

Current research project
Use of Growth factors in Tympanoplasty

Introduction:

Chronic Otitis media is a chronic inflammatory disease affecting the mucoperiosteal lining of the middle ear cleft. This disease is classified into Mucosal and squamosal type based on the location of the disease. If it is located in the middle ear due to obstruction to the Eustachian tube, then it is Mucosal type and if it involves attic region, it is Squamosal type. Patients with Mucosal type of ear disease present with tympanic membrane perforation. There are various types of graft materials used to close the perforation⁽¹⁾. Temporalis fascia graft is the conventional graft material that is being used till date. Other commonly used graft materials include cartilage, perichondrium and vein grafts. Though the success rates are more than 90% in any of these grafts, the fear of graft rejection is almost always present. Thus this study aims to augment this surgery by additional application of growth factors like Epidermal growth factor, Fibroblast growth factor, Platelet derived growth factor and insulin like growth factor. Thus this study aims to improve the success rates of tympanoplasty and myringoplasty.

Background

In chronic otitis media mucosal type, a central perforation is present in the pars tensa. If the perforation is small, there is epithelial migration and the defect is closed by forming an epithelial layer. In cases of large central perforation, the migration is hampered and thus the edges of the perforation is epithelialized with rounded margins. Thus it remains as a permanent perforation. If this perforation is not closed, the patient may experience loss of hearing and giddiness. The infection can spread to the inner ear and sometimes may involve the brain. Thus it becomes necessary to close the perforation surgically. Myringoplasty is a surgical procedure to close the perforation and Tympanoplasty is a procedure done to eradicate the disease in the middle ear and also close the perforation in the tympanic membrane. Various graft materials are used to close the perforation. Temporalis fascia is the graft that has been in use for many decades. This procedure is done under General anesthesia and sometimes under local anesthesia. Some of the other grafts that can be used are cartilage, perichondrium, fat, vein graft, etc⁽²⁾⁽³⁾⁽⁴⁾.

