

Advantage of Application of Topical Hyaluronic Acid in Reducing Post Tonsillectomy Pain; Cross Sectional Comparative Study

Ahmed Kareem Shiaan Al-Baidhani¹, Muthanna Saleem Abdulameer²

¹F.I.C.M.S (Otolaryngology)-Al-Sadiq Teaching General Hospital/Iraq, ²F.A.B.H.S (Otolaryngology), Lecturer, Hammurabi College of Medicine, University of Babylon/Iraq, ³Consultant Otolaryngology/Al-Sadiq Teaching General Hospital/Iraq

Abstract

Introduction: Tonsillectomy is common surgical operation performed in otolaryngology department. Various techniques could be used that include traditional cold dissection, powered instrumentation like electro cautery, harmonic scalpel, laser, and radiofrequency technique. As with any surgery, there are some risks can occur with tonsillectomy, these includes bleeding, pain at the site of surgery and/or referred otalgia, and infection. The aim of our study was to assess the postoperative use of topical hyaluronic acid with regards to safety, pain relief. **Method:** The research was considered a cross-sectional research made on 60 patients needing tonsillectomy from a period began from January to September 2018. The patients had been separated into two groups both from 30 patients, one group (group A) treated by using high molecular weight(HMW) Hyaluronic acid spray on tonsillar beds after operations , and the second group(group B) dealt as control. Early complications were registered in questionnaires and then the data were evaluated for each group. **Results:** The use of high molecular weight (HMW) Hyaluronic acid spray on tonsillar beds after surgery has reduces the pain significantly after 3 – 7 days (p-value = 0.0001) while has no implication on pain reduction within 12 - 24 hours p-value (0.17 and 0.3) respectively . **Conclusion:** The use of (HMW) hyaluronic acid spray can be used safely in post tonsillectomy patients. Hyaluronic acid spray can minimize post tonsillectomy pain.

Keywords: High molecular weight (HMW) hyaluronic acid (H.A.), tonsillectomy, pain

Introduction

The history of surgical removal of tonsils has been returned back to three thousand years ago¹, nowadays, Tonsillectomy is usual operation almost lead to open wound, so, connected with important postoperative pain that may last as long as 2 to 3 weeks period 2–5. This pain constitutes the major morbidity factor leading to poor nutrition, dysphagia, dehydration and delaying time for returning to work or school^{6,7}. Many factors contributes to the post-tonsillectomy pain as mucosal damage, irritation of vagal , glossopharyngeal nerves ,tissue inflammation ,retained debris and spasm of the muscles of the pharynx ^{5,8,9}.

Nonsteroidal anti-inflammatory drugs, codeine and paracetamol are frequently used to minimize the pain occurs following tonsillectomy ^{10,11}.Opioids are

associated with respiratory depression ,nausea, vomiting, depression of cough reflex and sedation^{5,10,12}. So, more safe opioid and non-opioid analgesia are used as pain killer to alleviate pain and discomfort after removal of the tonsils. Ibuprofen now suggested by American Academy of Otolaryngology— Head and Neck Surgery for pain relief following tonsillectomy ^{4,8,13}.

Optimal pain relief after tonsillectomy is challenging .Many researchers use different options for pain reduction whether systemic or topical like bupivacaine ^{14,15}, dexamethasone , lignocaine¹⁵ , sucralfate ¹⁶, etc.

Hyaluronic acid is high molecular weights, hydrophilic glycosaminoglycan that is a naturally component of connective tissue particularly seen in the synovial fluid of joint and inside the extracellular matrix of skin ^{17–19}. It provides a role in wound healing where

its secretion in proliferative phase stimulates fibroblast migration and proliferation 20,21. Finally it shows a suppressive effect on inflammatory mediators, tissue reactions to trauma so could be applied safely as an anti-inflammatory factor 21,22. Hyaluronic acid is a lubricant material with ability to stimulate growth so widely used to be the normally non-immunogenic, biocompatible and anti-inflammatory dressing biomaterial 22. Hyaluronic acid is reported to decrease pain, inflammation with stimulation of wound healing in pressure ulcers 19. It has a role in management of osteoarthritis and tendon problems 17, in burns, and chronic wounds 23,24 as well as in healing of vocal fold wounds 25.

