PROTOCOL OF A THESIS FOR PARTIAL FULFILLMENT OF MASTER DEGREE IN OTORHINOLARYNGOLOGY

Title of the Protocol:

The effect of systemic nonsteroidal anti-inflammatory drugs (NSAIDs) Vs intraoperative infiltration of steroids in tonsillar bed following tonsillectomy on post tonsillectomy pain: A prospective randomized controlled study.

Approval date :19/1/2025

Postgraduate Student: Abdurrahman Samir Mohamed Mohamed Harby
Degree: M.B.B.Ch, Ain Shams University (2021)
Resident at ENT department ,Ain Shams University Hospitals

Director: Prof. Dr. Samia Ahmed Mahmoud Fawaz
Academic Position: Professor
Department: Otorhinolaryngology

Co-Director: Dr. Peter MiladMikhail
Academic Position: Assistant Professor
Department: Otorhinolaryngology

Co-Director: Dr. Ahmed Mohamed Kamel
Academic Position: Lecturer
Department: Otorhinolaryngology

Co-Director: Dr. Omar Mostafa Yosef
Academic Position: Lecturer
Department: Otorhinolaryngology

Faculty of Medicine
Ain Shams University
2024

What is already known on this subject?
What does this study add?

Tonsillectomy operations are frequently performed surgical procedures among children. The removal of the tonsils and the adenoids is considered to be relatively safe with no known long-term immunological side effects. Pain is the number one perioperative concern and post-operative complaint in most patients, causing many health morbidities especially in children. Post-tonsillectomy pain is one of the most frequent morbidities of tonsillectomy surgery. This randomised controlled clinical trial study will compare the efficacy of adding paracetamol tosystemic non-steroidal anti-inflammatory drugs (NSAIDs) versus adding steroidsas local infiltration to paracetamol on post tonsillectomy pain control.

1. INTRODUCTION/ REVIEW

Tonsillectomy is one of the most commonly performed surgeries in the world, particularly in children. The palatine tonsils are encapsulated within the space formed between the anterior and posterior pharyngeal pillars known as the tonsillar fossa **(Cohen& Sommer, 2016)**.

Tonsillectomy consists of the complete removal of the tonsil tissue by dissection along the capsule, lifting the tonsil off the adjacent muscular wall. In children, this procedure is often performed in concert with adenoidectomy for various indications including recurrent tonsillitis. Less frequent indications for tonsillectomy include sleep disordered breathing or obstructive sleep apnea syndrome (OSAS), treatment of periodic fevers with aphthous stomatitis, pharyngitis and adenitis,treatment/biopsy for tonsillar malignancy (**Baugh et al., 2011**).

Although tonsillectomy is one of the most common surgical methods performed worldwide, postoperative morbidity remains a significant clinical problem despite advances in anaesthetic and surgical techniques (**Ali, 2004**).It is important to better understand the pathophysiology of post tonsillectomy pain. First, pain can ensue simply from the positioning of the patient, including the placement of a mouth retractor (e.g., Boyle–Davis mouth gag). This can cause pressure and venous congestion of the tongue and postoperative swelling and pain, as well as stretching of the temporomandibular joint. Patients frequently also complain of ear discomfort, presumably referred otalgia, mainly via the glossopharyngeal nerve. As well, removal of the tonsil triggers inflammatory cascades that facilitate healing, but also leaves an open wound in the pharynx with exposed nerve fibers and damaged muscle fibers **(Cohen & Sommer, 2016)**.

This combination of factors creates a postoperative wound that is vulnerable to mechanical trauma generated during swallowing. The tonsillectomy wound also displays

evidence of infection and inflammation by generation of a thick fibrin layer (**Sutters &Isaacson, 2014**), that increases in size during the first 3–4 days postoperatively, and begins to shed at about 7 days, usually allowing the bed to remucosalize by the end of 2 weeks (**Isaacson, 2012**). In accordance with this healing process, post-tonsillectomy pain can manifest a biphasic pattern, with peaks at 3 and 7 days postoperatively, but may persist past 2–3 weeks following surgery (**Stewart et al., 2012**).