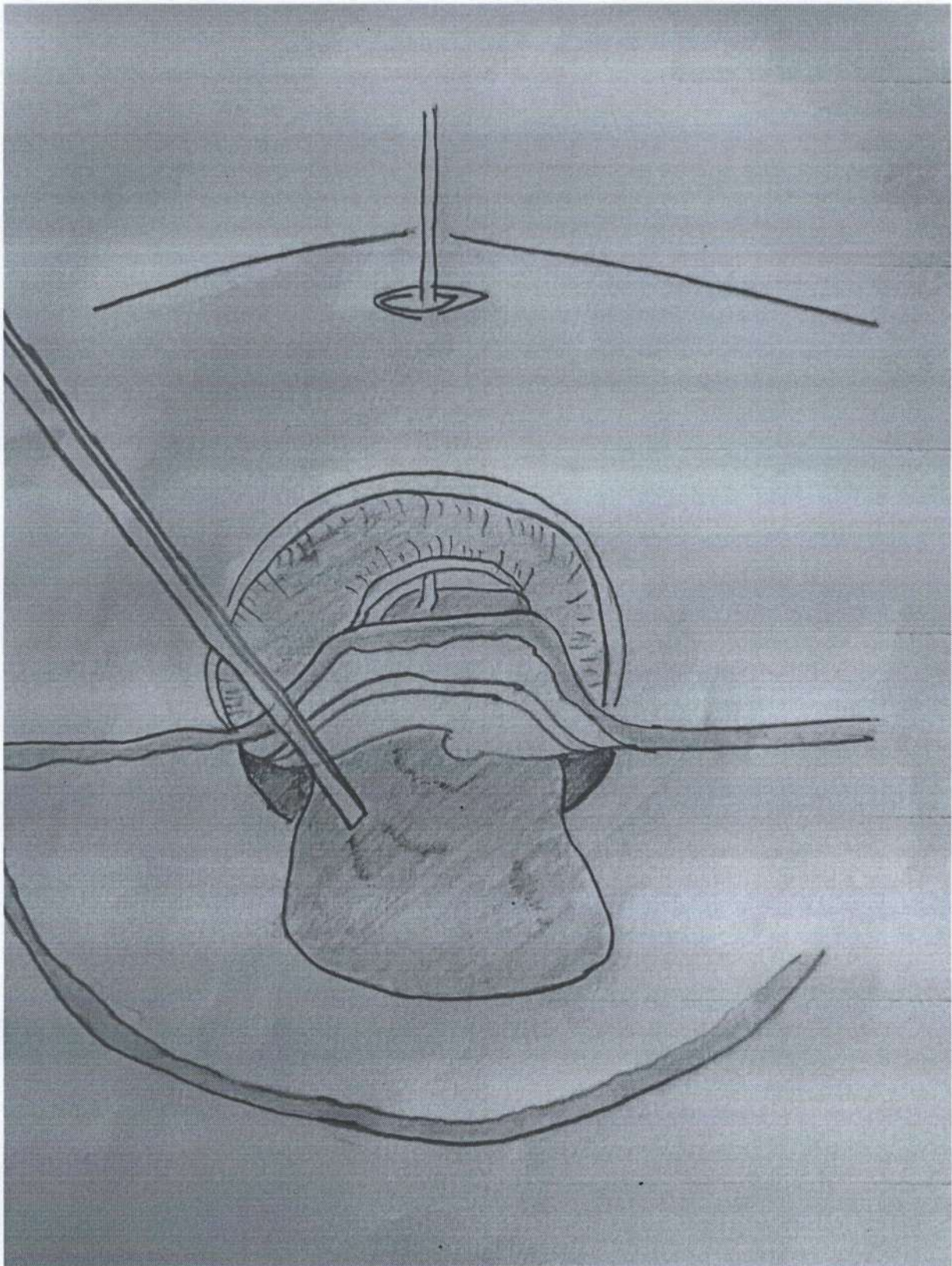


Fig 1 Temporalis fascia graft placed by underlay technique

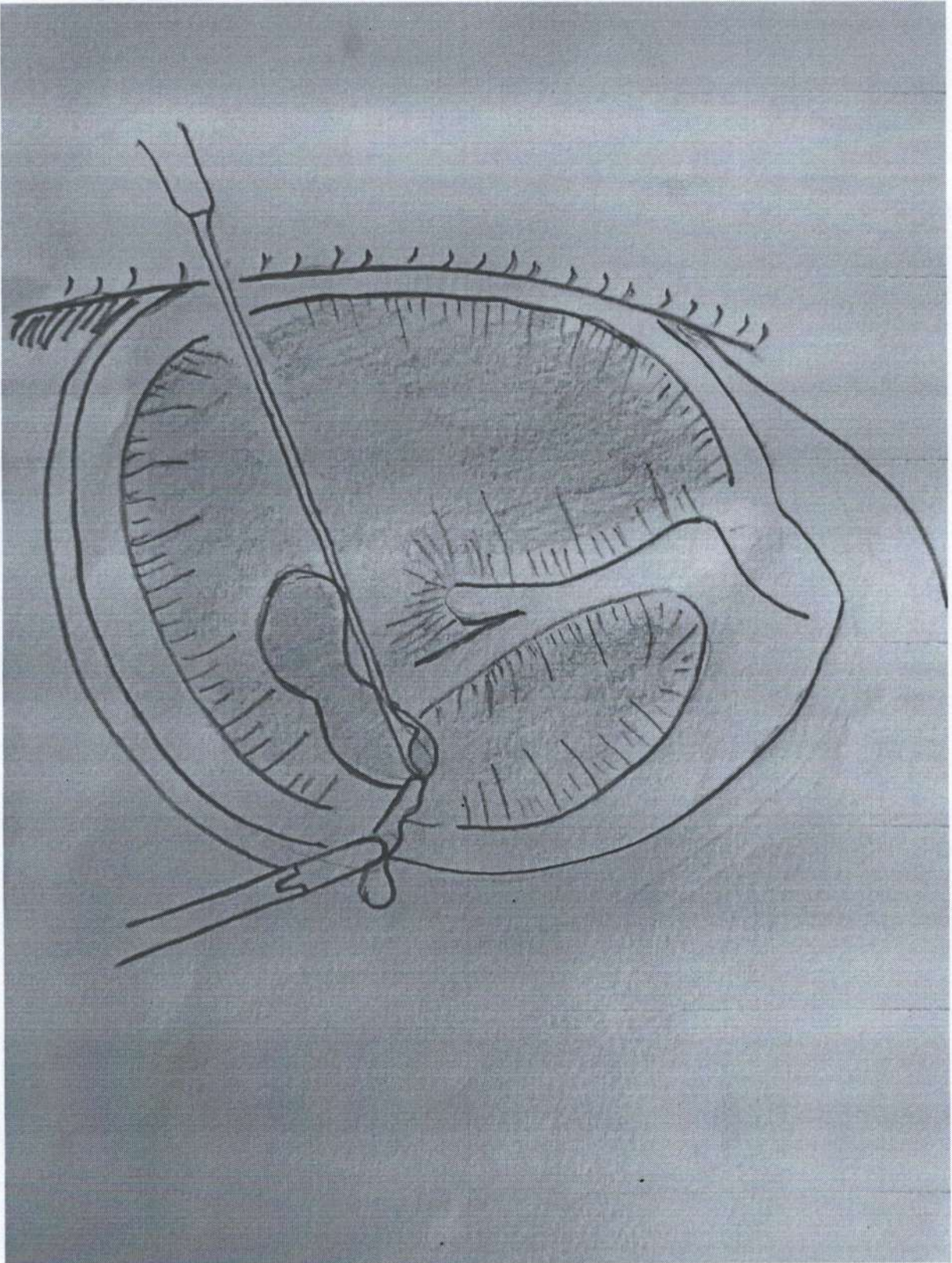


Fig 2 Temporalis fascia graft seen through the perforation

Study justification:

In tympanic membrane perforations, the edges are epithelialized and there is deficiency of growth factors. Thus healing of the perforation is hampered. While using temporalis fascia graft, there is no supplementation of growth factors and there are disadvantages like graft rejection or medialisation. Temporalis fascia is the most commonly used graft because of low BMR and its thickness is the same as that of tympanic membrane⁽⁵⁾. But because of graft rejection and graft medialisation, this graft is not commonly used nowadays. This study aims to use growth factors to augment the graft uptake. This may increase the chance of graft uptake and the healing may be faster.

Materials and methods:

Chronic Otitis media is a commonly presented condition. Thus all patients diagnosed with Chronic otitis media who fulfill the inclusion criteria is included in the study

Inclusion criteria:

- Patients below above 10 years of age and below 60 years of age
- Patients with chronic Otitis media mucosal type. Presence of a central perforation in the pars tensa is the diagnostic criteria
- Patients with dry ear
- Patients with good eustachian tube patency

Exclusion criteria

- Patients with intra temporal and extra temporal complications
- Patients not willing for the study

Based on the inclusion and exclusion criteria and obtaining consent from the patient, the patients are included in the study. The patients will then be divided into 5 groups.

- Group A are patients who undergo tympanoplasty with temporalis fascia graft only
- Group B are patients who undergo tympanoplasty with temporalis fascia and then topical application of ***Epidermal growth factor***
- Group C are patients who undergo tympanoplasty with temporalis fascia and then topical application of ***Fibroblast growth factor***