Materials and Method

A cross-sectional study carried out on 60 patients requiring tonsillectomy throughout the period began from January to September 2018. The study certified by hospital ethical committee with written informed consent was taken. The indications of surgery are recurrent attacks of acute tonsillitis, chronic tonsillitis and/or large obstructive tonsil with sleep apnea syndrome. Patients with quinsy, associated adenoiditis or adenoid hypertrophy, tonsillectomy for biopsy were excluded. Our study population was arising from those attended to Al-Sadiq teaching general hospital in Hilla city, Babylon, Iraq. The tonsillectomies have been done under general anesthesia, with placement of oral endotracheal intubation. The tonsils were removed by cold steel dissection method and hemostasis by ligatures, packs or cautery. The study sample were divided into 2 groups each from 30 patients, first group (group A) dealt with postoperative use of high molecular weight (HMW) Hyaluronic acid spray (0.01% topical spray) on tonsillar beds three to five times per day starting 3 hours postoperatively and the second group (group B) considered as a control. Pain assessment was done 12 hours, 24 hours, 3 days and 7 days post tonsillectomy using visual analogue scale from 0-10 (0 represents no pain at all, 10 represents the severe incapacitating pain). Data collected were comprised of age, gender, all data collected for both groups were analyzed by SPSS 22 used Mann - Whitney test for calculate P-value and another statistical analysis.

Results

In our study we take 60 patients all undergone tonsillectomy, 30 patients were used H.A. after tonsillectomy as a (case) and 30 patients not used H.A.

as a (control). 38(63.33%) of patients were female and 22(36.67%) were male as in figure 1.

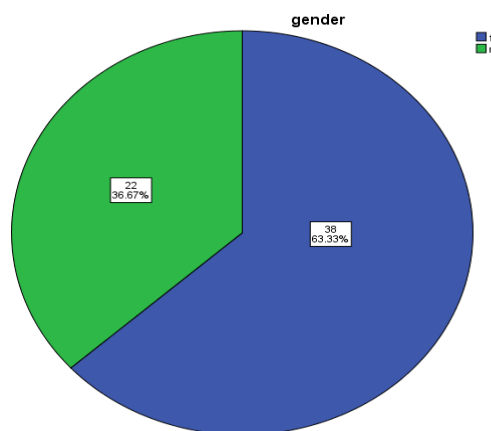


Figure1: gender distribution

Figure 2 shows gender distribution according to the type of sample.

Table 1 shows that the two groups (case and control) are similar regarding the age (p value > 0.05)

Table 1: Mean age of the study sample

| | Case Mean ±SD | Control Mean ±SD | Z- test | P value |
|-------------|---------------|------------------|---------|---------|
| Age (years) | 18.7 ± 3.6 | 18.9 ± 3 | 0.3 | 0.53 |

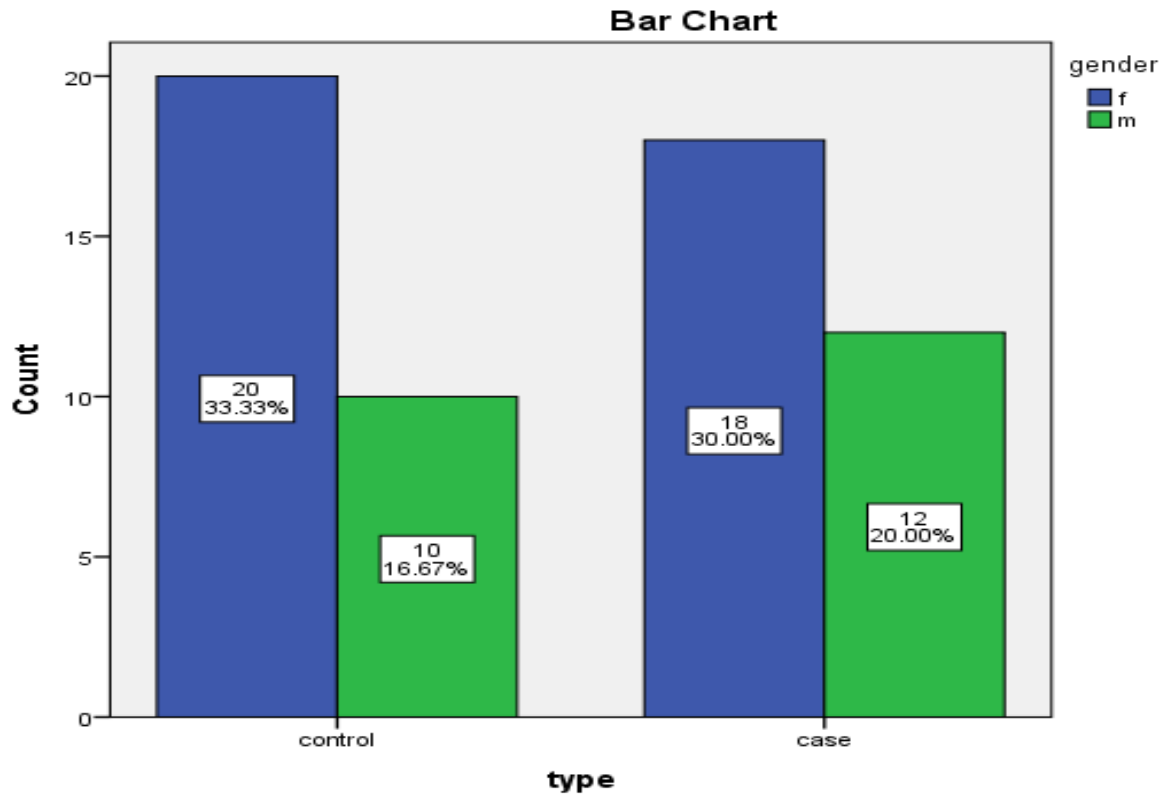
Z: Man-Whitney test; P- value <0.05 =significant.