Post-tonsillectomy pain can be severe enough to hinder the return to normal activities, and impair swallowing leading to an increased risk of dehydration, secondary infection and bleeding. Pain leads to more need for analgesic medication, higher risk of complication, increase days of hospitalization and greater number of missed school and work days(**Warnock &Lander, 1998**;**Robinson &Purdie, 2000**).

There are many different methods of tonsillectomy such as cold dissection (CD) or hot dissection as in monopolar–bipolar dissection (MBD) and coblation dissection (CBD). (**Álvarez et al., 2017**). Based on the methods of tissue dissection and hemostasis (control of bleeding) either, different techniques are used in tonsillectomy such as hot-hot, cold-hot, and cold-cold techniques. The choice of a specific technique in tonsillectomy can significantly influence postoperative outcomes such as pain, bleeding, and recovery time.**(Abdel-Aziz et al., 2023**)

The "hot-hot" technique, which uses electrocautery for both dissection and hemostasis, is effective in controlling bleeding but may cause increased thermal damage to surrounding tissues, leading to more postoperative pain**(Verma et al., 2017).** The "cold-hot" technique combines cold dissection with hot coagulation, offering a balance of tissue preservation with efficient bleeding control. In contrast, the "cold-cold" method, utilizing scalpel or scissors for dissection and manual hemostasis, results in less thermal injury and may reduce pain, though it may require more careful bleeding management**(Stavroulaki et al.,2007).** Studies have shown that hot techniques have shorter operative time and less intraoperative blood loss, while cold dissection technique has less postoperative pain and less postoperative complications especially secondary haemorrhage, with more rapid wound healing.**(Abdel-Aziz et al., 2023**).

Intraoperative steroids are frequently used to prevent postoperative nausea and vomiting, and have been used following tonsillectomy (**Steward, 2011**). Some studies have also looked at the role of steroids in pain control and some studies have shown improved analgesia with the use of oral steroids postoperatively (**Park, 2015**). However, there has also been controversy surrounding the use of systemic steroids and their possible association with bleeding (**Hermans, 2012**).

Systemic anti-inflammatory medications, such as nonsteroidal anti-inflammatory drugs

(NSAIDs) (e.g., ibuprofen) are well known to be potent analgesics and rival opioids in their capacity to control pain, while decreasing the risk of other operative complications such as nausea and vomiting. NSAIDs act by inhibiting cyclooxygenase enzymes that mediate inflammation and pain. This also results in inhibition of thromboxane, an important component in platelet aggregation, potentially resulting in an increased risk of bleeding. Consequently, many surgeons are reluctant to use NSAIDs to treat pain in their postoperative patients.**(Cohen & Sommer, 2016)**.

Also known as paracetamol, acetaminophen is a commonly used analgesic and antipyretic. Acetaminophen has been shown to be very safe for use in children and generally causes fewer side effects than NSAIDs. It is commonly used as a first line of treatment for surgical pain, and has been demonstrated to be an effective analgesic for post-tonsillectomy pain. However, when used alone, acetaminophen may be insufficient following tonsillectomy, and is therefore often used in combination with an NSAID or opioid to obtain adequate pain control **(Cohen & Sommer, 2016)**.

In order to reduce post-tonsillectomy pain, a number of strategies have been developed by anaesthetic and surgical staff including the use of corticosteroids. The use of local agents, either by topical application into the tonsillar fossa, or by infiltration either before or after tonsillectomy has been studied as a method of reducing post-tonsillectomy pain. The rationale behind the use of local agents with analgesic or anaesthetic action in the peri-operative period relates not only to its ability to block peripheral nociceptor transmission after tissue damage but also in preventing sensitization of the central nervous system(**Grainger, 2008**).

