## **Original Research Article**

DOI: http://dx.doi.org/10.18203/issn.2454-5929.ijohns20183695

# Study of effect of 1% sodium hyaluronate application on tympanic membrane perforation

### Dimple Sahni\*, Bikramjit Singh, K. S. Uppal, Sanjeev Bhagat, Dinesh Sharma, Girish Dogra

Department of Otorhinolarynogology, Government Medical College, Patiala, Punjab, India

Received: 28 May 2018 Revised: 18 July 2018 Accepted: 19 July 2018

#### \*Correspondence: Dr. Dimple Sahni,

E-mail: sawhneygirish@gmail.com

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

#### **ABSTRACT**

**Background:** Topical applications of hyaluronic acid have been found to have beneficial effects on closure of tympanic membrane perforations. The aim of the study was to evaluate the role of 1% sodium hyaluronate in the repair of small or medium sized dry central tympanic membrane perforation and improvement in hearing following closure of tympanic membrane perforation.

**Methods:** 50 patients with dry central perforation of inflammatory or traumatic origin were taken up. Maximum of 4 applications of 1% sodium hyaluronate were given at weekly intervals. Final mapping for closure of tympanic membrane perforation and hearing assessment was done after 3 months.

**Results:** 26 perforations closed completely while 18 perforations showed significant reduction in size. Thus 44 or 88% perforations showed positive response to 1% sodium hyaluronate application. Hearing Improvement was observed on pure tone audiometry with the average hearing gain in patients after complete closure of tympanic membrane perforation was 12.40 dB with p value of 0.001.

**Conclusions:** Study showed the beneficial effects of 1% sodium hyaluronate application in closure of small and medium size perforations of tympanic membrane perforation and improvement in hearing.

Keywords: Hyaluronic acid, Tympanic membrane perforation, Pure tone audiometry, Chemical cautery, Hearing loss

#### INTRODUCTION

The tympanic membrane is a unique structure which is important for sound transmission, a key in impedance matching for sound travelling from air to fluid and only true closing membrane remaining in fully developed human fetus.<sup>1</sup>

Perforation of tympanic membrane is a common presentation to an Otolaryngologist. The most common etiologies of tympanic membrane perforation include trauma, otitis media and grommets. The majority of these tympanic membrane perforations tend to heal spontaneously (88%).<sup>2</sup>

The perforation of tympanic membrane leads to hearing loss (conductive type). This is because of decreased drum area and the round window protection, so that the differential required to produce perilymph movement is reduced.<sup>3</sup> Untreated perforations may lead to increased susceptibility to infection and ear discharge, speech problems due to hearing loss and cholesteatoma formation.<sup>4</sup>

It is important that tympanic membrane perforations are diagnosed and treated as early as possible. Recently there has been more inclination towards the surgical repair of tympanic membrane perforations. Over the years, alternative methods and materials were applied in the outpatient settings that obviate the need for general anaesthesia have been extensively researched. Chemical cautery agents like hyaluronic acid/sodium hyaluronate, trichloroacetic acid, silver nitrate and urea are being used commonly for small dry central perforations. Chemical cautery makes the margins of the perforation raw and allows the epithelium to grow. In particular, hyaluronic acid has gained popularity following the discovery of its prominent roles in wound healing.<sup>5</sup>

Beneficial effect of hyaluronic acid application over other chemical agents for successful tympanic membrane repair has been seen. Hyaluronic acid has a vast range of biological functions in altering the integrity of tissues and plays an important role in inflammation and wound healing. Being a natural component of the extracellular matrix of many body tissues, it is highly biocompatible. <sup>6</sup>

Hyaluronic acid (hyaluronan) consists of an unbranched chain of repeating disaccharide units which contains D-glucuronic acid and N-acetyl glucosamine.<sup>7</sup> It is a glycosaminoglycan which are essential for maintaining structural integrity of many connective tissues.<sup>8</sup>

Hyaluronic acid has an important role in cell migration during morphogenesis and wound repair. It attracts water into extracellular matrix and thereby "loosen it up" may be important in this regard.<sup>7</sup>

Hyaluronic acid has influence in rapid restoration of the body tissue components. This helps in less scar formation and enhancement of structure and function of the healed tympanic membrane perforation.<sup>9</sup>

In the present study, 1% sodium hyaluronate (SH) was used for applications over tympanic membrane perforation. Commercially, it is available in the form of a prefilled syringe.

#### Aims and objectives

The study was conducted to evaluate the role of topically applied 1% sodium hyaluronate in the repair of small or medium sized dry central tympanic membrane perforation and hearing gain after perforation closure.

