Original Research Article

Treatment of tympanic membrane perforation with topical epidermal growth factor: progress towards clinical application

Puneeth S. Nayak, Anil S. Harugop, Prashant H. Patil, Prasad T. V. R. K., Lakshmi Goswami*

Department of ENT, Head and Neck Surgery J. N. Medical college, KLE Academy of higher education and research, Belagavi, Karnataka

Received: 07 January 2021
Revised: 03 March 2021
Accepted: 07 April 2021

*Correspondence:
Dr. Lakshmi Goswami,
E-mail: lakshmi.goswami05@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: Chronic otitis media is a widespread disease of developing countries, especially of the lower socioeconomic group. Medical cost in hospitals associated with tympanoplasty for treating CSOM is very high. Our study investigates the efficacy of epidermal growth factor along with chemical cautery in healing of chronic tympanic membrane perforation on an outpatient department (OPD) basis. Hence providing a cheaper and cost effective treatment alternative to the patients.

Methods: A total number of 70 patients with signs of COM attending ENT OPD were selected. The patients were randomly assigned into 2 groups each with a sample size of 35. Otoendoscopy and pure tone audiometry was performed. Group A was treated with EGF with chemical cautery and group B was treated with only chemical cautery. Both groups were followed up after 15 days, one month and second month of the procedure in ENT outpatient clinic.

Results: The success rate of these non-healing perforation was found to be significantly higher in group A (29 [82.86%]) compared with group B (17 [65.71%]) with P value of 0.0070*.

Conclusions: This study shows a statistically significant result with topical application of epidermal growth factor in small to medium non-healing central tympanic membrane perforation. Due to the promising result of epidermal growth factor, it could be considered as office myringoplasty.

Keywords: Chronic otitis media, Tympanic membrane perforation, Epidermal growth factor, Carbolic acid

INTRODUCTION

Chronic otitis media (COM) is a widespread disease in developing countries with higher prevalence in lower socioeconomic groups.1-4 The overall prevalence of chronic otitis media is 4.1 percent with 3.1 percent of the individuals having unilateral and 1.0 percent of the individuals having bilateral disease. There is no difference in male and female prevalence. Prevalence of chronic otitis media in the age group 41-80 was found twice as those in the age group of 18-40.4

Chronic otitis media is one of the most common causes of hearing loss that mainly results due to tympanic membrane perforation. Tympanoplasty is required for the treatment of majority of patients with chronic otitis media.1,2,7 Medical cost in hospitals associated with tympanoplasty is very high. This study was done to find a less expensive, simple, out patient and non-surgical procedure with epidermal growth factor which contributes to cell growth, the role of which in normal would healing is documented.2,9

The recent experimental animal study shows epidermal growth factor promotes healing of tympanic membrane perforation on topical application.11,12 It is hoped that epidermal growth factor will eventually prove to be a promising alternative to tympanoplasty for stimulating the
repair of chronic tympanic membrane perforation that would not otherwise heal on its own.

The objective of our study is to assess the efficacy of topical epidermal growth factor in the treatment of non-healing small central perforation.

**METHODS**

A single blind randomized controlled study was conducted in the department of ENT and HNS at KLE’S Dr. Prabhakar Kore Hospital and Medical Research Centre during the study period of 1 year from December 2018-December 2019. Every consecutive eligible patient fulfilling the inclusion and exclusion criteria was recruited into the study. Total sample size of our study was 70 patients calculated using the census method depending on the prevalence of COM patients in our hospital.

Patients aged 18-60 years having an inactive mucosal type of COM with non-healing perforation involving one quadrant, those having a traumatic perforation not healing for at least 1 month and those with a dry post tympanoplasty residual perforation were included in the study. Active chronic otitis media, sensory neural hearing loss and those with an active predisposing disease focus in the nose and throat were excluded.