Dexamethasone, a powerful synthetic steroid, is well-known as an effective antiemetic. Because of its anti-inflammatory andanti-edematous effects, the drug plays a primary role in pain therapy. Dexamethasone is preferred because of its absolute glucocorticoid and long-term effect of 36–72 hours. Short-term application, even in high doses, is not associated with severe side-effects, and the overall costs are low. Dexamethasone can be used in local infiltration to manage pain and inflammation during or after surgery. **(Egeli & Akkaya, 1997; Ali Maeed, 2004**).

2.AIM/OBJECTIVES

The aim of this study is to compare the efficacy of adding paracetamol to systemicnon-steroidal anti-inflammatory drugs (NSAIDs) versusadding dexamethasone as local infiltrationto paracetamol on post tonsillectomy pain control.

3.METHODOLOGY:
Patients and Methods/ Subjects and Methods/ Material and Methods

Type of Study

A Prospective Randomized Controlled study.

Study Setting

The study will be conducted at **Ain Shams University hospital, OtolaryngologyDepartment**.

Study Period

6 months from approval of the protocol.

Study Population

Participants will be recruited from outpatient ENT clinic,and ENT department inpatients.

Inclusion Criteria:

1- Age: Between 4-10 years.

2- Indications of tonsillectomy such as:
   a) Recurrent acute attacks at least 7 episodes in the past year or at least 5 episodes per year for 2 years or at least 3 episodes per year for 3 years.
   b) Chronic tonsillitis and hypertrophy of tonsils causing sleep apnea, difficulty in deglutition, interference in speech.

3- Tonsillectomy by cold dissection only.

4- American Society of Anesthesiologists (ASA) classification 1,2 (Normal Health, Mild systematic disease).

Exclusion Criteria:

1- Patients with age less than 4 and more than 10 years.
2- Indications of tonsillectomy other than chronic tonsillitis such as lymphoma.
3- Patients on chronic steroid therapy
4- Hemoglobin level less than 10 gm/dL
5- Presence of acute infection in the upper respiratory tract, acute tonsillitis

6- American Society of Anesthesiologists (ASA) classification ASA 3,4 (Severe systematic disease such as uncontrolled Diabetes, cardiac disease, liver or kidney disease, life threating medical conditions)
7- Regular use of analgesics within a week of surgery.

Sampling Method

The results were basedon Neupan et al. 2016, with the mean VAS on the fifth day with steroid infiltration 6.6 ± 6 while in the control group 13 ± 11. alpha error 5%, power of study 80%. The required sample size is 75 patients, 25 patients in each group. The program for sample size calculation is STATA 10.

Sample Size(study design)

The required sample size is 75 patients, will be subdivided randomly by computer-based program into 3 groups each consists of 25 patients.

1- First group: will receive local infiltration ofsteroids (dexamethasone) in tonsillar bed and paracetamol.
2- Second group: will receive systemic nonsteroidal anti-inflammatory drugs in the analgesic and anti-inflammatory dosage and paracetamol.
3- Third group: control group will receive NSAIDs, steroids and paracetamol as standard post tonsillectomy medications in our department.

Based on the results of Neupan et al. 2016, with the mean VAS on the fifth day with steroid infiltration 6.6 ± 6 while in the control group 13 ± 11. alpha error 5%, power of study 80%, the required sample size is 75 patients 25 patients in each group. The program for sample size calculation is STATA 10.

Ethical considerations: The approval of the Scientific Research Ethics Committee at the Faculty of Medicine, Ain Shams University will be obtained before starting work on the study.

Study medications

All the study medications are FDA approved and typically prescribed and used as post tonsillectomy surgery medications and the dosage will be adjusted according to the body weight of the patient.

1- Steroids as Dexamethasone will be injected by local infiltration method.0.1 to 0.5 mg/kg, with a typical maximum dose of 4 to 10 mg. The dosage ranges from 0.5 to 5 mg per site.
2- Systemic nonsteroidal anti-inflammatory drugs (NSAIDs) namely Ibuprofen in the analgesic and anti-inflammatory dose 10 mg/kg maximum 40 mg/kg/day.
3- Paracetamol will be used according to the weight of patient as 15 mg/kg per dose maximum 1 g per dose, and 4 g per day.