#### **METHODS**

This study was conducted at the outpatient department (OPD) of Otorhinolaryngology and Head & Neck surgery at Rajindra hospital, Government Medical College, Patiala between time periods of July, 2015 to August 2017. 50 patients were included in the study after obtaining the written and informed consent. The inclusion criteria were patients aged between 18 years and 70 years; size of perforation in Pars Tensa up to 3 mm which was dry for at least 3 weeks. In cases of traumatic perforations, when it was at least 6 weeks old to rule out

spontaneous closure; perforation in Pars Tensa; patent Eustachian tube; air bone gap on pure tone audiometry; patient's willingness to participate in the study.

Exclusion criteria were active suppuration; perforations of Pars Flaccida; posterior marginal defects; perforations whose margins were not visible; patient's refusal to participate in the study; postoperative cases of failed ear surgery.

Taking all aseptic precautions, margins of the perforation were made raw under the microscope using local anaesthesia. 0.2 ml of 1% sodium hyaluronate was applied on the perforation under strictly sterile conditions. A fine cannula was mounted over this syringe for sodium hyaluronate applications. Maximum of 4 applications were given at a weekly interval for a maximum of 1 month. Further applications were stopped, if there was healing of perforations before the maximum fixed number of 4 applications. Patients were followed up at weekly intervals for first 4 weeks. The final mapping was done 3 months after the last sodium hyaluronate application.

The data taken from this study was analyzed statistically using SPSS software version 21.

#### RESULTS

Out of total 50 patients taken, 27 (54%) were females and 23 (46%) were males. 56% patients were from rural background as compared to 44% from urban areas (Table 1).

Size of perforation was 1-2 mm in majority (56%) patients (Table 2).

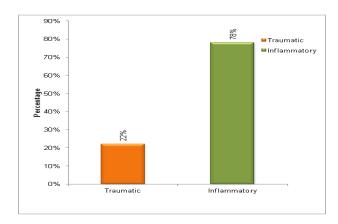
**Table 1: Demographic distribution of patients.** 

Demography	No. of patients	Percentage (%)	
Male	23	46	
Female	27	54	
Rural	28	56	
Urban	22	44	

Table 2: Size of tympanic membrane perforation.

Size of perforation (mm)	No. of Patients	Percentage (%)
Up to 1 mm	10	20
1-2 mm	28	56
2-3 mm	12	24
Total	50	100

Majority (78%) of the patients had perforations of inflammatory origin (Figure 1) with highest (44%) perforations in the antero-inferior quadrant of tympanic membrane (Figure 2).



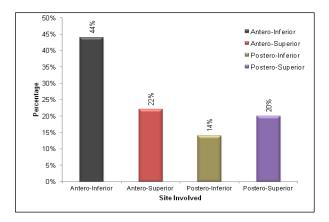


Figure 1: Aetiology of perforation.

Figure 2: Site involved.

Table 3: Initial hearing loss according to size of perforation.

Size of perforation (mm)	No. of patients	Hearing loss range (dB)	Average hearing loss (dB) ±SD
Up to 1 mm	10	20-37	23.90±5.32
1-2 mm	28	16-44	27.35±5.96
2-3 mm	12	22-81	39.70±20.10
Total	50	16-81	30.42±12.08

Table 4: Healing pattern according to size of perforation.

Size of perforation	No. of patients	Closed	Reduced	Persistent	% showing positive response
Up to 1 mm	10	7	3	0	100
1-2 mm	28	16	8	4	85.71
2-3 mm	12	4	7	2	83.33
Total	50	26	18	6	88

Table 5: Hearing gain (db) in healed perforations according to perforation size.

Perforation size (mm)	No. of cases completely	Avg. initial hearing loss (dB)	Avg. final hearing loss (dB)	Gain in hearing (dB)	P value
Up to 1	7	34.71±4.11	21.86±1.46	12.86±2.79	0.001
1-2	16	37.11±2.68	25.13±2.69	11.98±3.80	0.001
2-3	3	41.53±1.36	23.47±2.20	18.07±3.52	0.001
Total	26	37.78	25.39	12.40	0.001

Average initial hearing loss was found to be 30.42±12.08 dB (Table 3).

Perforations of small size responded well and showed better positive response (Table 4).

Avergae final hearing gain was calculated to be 12.40 dB after closure of tympanic membrane perforation (Table 5).

#### **DISCUSSION**

Chronic Otitis media is a very common disease in India. It is also considered to be the major cause of deafness in general population, accounting for about 2-4%. <sup>10</sup>

Perforations of tympanic membrane are common although it is very well protected deep in the external auditory canal. 11 Chronic perforations of tympanic membrane occur in association with chronic otitis media. 5 Various materials had been used to repair the tympanic membrane perforation e.g. full thickness skin, fascia, cartilage with perichondrium, vein, heart valves. 12 Though results were acceptable but these techniques were invasive.