- Group D are patients who undergo tympanoplasty with temporalis fascia and then topical application of ***Platelet Derived Growth factor***
- Group E are patients who undergo tympanoplasty with temporalis fascia and then topical application of ***Insulin like growth factor***

All patients will be subjected to Otoscopy and Otomicroscopy to assess the size and shape of the perforation. Pure tone audiogram is done to assess the hearing.. In case of suspected erosion of adjacent structures or ossicles, Computed tomography of Temporal bone is done. Patients are then evaluated for fitness for surgery. The procedure is done under Local anesthesia or general anesthesia. Supra aural or post aural incision is made and temporalis fascia graft is harvested.

During tympanoplasty, after elevating the tympano meatal flap, the temporalis fascia graft is placed. After placing the graft, the growth factors are applied over the graft.

Group A is taken as the control group. The components that are assessed include duration for complete Graft healing, residual perforation, medialisation of graft and presence of active discharge.

The patient is reviewed after 1 week, 2 weeks, 3 weeks and 4 weeks. The graft healing is compared among the groups. The findings are recorded endoscopically. Presence of a complete neotympanum suggests good healing.

Discussion

The use of growth factors in tympanoplasty is an emerging innovation. There are few studies which show that the application of epidermal growth factor and fibroblast growth factor has enhanced graft uptake. There are no studies to show the efficiency of insulin like growth factor. This study aims to compare the efficacy of all these growth factors in tympanoplasty.

Epidermal growth factor stimulated DNA, RNA and proteins and is expressed as a part of reparative process⁽⁶⁾. Ramsay et al ⁽⁷⁾ studied the use of EGF as drops post surgery. It was found to have better graft healing and uptake.