Gender Chi square = 0.3 with P-value= 0.79 no difference between gender in case and control sample.

Figure 2: gender distribution according to type of sample

Table 2 shows that there is no difference in pain score at 12 hours and 24 hours postoperatively after using H.A. between the case and control group (p - value 0.17 and 0.3) respectively. However the use of H.A. spray post tonsillectomy in case group results in significant decrease in pain after 3 days and 7 days postoperatively (p value <0.05).

Table 2: Pain assessment by visual analogue scale post operatively



| Time | Case Mean ±SD | Control Mean ±SD | Z- test | P-value |
|----------------|---------------|------------------|---------|----------|
| After 12 hours | 7.20±1 | 7.60±1.1 | 1.37 | 0.17 |
| After 24 hours | 7.13±1 | 7.40±1.2 | 1.078 | 0.3 |
| After 3 days | 4.60±1.2 | 6.60±1.7 | 4.491 | 0.0001** |
| After 7 days | 2.47±1.3 | 4.07±1.34 | 4.071 | 0.0001** |

Z: Man-Whitney test; P- value <0.05 =significant.

Discussion

Pain management after tonsillectomy is a crucial factor in decreasing postoperative morbidity and complications like poor oral intake, dehydration, dysphagia and disturbed sleep 10,11,26. The pain and inflammatory reactions following oral surgery may reach its maximum level two days postoperatively and decrease through 7-10 days 27

Hyaluronic acid is a linear polysaccharide found in many tissues especially connective tissues where its responsible for tissue elasticity ,control of hydration of connective tissues and synovial fluid elastoviscosity .It

is an important factor in the process of wound healing 28,29. In our study it was found that postoperative pain following tonsillectomy was dramatically reduced by using topical (HMW) Hyaluronic acid spray especially after 3 days. This may be explained by the fact that this substance has a role in repairing tissue and cover the exposed wound of tonsillectomy as well as its minimize the risk of post tonsillectomy infection .These effects were clearly described to induce healing for pressure ulcers and to increase the rate of healing in diabetic foot30. Hyaluronic acid also has anti-inflammatory effects; decreasing leukocyte infiltration and enhance the angiogenesis31. H.A. is effective in management of osteoarthritis pain17 and pain of temporomandibular joint disorder18, where it used for intra articular

injection²¹. Researchers from turkey studied the effect of applying hyaluronic acid gel during tonsillectomy and found that the pain decrease significantly postoperatively with rapid wound healing. In our study the maximum benefit from applying the H.A. spray was between 3-7 days (p value <0.05) while no significant pain reduction was observed within 24 hours postoperatively. This may indicate that immediate effect of H.A. need time to act as anti-inflammatory, coating material and stimulatory for wound healing.

Several studies test the effect of hyaluronic acid following teeth extraction especially third molar teeth and found significant pain reduction with decrease in analgesics need ^{32,33}. Little researches studied the effect of hyaluronic acid following tonsillectomy so researchers should be encouraged to explore its effects, adverse effects with a larger study samples.