The possibility of tympanic membrane perforation closure with sodium hyaluronate was first evaluated in animal models'. Significantly accelerated rate of healing was reported in that study. The similar results have been observed in humans too. <sup>13</sup>

Healing of tympanic membrane wound is unique and distinct as compared to other sites of the body. In response to injury, normally tissue undergoes four phases that are haemostasis, inflammation, proliferation, and migration. In case of tympanic membrane healing, the latter two stages occur in reverse order. The chemo-attractive properties of hyaluronic acid accelerate the ongoing inflammatory process by inducing inflammatory cells such as granulocytes and macrophages. The migratory stage causes squamous epithelium bridging across the perforation by a keratin spur. The keratin layer serves as a scaffold. Hyaluronic acid stimulates the production of this keratin and forms a film of keratin-hyaluronate. The later allows the migration of squamous epithelium which is centripetal migration.<sup>5</sup>

Patients with dry and central perforations of tympanic membrane with sufficient rim area around the perforation with no cholesteatoma and a patent eustachian tube are the ideal candidates for closure of perforation. <sup>14</sup> The condition of the mucous membrane is important in healing of tympanic membrane perforation. Formation of neovascularisation is required for the development of epithelial and fibrotic layers.

In this study, total 50 patients were included with 54% female and 46% male. Majority (56%) of the patients were with perforation size of 1-2 mm. 22% patients had traumatic perforation while rest 78% had perforations of inflammatory origin. Similar study was conducted by Kaur et al on thirty patients of tympanic membrane perforation with 8 males and 22 females. The age of the patients was 15-60 years. Makwana et al published a study with TCA cautery on 60 patients of tympanic membrane perforations with age 18-60 years. 27 were male patients while 33 were female patients.

In our study, 22 (44%) patients had anterior inferior quadrant involvement of the tympanic membrane, 11 (22%) patients were with anterosuperior quadrant, 10 (20%) patients had posterosuperior quadrant involvement and 7 (14%) patients had posteroinferior quadrant involved. The size of the perforation was between 1-3 mm. Kaur et al had conducted their study with 40% cases of anteroinferior quadrant involvement, posteroinferior being 30%, antero-superior 16.67% and posterosuperior quadrant involvement in 13.33%. Size of the perforation was 1-3 mm. Makwana et al done treatment on 60 patients. Majority of the patients had small central perforation involving one quadrant of the tympanic membrane. 13

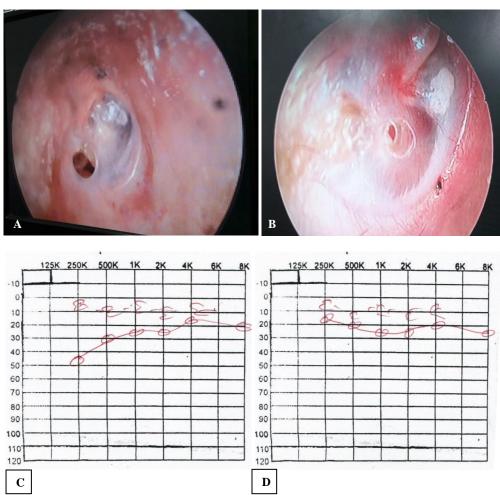


Figure 3: Tympanic membrane perforation. (A) before SH application; (B) after SH application; (C) audiogrambefore perforation closure; (D) audiogram-after perforation closure.

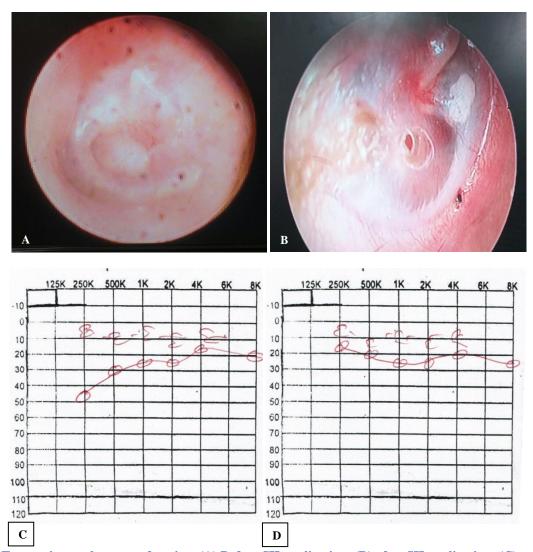


Figure 4: Tympanic membrane perforation. (A) Before SH application; (B) after SH application; (C) audiogrambefore perforation closure; (D) audiogram-after perforation closure.

