relief for breakthrough swallowing pain by directly targeting the sensitized nerve endings in the tonsillar fossa (Grainger and Saravanappa, 2008), providing a non-invasive tool for patients to manage their symptoms at home.

The strong dose-response relationship observed suggests that a threshold concentration is required to penetrate the surgical slough and reach the deeper nociceptors. While 0.3% oxybuprocaine (Group A) achieved the highest pain reduction, its high rate of tongue numbness (over 50%) is a major drawback. Excessive oral numbness in a surgical patient can cause anxiety and theoretically increase the risk of aspiration or tongue biting during meals (Hung *et al.*, 2010).

Group B (0.15%) appears to be the most practical choice for clinical integration. It maintained a statistically significant VAS reduction (1.08 points) while keeping adverse reactions at a manageable level (33.3%). In the context of multimodal therapy, even a 1-point reduction on the VAS is considered clinically significant, particularly when it addresses the patient's primary trigger for pain-swallowing (Geißler *et al.*, 2019; Guntinas-Lichius *et al.*, 2023).

While invasive peritonsillar infiltration with agents like levobupivacaine provides excellent intraoperative and early (24 hr) relief (Abo Elfadl *et al.*, 2022; Kasapoglu *et al.*, 2013), its

Table 2: Comparison of Pain Scores and Safety.

Group	VAS Reduction (Mean±SD)	Adverse Reactions n (%)	*p*-value (vs. Control)
Control	0.06±0.12	0 (0.0%)	-
Group A (0.3%)	2.71±1.17	8 (53.3%)	<0.001
Group B (0.15%)	1.08±0.71	5 (33.3%)	<0.001
Group C (0.06%)	0.50±0.44	3 (20.0%)	0.101

Table 1: General Clinical Indicators (*n*=60).

Variable	Control (*n*=15)	Group A (0.3%)	Group B (0.15%)	Group C (0.06%)	*p*-value
Age (years)	37.00±13.73	32.80±9.63	36.40±10.26	31.80±10.11	0.488
Sex (M/F)	11 / 4	8 / 7	7 / 8	9 / 6	0.494
Surgery Time (min)	33.53±12.50	27.53±12.00	28.93±7.82	26.80±5.13	0.249

Table 3: Pairwise Comparison of Adverse Reactions.

Comparison Pair	Fisher's Exact (Value)	*p*-value
Control vs. Group A	10.909	0.001*
Control vs. Group B	6.000	0.014*
Group A vs. Group B	1.222	0.269
Group B vs. Group C	0.682	0.409

effect wanes quickly. Non-invasive gargles provide patients with a "rescue" tool they can self-administer at home during peak pain periods (Geißler *et al.*, 2025; Ugur *et al.*, 2013). This could reduce the reliance on rescue opioids, which are associated with significant side effects like nausea and constipation (Aldamluji *et al.*, 2021). Furthermore, by effectively controlling acute pain on the first postoperative day, this intervention may help prevent the development of chronic postsurgical pain syndromes.

This study has several limitations inherent to its pilot design. The sample size (*n*=60) is sufficient for exploratory purposes but lacks the power to detect subtle differences in recovery metrics like time to resume a normal diet or secondary hemorrhage rates. Additionally, the lack of a double-blind design may have introduced reporting bias. Future large-scale, multi-center Randomized Controlled Trials (RCTs) should employ blinded assessments and extend follow-up to evaluate long-term functional outcomes and quality of life (Geißler *et al.*, 2025).

CONCLUSION

Topical gargling with 0.15% Oxybuprocaine hydrochloride is a feasible, safe, and effective adjunct for managing adult post-tonsillectomy pain. It effectively bridges the gap between systemic analgesia and breakthrough swallowing pain.

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ABBREVIATIONS

ASA: American Society of Anesthesiologists; **NaCl:** Sodium Chloride; **VAS:** Visual Analog Scale; **NSAIDs:** Non-Steroidal Anti-Inflammatory Drugs; **RCTs:** Randomized Controlled Trials; **hr:** Hour; **min:** Minutes; **n:** Number (sample size); **p:** Probability value (statistical significance); **±:** Plus–minus (standard deviation representation).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICAL APPROVAL AND INFORMED CONSENT STATEMENTS

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Review Committee of the Second Affiliated Hospital of Kunming Medical University (Approval No. PJ - Department - 2022 - 155) on March 2024, and all participants provided written informed consent.

DATA AVAILABILITY STATEMENT

The datasets generated during and analysed during the current study are available from the corresponding author on reasonable request.