Conclusion

The use of topical (HMW) Hyaluronic acid spray is recommended post tonsillectomy to decrease post tonsillectomy pain and decrease the need for analgesia. Its shows maximum effect after 3 days postoperatively which may help to speed recovery, decrease morbidity and ensure early return to school and work.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

Funding: Self-funding

References

- Flávio J, Júnior N, Hermann DR, Américo R, Stamm RG, Hirata CW. Breve História da Tonsilectomia A Brief History of Tonsillectomy. 2006:314-317.
- Stelter K. Tonsillitis and sore throat in children. *GMS Curr Top Otorhinolaryngol - Head Neck Surg.* 2014.
- Howard D, Davis KF, Phillips E, et al. Pain management for pediatric tonsillectomy: An integrative review through the perioperative and home experience. *J Spec Pediatr Nurs.* 2014. doi:10.1111/jspn.12048
- Isaacson G. Tonsillectomy Care for the Pediatrician. *Pediatrics.* 2012. doi:10.1542/peds.2011-3857
- Aysenur D, Mine C, Ozgur Y, et al. Pre-emptive peritonsillar dexamethasone vs. levobupivacaine infiltration for relief of post-adenotonsillectomy pain in children: A controlled clinical study. *Int J Pediatr Otorhinolaryngol.* 2014. doi:10.1016/j.ijporl.2014.06.010
- Vasan NR, Stevenson S, Ward M. Preincisional bupivacaine in posttonsillectomy pain relief: A randomized prospective study. *Arch Otolaryngol - Head Neck Surg.* 2002. doi:10.1001/archotol.128.2.145
- Ohlms LA. Injection of Local Anesthetic in Tonsillectomy. *JAMA Otolaryngol Neck Surg.* 2001;127(10):1276-1278. doi:10.1001/archotol.127.10.1276
- Sutters KA, Isaacson G. Posttonsillectomy pain in children. *Am J Nurs.* 2014. doi:10.1097/01.NAJ.0000443769.04764.65
- Rakesh S, Anand TS, Payal G, Pranjali K. A Prospective, Randomized, Double-Blind Study of Coblation versus Dissection Tonsillectomy in Adult Patients. *Indian J Otolaryngol Head Neck Surg.* 2012. doi:10.1007/s12070-011-0355-y
- Subramanyam R, Varughese A, Willging JP, Sadhasivam S. Future of pediatric tonsillectomy and perioperative outcomes. *Int J Pediatr Otorhinolaryngol.* 2013. doi:10.1016/j.ijporl.2012.10.016
- Ju NY, Cui GX, Gao W. Ropivacaine plus dexamethasone infiltration reduces postoperative pain after tonsillectomy and adenoidectomy. *Int J Pediatr Otorhinolaryngol.* 2013. doi:10.1016/j.ijporl.2013.08.037
- Javid MJ, Hajjafari M, Hajipour A, Makarem J, Khazaeipour Z. Evaluation of a Low Dose Ketamine in Post Tonsillectomy Pain Relief: A Randomized Trial Comparing Intravenous and Subcutaneous Ketamine in Pediatrics. *Anesthesiol Pain Med.* 2012. doi:10.5812/aapm.4399
- Moss JR, Watcha MF, Bendel LP, McCarthy DL, Witham SL, Glover CD. A multicenter, randomized, double-blind placebo-controlled, single dose trial of the safety and efficacy of intravenous ibuprofen for treatment of pain in pediatric patients undergoing tonsillectomy. *Paediatr Anaesth.* 2014. doi:10.1111/pan.12381
- Kountakis SE. Effectiveness of perioperative