In our study, we found that 1% sodium hyaluronate applications resulted in closure of 26 (52%) perforations, size reduction in 18 (36%) perforations out of total 50 perforations. 6 perforations did not show any significant reduction in size (persistent perforations). Small perforation (up to 1mm) showed 100% result while perforations in the size group 2-3 mm showed results of 83.33%. Total 44 perforations (88%) showed reduction in size [Figure 3 (A, B) and Figure 4 (A, B)]. Improvement in hearing was seen after closure of perforation on Pure Tone Audiometry [Figure 3 (C, D) and Figure 4 (C, D)]. A similar study by Kaur et al got results of 86.67% in a study on 30 patients after applications of 1% sodium hyaluronate on tympanic membrane perforations. Alzahrani and Saliba conducted a study using hyaluronic acid fat graft myringoplasty and got results of 80% in perforation closure. Parmar et al got results ranging between 65.8-93% in different categories of patients with chemical cautery for tympanic membrane closure.

#### **CONCLUSION**

The treatment under study was simple, short and convenient to patients. No adverse effects were reported by any patient in this study.

The results obtained with the present study are not far behind as compared to tympanoplasty. Tympanoplasty is an invasive procedure with few days of hospital stay also. Moreover, cost of the surgery can be high which many patients may not afford. Sometimes patients do not get medical fitness for surgery due to some other illness thus leading to delay in the treatment. The procedure done in this study can be tried as an alternative for small and medium size perforation before the patient is taken up for surgery.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

Institutional Ethics Committee

#### **REFERENCES**

- Puleck JL. Disease of tympanic membrane. In: Paparella MM, Shumrick DA, editors Otolaryngology 2nd ed. Otology and Neurology, Philadelphia: WB Saunders Company; 1980: 1381-1401.
- Alzahrani M, Saliba I. Hyaluronic Acid Fat Graft Myringoplasty vs Fat Patch Fat Graft Myringoplasty: Eur Arch Otorhinolaryngol. 2015;272(8):1873-7.
- 3. Ormerd FC, McLay K. The technique of plastic operations on the sound conducting apparatus. J Laryng Otol. 1956;70:648-63.
- 4. Hong P, Bance M, Gratzer PF.; Repair of tympanic membrane perforation using novel adjuvant therapies: A contemporary review of experimental and tissue engineering studies,2012; Int J Pediatr Otorhinolaryngol. 2013;7:3-12.
- 5. The BM, Shen Y, Friedland PL, Atlas DM, Marano JR. A review on the use of hyaluronic acid in tympanic membrane wound healing, 2012; Expert Opin Biol Ther. 2012;12(1):23-36.
- Gun T, Boztepe OF, Atan D, Lkinciogullari A, Dere H. Comparison of Hyaluronic Acid Fat Graft Myringoplasty, Fat Graft Myringoplasty and Temporalis Fascia Techniques for the closure of Different Sizes and Sites of tympanic Membrane Perforations, 2016.
- 7. Murray Robert K, Keeley Fredrick W. The extracellular matrix. Harper's Biochemistry, ed

- 24th.Stamford:Appleton and Lounge Co. 1996:667-685
- 8. Ahn JH, Lim HW, Hong HR. The clinical application and efficacy of sodium hyaluronate-carboxymethylcellulose during tympanomastoid surgery. Laryngoscope. 2012;122(4):912-5.
- 9. Baba EIB, Barake C, Roger M, Jurjus R, Sertel S, Jurjus A. Stem Cells in the Management of Tympanic Membrane Perforation: An Update. Neurological Regeneration. 2017: 181-194.
- 10. Bali K, Sood VP. Intact canal wall tympanoplasty with mastoidectomy. Ind J Otolaryngol. 1973;25:196.
- 11. Paprella MM. Treatment of permanent perforation of tympanic membrane. Otolaryngology Ed. 3 (II), Philadelphia, WB Sunders Co, 1991: 1364.
- 12. Stenofars LE. Repair of tympanic membrane perforations using hyaluronic acid: An alternative to myringoplasty. J Laryngol Otol. 1989;103:39-40.
- 13. Reijnen CJH, Kuijpers W. The healing pattern of drum membrane. Acta Otolaryngologica 1971;(Suppl 287):1-74.
- 14. Dunlap AM, Schuknecht HF. Closure of perforation of tympanic membrane. Laryngoscope (St. Louis) 1947:57:479.

Cite this article as: Sahni D, Singh B, Uppal KS, Bhagat S, Sharma D, Dogra G. Study of effect of 1% sodium hyaluronate application on tympanic membrane perforation. Int J Otorhinolaryngol Head Neck Surg 2018;4:1246-51.