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Original Research Article

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

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ABSTRACT

Background: Chronic otitis media is a widespread disease of developing countries, especially of the lower socio-economic 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.[1,7] 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.[7,9]

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 it's 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 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 csom 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 bactrigras 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 analgesic tablets 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 intergroup continuous variable were compared using suitable tools of statistics like a normal test, unpaired student's t-test. Two quantitive 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%.

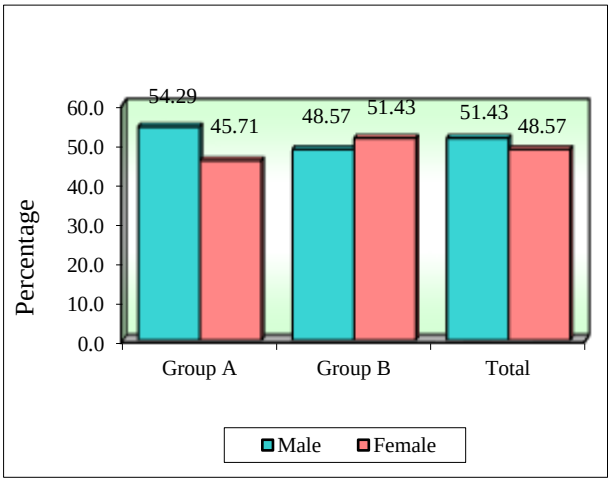

Figure 1: Distribution of male and females in group A and group B.

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.

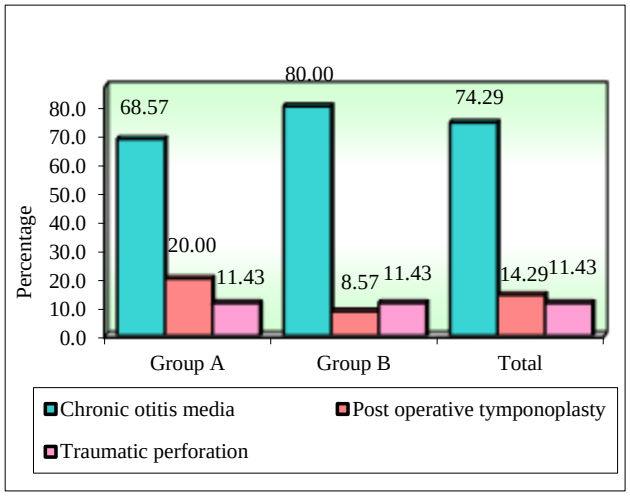

Figure 2: Comparison of group A and group B by diagnosis.

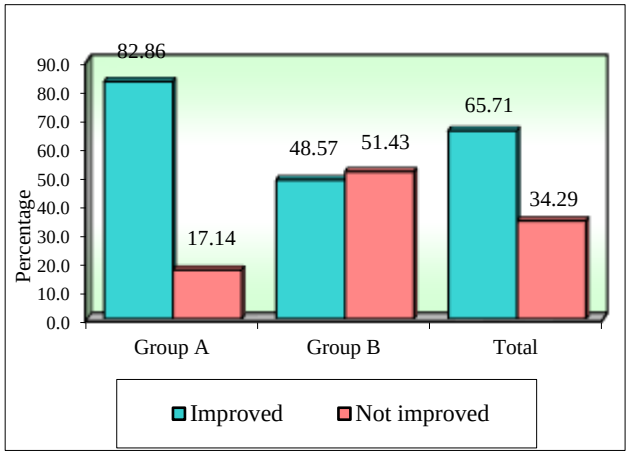

Figure 3: Comparison of group A and group B by results.

Figure 3 Comparison of Group A and Group B by results *p<0.05 Group A percentage of improved 82.86%, in group B percentage of improved 65.71% p<0.05 which is significant.

Figure 4 *p<0.05 Group A complete closure 60.00% in group B complete closure 28.57% p< 0.05 which is significant.

The success rate was found to be significantly higher in group 1(29 [82.86%]) compared with group 2 (17 [65.71%]). P value is 0.0070*.

Hearing gain in the perforation that closed

The hearing gain was assessed in both groups to remove that completely closed after 3 months of follow up. There was a hearing gain in both A (80.2%) and B (72%) groups which is statistically significant.

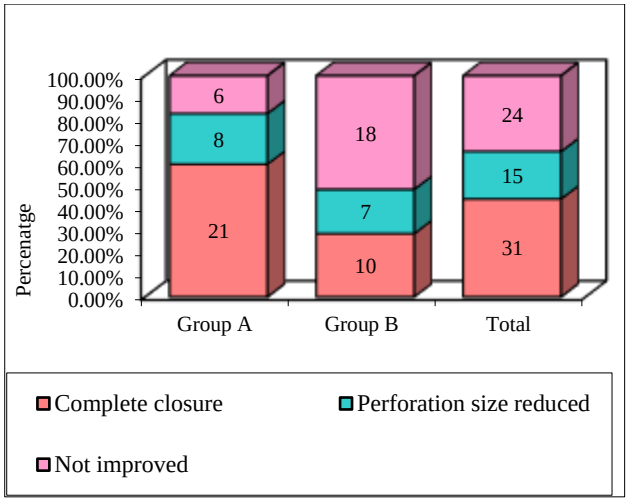

Figure 4: Comparison of group A and group B by results.

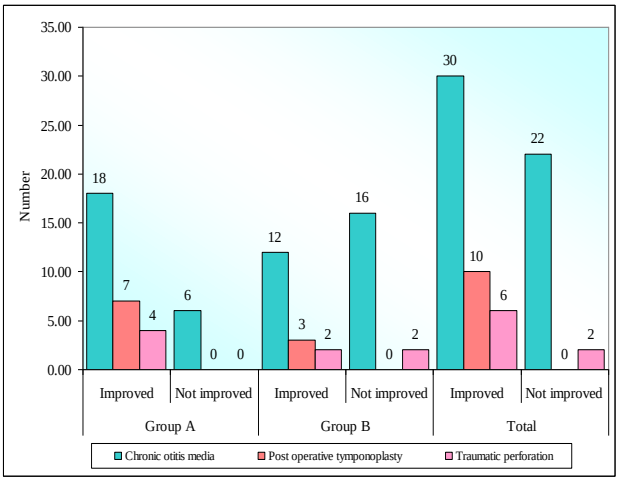

Figure 5: Association between the outcome of results and diagnosis in group A and group B.

DISCUSSION

Chronic otitis media is a widespread disease of developing countries, especially the low socio-economic group.[1] Changes like granulation, ossicular necrosis, tympanosclerosis and recurrent ear discharge are the common problems for non-healing tympanic membrane perforation.[14]

The healing of TM perforation involves biological process like epithelial proliferation, epithelial migration, fibroblast proliferation, neoangiogenesis and tissue remodelling.[9] Epidermal growth factor is involved in normal tympanic membrane perforation healing by epithelial proliferation, tissue neoangiogenesis.[7] Topical application of EGF and fibroblast growth factor have reported to enhance the closure of tympanic membrane perforation.[9]

Topical treatment of EGF on TM perforation has been reported since 1990.[3] 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.[7] 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.[8] In Cho et al study showed growth promoters facilitate healing of the tympanic membrane perforation.[9] 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.[14]

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.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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