**Methodology**

Prospective study candidates were examined and investigated in the ENT outpatient clinic to confirm eligibility. A full valid written consent was taken from all eligible candidates. Total sample size was of 70 patients. Pure tone audiometry was done to record the type and degree of hearing loss. A diagnostic nasal endoscopy was done to rule out any predisposing focus in the nose and otomicroscopy was done to examine the perforation.

Pre-procedural pictures of the patients were taken. The patients were randomly assigned into 2 groups, group A patients underwent treatment with EGF with chemical cautery and group B underwent treatment with only chemical cautery. All the treatment procedures were performed under local anesthesia by applying 4% lignocaine drops to the ear 10 minutes before the procedure. Under otomicroscopic visualisation the margins of Tympanic membrane perforations were cauterized using a Jobson Horne Probe with carbolic acid solution at its tip. A thorough normal saline wash was given and the remaining Carbolic acid solution was suctioned out from the middle ear and external auditory canal. Recombinant human EGF (epidermal growth factor) gel was applied directly over the edges of tympanic membrane perforation. A small piece of dry gel foam was kept over the tympanic membrane to help in epithelization. The external auditory canal was packed with bactigras of povidone-iodine.

In group B: After performing carbolic acid cauterization and saline wash, a small piece of dry gel foam was kept over it. The external auditory canal was packed with bactigras of povidone-iodine.

Patients in both the groups were treated with amoxicillin-clavulanic acid (625 mg) oral/bd for 5 days, levocetirizine 5 mg + phenylephrine 60mg tablets one at night for 15 days and analgesics for 3 days.

The patients were followed up on post op day 15, one month and second month after the procedure in ENT outpatient clinic. Pack removed from the external auditory canal at the first visit. During each follow up the patient underwent otomicroscopic examination to access the perforation size and to rule out secondary complications. Pure tone audiometry was performed at the third visit in patients whose perforation had closed. Closure of the perforation and decrease in perforation was the primary outcome measured. Hearing gain was the secondary outcome considered.

**Statistical analysis**

The study is focused on a comparison of two groups. The inter-group continuous variable were compared using suitable tools of statistics like a normal test, unpaired student’s t-test. Two quantitative variables, within a group, were compared using the student’s paired t-test. The association between the outcome, clinical, and demographics were tested using a chi-square test. For all the tests the value of p less than 5% (0.05) were considered significant.

**RESULTS**

Male preponderance is 51.43%.

![Figure 1: Distribution of male and females in group A and group B.](image)

Figure 2 in group A out of 35 patients 24 were of chronic otitis media, 7 of post-operative tympanoplasty, 4 of
traumatic perforation. In group B out of 35 patients 28 were of chronic otitis media, 3 of post-operative tympanoplasty, 4 of traumatic perforation.

was a hearing gain in both A (80.2%) and B (72%) groups which is statistically significant.

**DISCUSSION**

Chronic otitis media is a widespread disease of developing countries, especially the low socio-economic group. Changes like granulation, ossicular necrosis, tympanosclerosis and recurrent ear discharge are the common problems for non-healing tympanic membrane perforation. The healing of TM perforation involves biological process like epithelial proliferation, epithelial migration, fibroblast proliferation, neoangiogenesis and tissue remodelling. Epidermal growth factor is involved in normal tympanic membrane perforation healing by epithelial proliferation, tissue neoangiogenesis. Topical application of EGF and fibroblast growth factor have reported to enhance the closure of tympanic membrane perforation.
Topical treatment of EGF on TM perforation has been reported since 1990. In a study conducted by Chauvin et al the EGF group produced the thickest tympanic membrane at all 3 sample sites compared with other growth promoters, primarily increase in fibrous layer thickness. EGF was not used alone in the tympanic membrane perforations, as the perforation edges where squamous epithelium which does not remove with EGF alone. In Ramsay et al study EGF treatment applied locally without freshened the margins does not have the desired effect on the healing of tympanic perforation. In Cho et al study showed growth promoters facilitate healing of the tympanic membrane perforation. In a study conducted by Bhat et al, the application of EGF topically on non-healing tympanic membrane perforation were shown good outcomes compare with the control group.