- bupivacaine infiltration in tonsillectomy patients. *Am J Otolaryngol - Head Neck Med Surg.* 2002. doi:10.1053/ajot.2002.28771
15. Kaygusuz I, Susaman N. The effects of dexamethasone, bupivacaine and topical lidocaine spray on pain after tonsillectomy. *Int J Pediatr Otorhinolaryngol.* 2003. doi:10.1016/S0165-5876(03)00091-0
 16. Siupsinskiene N, Žekonienė J, Padervinskis E, Žekonis G, Vaitkus S. Efficacy of sucralfate for the treatment of post-tonsillectomy symptoms. *Eur Arch Oto-Rhino-Laryngology.* 2014. doi:10.1007/s00405-014-3023-5
 17. Abate M, Schiavone C, Salini V. The Use of Hyaluronic Acid after Tendon Surgery and in Tendinopathies. *Biomed Res Int.* 2014. doi:10.1155/2014/783632
 18. Gencer ZK, Özkiriş M, Okur A, Korkmaz M, Saydam L. A comparative study on the impact of intra-articular injections of hyaluronic acid, tenoxicam and betametazon on the relief of temporomandibular joint disorder complaints. *J Cranio-Maxillofacial Surg.* 2014. doi:10.1016/j.jcms.2014.01.041
 19. Ramos-Torrecillas J, García-Martínez O, De Luna-Bertos E, Ocaña-Peinado FM, Ruiz C. Effectiveness of Platelet-Rich Plasma and Hyaluronic Acid for the Treatment and Care of Pressure Ulcers. *Biol Res Nurs.* 2015. doi:10.1177/1099800414535840
 20. MacKay D, Miller AL. Nutritional Support for Wound Healing. *Altern Med Rev.* 2003.
 21. Voigt J, Driver VR. Hyaluronic acid derivatives and their healing effect on burns, epithelial surgical wounds, and chronic wounds: A systematic review and meta-analysis of randomized controlled trials. *Wound Repair Regen.* 2012. doi:10.1111/j.1524-475x.2012.00777.x
 22. J.S. B, K.H. M, H.N.E. S. Wound healing dressings and drug delivery systems: A review. *J Pharm Sci.* 2008. doi:http://dx.doi.org/10.1002/jps.21210
 23. Onesti MG, Fino P, Ponzo I, Ruggieri M, Scuderi N. Non-surgical treatment of deep wounds triggered by harmful physical and chemical agents: A successful combined use of collagenase and hyaluronic acid. *Int Wound J.* 2016. doi:10.1111/iwj.12215
 24. Magdy EA, Elwany S, El-Daly AS, Abdel-Hadi M, Morshedy MA. Coblation tonsillectomy: A prospective, double-blind, randomised, clinical and histopathological comparison with dissection-ligation, monopolar electrocautery and laser tonsillectomies. *J Laryngol Otol.* 2008. doi:10.1017/S002221510700093X
 25. J. G. Hyaluronic acid hydrogels for vocal fold wound healing. *Biomatter.* 2013.
 26. Cho HK, Kim KW, Jeong YM, Lee HS, Lee YJ, Hwang SH. Efficacy of ketamine in improving pain after tonsillectomy in children: Meta-analysis. *PLoS One.* 2014. doi:10.1371/journal.pone.0101259
 27. van Wijk A, Kieffer JM, Lindeboom JH. Effect of Third Molar Surgery on Oral Health-Related Quality of Life in the First Postoperative Week Using Dutch Version of Oral Health Impact Profile-14. *J Oral Maxillofac Surg.* 2009. doi:10.1016/j.joms.2008.12.041
 28. Radice M, Brun P, Cortivo R, Scapinelli R, Battaliard C, Abatangelo G. Hyaluronan-based biopolymers as delivery vehicles for bone-marrow-derived mesenchymal progenitors. *J Biomed Mater Res.* 2000. doi:10.1002/(SICI)1097-4636(200005)50:2<101::AID-JBM2>3.0.CO;2-M
 29. Sahayata VN, Bhavsar N V, Brahmabhatt NA. An evaluation of 0.2% hyaluronic acid gel (Gengigel®) in the treatment of gingivitis: a clinical & microbiological study. *Oral Health Dent Manag.* 2014.
 30. Chen CP, Hung W, Lin SH. Effectiveness of hyaluronic acid for treating diabetic foot: A systematic review and meta-analysis. *Dermatol Ther.* 2014. doi:10.1111/dth.12153
 31. Gocmen G, Gonul O, Oktay NS, Yarat A, Goker K. The antioxidant and anti-inflammatory efficiency of hyaluronic acid after third molar extraction. *J Cranio-Maxillofacial Surg.* 2015. doi:10.1016/j.jcms.2015.04.022
 32. Shuborna NS, Chaiyasamut T, Sakdajeyont W, Vorakulpipat C, Rojvanakarn M, Wongsirichat N. Generation of novel hyaluronic acid biomaterials for study of pain in third molar intervention: a review. *J Dent Anesth Pain Med.* 2019. doi:10.17245/jdapm.2019.19.1.11
 33. Yilmaz N, Demirtas N, Kazancioglu HO, Bayer S, Acar AH, Mihmanli A. The efficacy of hyaluronic acid in postextraction sockets of impacted third molars: A pilot study. *Niger J Clin Pract.* 2017. doi:10.4103/1119-3077.224131