Fibroblast growth factor is known to enhance epidermal cells proliferation and growth of connective tissue cells ⁽⁸⁾. Over use of Fibroblast growth factor used as drops was seen to have some adverse effects like persistent otorrhea and in few cases, cholesteatoma formation ⁽⁹⁾. However if properly used, it is known to augment the healing of perforations.

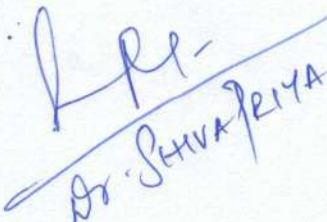
Platelet therapy in tympanoplasty is vastly under research. Platelet derived plasma, use of platelet rich fibrin membrane are all under trials. The use of growth factors was seen to have faster healing rate ⁽¹⁰⁾.

Insulin like growth factor has not been studied and also not reported in literature. This study aims to study the receptors for IGF. If the expression is seen, the patients will be treated with insulin growth factor post tympanoplasty. Insulin promotes wound healing and hence it is used in treatment of chronic non healing ulcers and wounds⁽¹¹⁾. Considering the epithelial nature of the tympanic membrane perforation, Insulin may promote healing but this can be confirmed only if the insulin growth factors are expressed.

References

1. Marcos Rabelo de Freitas, Thiago Corrêa de Oliveira, The role of different types of grafts in tympanoplasty, Brazilian Journal of Otorhinolaryngology, Volume 80, Issue 4, 2014, Pages 275-276, ISSN 1808-8694, <https://doi.org/10.1016/j.bjorl.2014.05.018>.
2. Vadiya, Sohil I. "Technique and results of cartilage shield tympanoplasty." Indian Journal of Otology 20.4 (2014): 196-198.
3. Ali Bayram, Nuray Bayar Muluk, Cemal Cingi, Sameer Ali Bafaqeeh. Success rates for various graft materials in tympanoplasty – A review, Journal of Otology, Volume 15, Issue 3, 2020, Pages 107-111, ISSN 1672-2930, <https://doi.org/10.1016/j.joto.2020.01.001>

4. Dolhi N, Weimer AD. Tympanic Membrane Perforations. [Updated 2023 Aug 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK557887/>
5. Alkan S, Baylançiçek S, Sözen E, Başak T, Dadaş B. Effect of the use of dry (rigid) or wet (soft) temporal fascia graft on tympanoplasty. *J Otolaryngol Head Neck Surg*. 2009 Feb;38(1):126-32. PMID: 19344622.
6. Lou, Zhengcai. "The effect of epidermal growth factor on the pseudo-healing of traumatic tympanic membrane perforations." *Brazilian Journal of Otorhinolaryngology* 87 (2021): 53-58.
7. Ramsay, Hans A., Erkki J. Heikkonen, and Pekka K. Laurila. "Effect of epidermal growth factor on tympanic membranes with chronic perforations: a clinical trial." *Otolaryngology—Head and Neck Surgery* 113.4 (1995): 375-379.
8. Zheng-Cai, L., and L. Zi-Han. "The short-and long-term adverse effects of FGF-2 on tympanic membrane perforations." *Acta Otorhinolaryngologica Italica* 38.3 (2018): 264.
9. Hakuba, N., et al. "Epithelial pearl formation following tympanic membrane regeneration therapy using an atelocollagen/silicone membrane and basic fibroblast growth factor: our experience from a retrospective study of one hundred sixteen patients." *Clinical Otolaryngology* 38.5 (2013): 394.
10. Yadav, S., Malik, J., Malik, P., Sehgal, P., Gulia, J., & Ranga, R. (2018). Studying the result of underlay myringoplasty using platelet-rich plasma. *The Journal of Laryngology & Otology*, 132(11), 990-994. doi:10.1017/S0022215118001846
11. Garoufalia Z, Papadopetraki A, Karatza E, Vardakostas D, Philippou A, Kouraklis G, Mantas D. Insulin-like growth factor-I and wound healing, a potential answer to non-healing wounds: A systematic review of the literature and future perspectives. *Biomed Rep*. 2021 Aug;15(2):66. doi: 10.3892/br.2021.1442. Epub 2021 Jun 8. PMID: 34155450; PMCID: PMC8212444


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