The effect of topical estrogen on healing of chronic tympanic membrane perforations and hearing threshold
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Introduction

History always provides an insight into the future. The history of tympanoplasty nearly sums up the history of evolution of otology as a whole. The goal for each surgeon is to eradicate underlying disease and provide a functional hearing to the patient as far as practicable. The question is still on how to devise a method so as to give maximum postoperative hearing using minimal instrumentation [1,2]. In 1878, Emil Berthold was the first to describe the surgical procedure of myringoplasty, using a free skin graft from the forearm [3]. For surgical treatment of tympanic membrane (TM) perforations, the use of autologous autografts, including muscle fascia or perichondrium, is reported in most studies, with a success rate between 88 and 97%. However, surgical treatment involves higher costs, more effort, and surgical risks. Therefore, many investigators have studied topical use of substances to facilitate TM repair. Estrogen can influence the various phases of wound healing in cutaneous repair. Topical estrogen application may influence the repair of TM perforations.

Aim of the work

The aim of the work was to evaluate a new procedure for repairing TM perforation and improving hearing threshold after 30 days using estrogen paper patch.

Patients and methods

After obtaining informed consent, patients were randomly allocated into two groups. One group was treated with estrogen paper patch (paper patch impinged with 1% estrogen ointment to act as the study group), and the second group was treated with paper patch impinged with local antibiotic ointment to act as the control group (we used 1% tetracycline ointment in our study).

Conclusion

Perhaps, there is a significant and promising result for estrogen paper patching as a method of repairing TM perforation.

Keywords:
estrogen, myringoplasty, paper patch, tympanic membrane perforation

Background

Tympanic membrane (TM) perforations can arise from a variety of causes. Major causes include trauma and middle ear disease. Surgical treatment involves higher costs, more effort, and surgical risks. Therefore, many investigators have studied topical use of substances to facilitate TM repair. Estrogen can influence the various phases of wound healing in cutaneous repair. Topical estrogen application may influence the repair of TM perforations.

Aims and objectives

The aim of the work was to study the effect of topical estrogen on healing of chronic TM perforations as an office procedure for myringoplasty.
Participants and methods
It was an office procedure carried out during the period from November 2013 to November 2014.

Inclusion criteria
Inclusion criteria were as follows: presence of central perforation for more than 3 months, unilateral perforation, perforation size less than 40% of the total area of the TM, dry ear for at least 2–3 months preoperatively, air–bone gap less than 30 dB in the affected ear, and absence of ossicular or mastoid pathology as evidenced in computed tomography scan.

Exclusion criteria
Exclusion criteria were as follows: perforation size greater than 40% of the total area of the TM, presence of cholesteatoma or granulation tissue or polyp in the middle ear, presence of otorrhea in the past 3 months, presence of marginal perforation or recent perforation of the TM, infected external auditory canal, previously operated ear, or nonfunctioning Eustachian tube.

Informed consent was obtained from all patients. All patients were subjected to complete history taking, general examination, full ENT examination, and pure-tone audiometry. Patients were followed up weekly for reduction in size of perforation until complete closure at the end of fourth week.

The office procedure was performed by the same ENT surgeon as follows.

Patients were randomly allocated into two groups of 15 each. Under vision of an operating microscope, local anesthesia was induced using 10% lidocaine spray applied inside the external auditory canal. The margin of the perforation was refreshed with a sharp curved needle to create a fresh edge. Using a crocodile forceps, patches were placed and spread over the perforation using a straight blunt-ended needle (Fig. 1). Paper patch should be more than one and half the size of the perforation. The external ear canal was filled with gel foam to stabilize the patch. Thereafter, the external ear was slightly packed with small sterile gauze soaked in tetracycline ointment, and the sterile gauze and adhesive plaster were placed over the auricle. Medications included antibiotic ear drops three times per day (we used cipro ear drops), prophylactic antibiotic, and antihistaminic. Patients were instructed to prevent water from entering the ear and notify if any discharge occurs. The procedure was nearly painless and took 15 min or less. The patients returned to the office a week later for removal of aural pack. Medical treatment was stopped and weekly examination of the ear was carried out under microscope. After 2 weeks, suction of the gel foam was carried out. Thereafter, at the end of 1 month after the procedure, a photograph of the TM was taken for assessing the size of the perforation (Fig. 2), and complete closure was detected (Fig. 3). Pure-tone audiogram was performed after 1 month of the procedure (Figs. 4–7).