This study investigated the efficacy of EGF on chronic tympanic membrane perforation reducing the medical cost and avoiding inconvenience to the patient. Active predisposing disease foci in the nose and throat were treated before including in this study. Carbolic acid was used to freshen the margins of tympanic membrane perforation along with EGF application to enhance the healing effect of tympanic membrane perforation.

CONCLUSION

This study shows a statistically significant result with topical application of epidermal growth factor in small to medium nonhealing central tympanic membrane perforation. Due to the promising result of the epidermal growth factor, it could be considered as office myringoplasty. It proved to be reliable in hastening the healing of small to medium central tympanic membrane perforation without untoward complications. Medical expenditure associated with tympanoplasty has compelled investigators to search for a less expensive, simple nonsurgical outpatient procedure to close tympanic membrane perforation, the epidermal growth factor is an applicant for medical tympanoplasty.

ACKNOWLEDGEMENTS

I would like to thank my teachers and post graduate colleagues and clerical staff from the department of otorhinolaryngology and Head and Neck Surgery for their invaluable help and time. A special note of thanks to my beloved parents for their constant encouragement, enthusiasm and faith in me throughout.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Berman S. Otitis media in developing countries. Pediatrics. 1995;96:126-31.
2. Dvorak DW, Abbas G, Ali T, Stevenson S, Welling DB. Repair of chronic tympanic membrane perforations with long-term epidermal growth factor. Laryngoscope. 1995;105(12 Pt 1):1300-1304.
3. Ma Y, Zhao H, Zhou X. Topical Treatment with Growth Factors for Tympanic Membrane Perforations: Progress Towards Clinical Application. Acta Oto-Laryngologica. 2002;122(6):586-599.
4. Browning GG. The prevalence of middle ear disease in the adult British population. Clin Otolaryngol Allied Sci. 1992;17(4):317-21.
5. Bennett KE, Haggard MP. Accumulation of factors influencing children's middle ear disease: risk factor modeling on a large population cohort. J Epidemiol Community Health. 1998;52(12):786-793.
6. Tsang MW, Wong WK, Hung CS, et al. Human epidermal growth factor enhances healing of diabetic foot ulcers. Diabetes Care. 2003;26(6):1856-1861.
7. Chauvin K, Bratton C, Parkins C. Healing large tympanic membrane perforations using hyaluronic acid, basic fibroblast growth factor, and epidermal growth factor. Otolaryngol Head Neck Surg. 1999;121(1):43-473.
8. Ramsay HA, Helkkonen EJ, Laurila PK. Effect of epidermal growth factor on tympanic membranes with chronic perforations: a clinical trial. Otolaryngol Head Neck Surg. 1995;113(4):375-3793.
9. Cho, Lee KS Shin DG, Park D, Chon YD, Myong K. The importance of vascular endothelial growth factor in the healing of acute tympanic membrane perforation. Am J Otolaryngol. 2009;31:309-14.
10. Johnson AP, Smallman LA, Kent SE. The Mechanism of Healing of Tympanic Membrane Perforations. Acta Oto-Laryngologica. 1990;109:5-6:406-415.
11. Maria SPL, Redmond SL, Atlas MD, Ghassmir F. The role of epidermal growth in the healing tympanic membrane following perforation in rats. J Mol Histol. 2010;41(6):309-314.
12. Brown GL, Nanney LB, Griffen J. Enhancement of wound healing by topical treatment with epidermal growth factor. N Engl J Med. 1989;321:76-9.
13. Altman DG, Schulz KF, Moher D. CONSORT GROUP. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. Ann Intern Med. 2001;134(8):663-694.
14. Vikram B, Bijiraj V, Vidyashree M. Effect of Silver Nitrate and Epidermal Growth Factor on Nonhealing Tympanic Membrane Perforations: A Randomized Controlled Study. Ann Otol Neurotol. 2018;01:029-033.900-6.