Study Procedures

All patients will undergo tonsillectomy by cold dissection under GA. The intervention will be done to the first group (25 patients) by the study investigator**.** Following tonsillectomy**,**

peritonsillar infiltration will be done.The investigator will infiltrate the study medications superficially into the peritonsillar fossae using the aspiration injection technique at the upper pole, lower pole, and midway between the two previous injection points at tonsillar bed in subcapsular plane (3–5 ml/tonsil) using a straight 23-G/25-G needle. Patients will be observed in the post anesthesia care unit (PACU) for 30 min, at least, before transference to the ward. Patients will be instructed how to use a 0–10 VAS (0: no pain–10: worst pain) (***Figure 1***).

Primary outcome

The primary endpoints that will be used is resting pain scores at 6, 24h and five days post-operatively. Where pain score will be measured at multiple points during the outcome intervals, the pain scores at the time closest to six and 24h will be used.

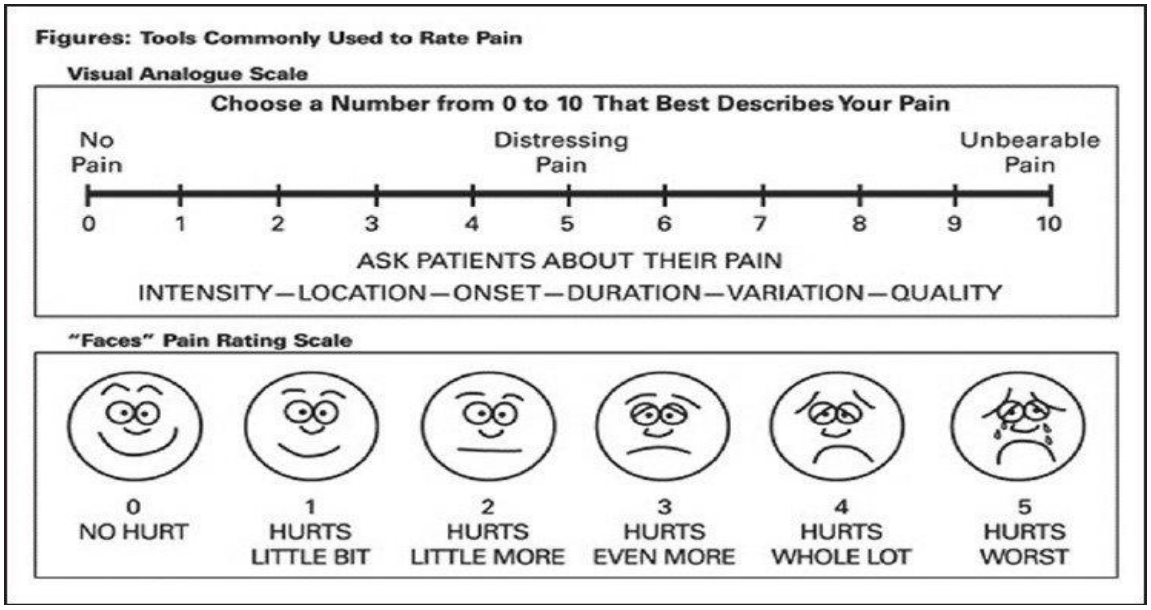

Figure 1*: *Wong-Baker FACES (VAS Score)

Secondary outcomes

1- The percentage of the patients in group 1 and 2 that will need extra analgesia
2- Patient satisfaction and return to normal activity.
3- Adverse effects noticed such as nausea, vomiting, infection and post tonsillectomy bleeding.

Statistical analysis

The data will be analysed using intent-to-treat analysis to ensure unbiased comparisons

between treatment groups. Numerical data will be presented as means and standard deviations, and the difference between the two groups will be tested using appropriate tests. Categorical data will be presented as frequencies and percentages, and the Chi-square test will be used for comparisons between groups when appropriate. A p-value < 0.05 will be considered statistically significant.