Results
As regards age, sex, and duration of symptoms, the difference was not significant ($P > 0.05$). At the end
of the study, pure-tone audiogram was performed for both groups. The results revealed that in the study...
group the mean air bone gap (ABG) was markedly reduced to 1.33 dB with SD 3.52 dB, whereas the mean ABG in the control group was 7.33 dB with SD 4.17 dB. The difference ($P < 0.001$) between postoperative and preoperative ABG was statistically significant (Table 1 and Fig. 8).

Overall, as shown in Table 2 and Fig. 9, 13 of 15 cases (86.7%) in the study group showed complete healing and only two cases showed failure (13.3%). In the control group, only one case (6.7%) showed complete healing, whereas 14 cases (93.3%) showed failure. The difference was significant, with a $P$ value less than 0.001.

### Discussion

The repair of the TM has been attempted with a large variety of synthetic, homologous and autogenous tissue. However, the temporalis fascia, areolar tissue, and the perichondrium are used most commonly today. Nevertheless, it is limited by the need for expensive equipment in the operating room, microsurgical skills of the surgeon, and donor site morbidity [5]. The trend toward increasingly less-invasive medical procedures, with shorter hospitalization stay, has led to a demand for materials to replace autologous grafts. Theoretical advantages include the elimination of morbidity related to graft harvesting, faster healing, no visible scarring, less pain, and less risk for infection, in addition to a faster procedure and early discharge. These grafts, however, make the procedure more expensive and have shown no real advantages thus far [3]. Paper patching is technically simple, time saving, safe to perform, cost-effective, and suitable as an outpatient procedure and has a good success rate [6]. Numerous growth factors have been investigated to stimulate healing of TM perforations, including epidermal growth factor, fibroblast growth factor, and platelet-derived growth factor, with mixed results. Topical insulin application in acute TM perforations in guinea pigs showed no

<table>
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<th>Variable</th>
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<th>Control ($n = 15$)</th>
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</table>

Figure 7

*Figure 7*

Case B: 1 month after procedure showing normal PTA.

Figure 8

*Figure 8*

Comparison of the study group and the control group with regard to ABG before and after the procedure.
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ficial effect on closure rate, epithelial thickness, and TM thickness [7]. Previous studies showed that the benefits of paper patching were low and limited to small perforations. Closure rates using rice paper patching after excision of the perforation margin under local anesthesia for persistent TM perforation were lower than 30% [8]. Our study was conducted to find a simple, noninvasive, effective procedure for repairing TM perforations with the criteria mentioned earlier, avoiding the disadvantages of the ordinary techniques. The present study showed that myringoplasty with estrogen paper patch was performed for 15 patients: closure of the TM perforation failed in two patients, one case developed severe upper respiratory tract infection shortly after the operation, followed by middle ear infection, and the other case did not follow the instructions after procedure and removed the aural pack shortly.

This good result in audiology was attributed mainly to estrogen effect, selection of the patients depending on the preoperative audiometry, which can exclude any ossicular pathology and good preoperative examination for the state of air conduction and computed tomography scan to exclude any hidden mastoid pathology. As regards the hearing improvement with estrogen paper patch, the mean A–B gap was 8.67 dB preoperatively. After the procedure, the mean A–B was 1.33 dB ($P < 0.001$). In the control group the mean preoperative ABG was 7.67 dB and the postoperative ABG was 7.33 ($P > 0.05$).

Conclusion
Day-stay surgery has become an integral part of modern otolaryngology. Myringoplasty under local anesthesia is a short, simple, cost-effective, and minimally invasive technique compared with traditional myringoplasty [9]. Considering the presence of squamous epithelial cells and fibroblasts in the TM, topical estrogen application may influence the repair of TM perforations [1]. Perhaps, there is a significant and promising result for estrogen paper patching as a method of repairing TM perforation and improving hearing threshold as shown in our study.

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Nil.

Conflicts of interest
There are no conflicts of interest.

References