REFERENCES

Abo Elfadl, G. M., AbdelRady, M. M., Osman, H. M., Gad, M. O., Abd El-Rady, N. M., and Ali, W. N. (2022). Efficacy of Levobupivacaine Versus Levobupivacaine Plus Dexmedetomidine Infiltration for Post-Tonsillectomy Analgesia: A Randomized Controlled Trial. *Pain Res Manag*, *2022*, 9958668. https://doi.org/10.1155/2022/9958668

Afman, C. E., Welge, J. A., and Steward, D. L. (2006). Steroids for post-tonsillectomy pain reduction: meta-analysis of randomized controlled trials. *Otolaryngol Head Neck Surg*, *134*(2), 181-186. https://doi.org/10.1016/j.otohns.2005.11.010

Aldamluji, N., Burgess, A., Pogatzki-Zahn, E., Raeder, J., and Beloeil, H. (2021). PROSPECT guideline for tonsillectomy: systematic review and procedure-specific postoperative pain management recommendations. *Anaesthesia*, *76*(7), 947-961. https://doi.org/10.1111/anae.15299

Alm, F., Lundeberg, S., and Ericsson, E. (2021). Postoperative pain, pain management, and recovery at home after pediatric tonsil surgery. *Eur Arch Otorhinolaryngol*, *278*(2), 451-461. https://doi.org/10.1007/s00405-020-06367-z

Caixeta, J. A. S., Sampaio, J. C. S., da Costa, P. S. S., and Avelino, M. A. G. (2020). Analgesia for adenotonsillectomy in children: a comparison between peritonsillar infiltration of tramadol, ketamine, and placebo. *Eur Arch Otorhinolaryngol*, *277*(6), 1815-1822. https://doi.org/10.1007/s00405-020-05878-z

Geißler, K., Ducke, M., Volk, G. F., Meißner, W., and Guntinas-Lichius, O. (2019). Pain on the first postoperative day after tonsillectomy in adults: A comparison of metamizole versus etoricoxib as baseline analgesic. *PLoS One*, *14*(8), e0221188. https://doi.org/10.1371/journal.pone.0221188

Geißler, K., Scham, D., Meißner, W., Schlattmann, P., and Guntinas-Lichius, O. (2025). Systematic review and meta-analysis of pain management after tonsillectomy. *Sci Rep*, *15*(1), 1476. https://doi.org/10.1038/s41598-024-85008-5

Gerbershagen, H. J., Aduckathil, S., van Wijck, A. J., Peelen, L. M., Kalkman, C. J., and Meissner, W. (2013). Pain intensity on the first day after surgery: a prospective cohort study comparing 179 surgical procedures. *Anesthesiology*, *118*(4), 934-944. https://doi.org/10.1097/ALN.0b013e31828866b3

Grainger, J., and Saravanappa, N. (2008). Local anaesthetic for post-tonsillectomy pain: a systematic review and meta-analysis. *Clin Otolaryngol*, *33*(5), 411-419. https://doi.org/10.1111/j.1749-4486.2008.01815.x

Guntinas-Lichius, O., Geißler, K., Mäkitie, A. A., Ronen, O., Bradley, P. J., Rinaldo, A., Takes, R. P., and Ferlito, A. (2023). Treatment of recurrent acute tonsillitis-a systematic review and clinical practice recommendations. *Front Surg*, *10*, 1221932. https://doi.org/10.3389/fsurg.2023.1221932

Hung, C. H., Liu, K. S., Shao, D. Z., Cheng, K. I., Chen, Y. C., and Chen, Y. W. (2010). The systemic toxicity of equipotent proxymetacaine, oxybuprocaine, and bupivacaine during continuous intravenous infusion in rats. *Anesth Analg*, *110*(1), 238-242. https://doi.org/10.1213/ANE.0b013e3181bf6acf

Kasapoglu, F., Demir, U. L., Kaya, F. N., Cetin, Y. S., and Yavascaoglu, B. (2013). The effects of levobupivacaine infiltration on post-tonsillectomy pain relief in adults: a single-blinded, randomized, and controlled clinical study. *Eur Arch Otorhinolaryngol*, *270*(2), 761-766. https://doi.org/10.1007/s00405-012-2194-1

Roskvist, M., Alm, F., Nerfeldt, P., and Ericsson, E. (2024). Pain management after tonsil surgery in children and adults-A national survey related to pain outcome measures from the Swedish Quality Register for tonsil surgery. *PLoS One*, *19*(3), e0298011. https://doi.org/10.1371/journal.pone.0298011

Ugur, K. S., Karabayirli, S., Demircioğlu, R., Ark, N., Kurtaran, H., Muslu, B., and Sert, H. (2013). The comparison of preincisional peritonsillar infiltration of ketamine and tramadol for postoperative pain relief on children following adenotonsillectomy. *Int J Pediatr Otorhinolaryngol*, *77*(11), 1825-1829. https://doi.org/10.1016/j.ijporl.2013.08.018

Whitehead, A. L., Julious, S. A., Cooper, C. L., and Campbell, M. J. (2016). Estimating the sample size for a pilot randomised trial to minimise the overall trial sample size for the external pilot and main trial for a continuous outcome variable. *Stat Methods Med Res*, *25*(3), 1057-1073. https://doi.org/10.1177/0962280215588241

Wong Chung, J., van Benthem, P. P. G., and Blom, H. M. (2018). Tonsillotomy versus tonsillectomy in adults suffering from tonsil-related afflictions: a systematic review. *Acta Otolaryngol*, *138*(5), 492-501. https://doi.org/10.1080/00016489.2017.1412500

Xiaoning, Z., Ying, W., and Xijia, S. (2023). Effects of oxybuprocaine hydrochloride gel on analgesia after pediatric tonsillectomy. *Journal of China Medical University* *52*(02), 182-185. https://link.cnki.net/urlid/21.1227.R.20230130.1458.015

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