4. ETHICAL CONSIDERATIONS

This study will start after the approval of the" Research Ethics Committee" of Faculty of Medicine, Ain Shams University and an informed consent will be obtained from the participants or his/her caregiver, after explaining the study purpose and methods to the subjects.

5. REFERENCES

1- **Abdel-Aziz, M., Atef, A., Sabry, O. A., et al. (2023).** Different tonsillectomy techniques in Egypt: Advantages and disadvantages—Experience and review of literature. The Egyptian Journal of Otolaryngology, 39(1), 127.

2- **Ali Maeed, M. A. (2004).** Steroid therapy for posttonsillectomy symptoms in adults: A randomized, placebo-controlled study. Annals of Saudi Medicine, 24(5), 365–367.

3- **Álvarez Palacios, I., González-Orús Álvarez-Morujo, R., Alonso Martínez, C., et al. (2017).** Postoperative pain in adult tonsillectomy: Is there any difference between the technique? Indian Journal of Otolaryngology and Head & Neck Surgery, 69, 187–193.

4- **Baugh, R. F., Archer, S. M., Mitchell, R. B., et al. (2011).** Clinical practice guideline: Tonsillectomy in children. Otolaryngology–Head and Neck Surgery, 144(1 Suppl), S1–S30.

5- **Cohen, N., & Sommer, D. D. (2016).** Post-tonsillectomy pain control: consensus or controversy?. Pain management, *6*(1), 31-37.

6- **Egeli, E., & Akkaya, S. (1997).** The effect of peritonsillar corticosteroid infiltration in tonsillectomy. Auris Nasus Larynx, 24, 179–183.

7- **Grainger, J., & Saravanappa, N. (2008).** Local anesthetic for post-tonsillectomy pain: A systematic review and meta-analysis. Clinical Otolaryngology, 33, 411–419.

8- **Hermans, V., De Pooter, F., De Groote, F., et al. (2012).** Effect of dexamethasone on nausea, vomiting, and pain in pediatric tonsillectomy. British Journal of Anaesthesia, 109(3), 427–431.

9- **Isaacson, G. (2012).** Tonsillectomy healing. Annals of Otology, Rhinology & Laryngology, 121(10), 645–649.

10- **Park, S. K., Kim, J., Kim, J. M., et al. (2015).** Effects of oral prednisolone on recovery after tonsillectomy. Laryngoscope, 125(1), 111–117.

11- **Robinson, S. R., & Purdie, G. L. (2000).** Reducing post-tonsillectomy pain with cryoanalgesia: A randomized controlled trial. Laryngoscope, 110, 1128–1131.

12- **Stavroulaki, P., Skoulakis, C., Theos, E., et al. (2007).** Thermal welding versus cold dissection tonsillectomy: A prospective, randomized, single-blind study in adult patients. Annals of Otology, Rhinology & Laryngology, 116(8), 565–570.

13- **Steward, D. I., Grisel, J., & Meinzen-Derr, J. (2011**). Steroids for improving recovery following tonsillectomy in children. Cochrane Database of Systematic Reviews, 8, CD003997.

14- **Stewart, D. W., Ragg, P. G., Sheppard, S., et al. (2012).** The severity and duration of postoperative pain and analgesia requirements in children after tonsillectomy, orchidopexy, or inguinal hernia repair. Paediatric Anaesthesia, 22(2), 136–143.

15- **Sutters, K. A., & Isaacson, G. (2014).** Post-tonsillectomy pain in children. American Journal of Nursing, 114(2), 36–42.

16- **Verma, R., Verma, R. R., & Verma, R. R. (2017).** Tonsillectomy: Comparative study of various techniques and changing trend. Indian Journal of Otolaryngology and Head & Neck Surgery, 69(4), 549–558.

17- **Warnock, F., & Lander, J. (1998).** Pain progression, intensity and outcomes following tonsillectomy. Pain, 75, 37–45.