

A comparative study of outcome of myringoplasty with and without use of autologous platelet rich fibrin

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Abstract: *Introduction:* Chronic suppurative otitis media is one of the commonest causes of hearing loss. In myringoplasty the most widely used and accepted method is underlay graft of temporalis fascia. Platelet-rich fibrin is a second-generation platelet concentrate; It serves as a resorbable membrane that offers both mechanical and inflammatory protection to the tympanic membrane graft. It accelerates cell proliferation and matrix remodelling; it does not induce any undesirable tissue reactions. *Objectives:* To study the efficiency of use of autologous platelet rich fibrin in closure of tympanic membrane perforation during myringoplasty by preventing graft lateralization, graft site infection, promoting quicker healing and improving the overall outcome. *Methods:* This study included 50 patients presented to the Department of Otorhinolaryngology, Al Ameen Medical College, Vijayapura from November 2019 to December 2021 with chronic suppurative otitis media. 50% of patients underwent myringoplasty with autologous PRF and remaining 50% without PRF, they served as control. Routine follow-up at the 21 days, 1 month and 3 months after surgery. Postoperative PTA was done at 3 months. *Results:* The graft uptake rate was found to earlier in PRF group at 3 weeks and 1 month in comparison to controls, which was statistically significant ($p < 0.05$). *Conclusion:* PRF is a cheap and cost effective platelet concentrate with enriched growth factors. It accelerates the tympanic membrane closure, prevents graft migration, site infection and improves overall success rate in myringoplasty. It has no noticeable side effects.

Keywords: Chronic Suppurative Otitis Media, Myringoplasty, PRF, Graft Uptake, Audiometry.

Introduction

The WHO defines CSOM as “a stage of ear disease in which there is a chronic infection of the middle ear cleft i.e., Eustachian tube, middle ear, and mastoid, and in which a perforated tympanic membrane and discharge are present. The prevalence of CSOM in India according to WHO reports is 7.8%, [1] which puts India amongst the group with highest prevalence. Myringoplasty is a tympanoplasty without ossicular reconstruction. Over the years many methods have been used for closing perforations.

The most widely used and accepted method is underlay graft of temporalis fascia. The successful closure rate in myringoplasty vary from 64-88% from various studies. Platelet concentrates [2-3] have been used extensively by maxillofacial surgeons, plastic surgeons, and orthopedic surgeons to augment wound healing.

The different platelet concentrates that have been studied are platelet-rich plasma and platelet rich fibrin. Platelet-rich fibrin [4] is a second-generation platelet concentrate, which is rich in platelets, cytokines, growth factors, and leukocytes that are trapped and released over a period. It serves as a resorbable membrane that offers both mechanical and inflammatory protection to the tympanic membrane. It accelerates cell proliferation and matrix remodelling.

Being an autologous biomaterial, it does not induce any undesirable tissue reactions. Moreover, it is easy, quick, and cheap to produce, and can easily be manipulated during surgical procedures. As it has strong elastic fibrin rich with growth factors, it is considered an ideal patch material for tympanic membrane perforation. Leukocytes embedded in the platelet-rich fibrin scaffold also play a

role in the release of growth factors, immune regulation, antimicrobial response, matrix remodelling and wound healing. The present study is a Cross-sectional comparative study conducted in the Department of Otorhinolaryngology, Al-Ameen Medical College, Vijayapura, among 50 patients presented with chronic suppurative otitis media, who underwent Myringoplasty with and without PRF membrane. The outcome was analysed in postoperatively by clinical examination and audiometry during follow-up.

Aims: To study the efficiency of use of autologous platelet rich fibrin in closure of tympanic membrane perforation during myringoplasty by promoting quicker healing, preventing lateralization of graft and improving the overall outcome.

Objectives: To assess the outcome of Myringoplasty with and without autologous Platelet rich Fibrin. To compare the outcome of Myringoplasty in study and control group, with and without use of autologous Platelet rich Fibrin.

Platelet Rich Fibrin [5-6]: Platelets have been described as key components affecting the early phases of tissue regeneration important during haemostasis and fibrin clot formation. Platelets have also been shown to secrete a number of important growth factors including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), coagulation factors, adhesion molecules, cytokines/chemokines, and a variety of other angiogenic factors capable of stimulating the proliferation and activation of cells involved in the wound healing process including fibroblasts, neutrophils, macrophages, and mesenchymal stem cells.

Platelets and macrophages release an abundance of factors including transforming growth factor beta-1 (TGF- β 1), platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and insulin-like growth factor (IGF).

Material and Methods

A cross-sectional comparative study in conducted at the Department of Otorhinolaryngology, Al Ameen Medical College, Vijayapura, Karnataka, under Rajiv Gandhi University of Health

Sciences, Bangalore, Karnataka. The collection of data was done between November 2019- December 2021 for a period of 2 years. The study group included 50 patients presented with chronic suppurative otitis media to the department of Otorhinolaryngology, Al Ameen Medical College, Vijayapura, Karnataka.

Inclusion Criteria: Age group of 12- 55 years, Patient willing to give informed consent, Chronic otitis media inactive mucosal disease (central perforation with dry ear) without discharge for at least 6 to 8 weeks.

Exclusion Criteria: Patient not willing to give informed consent, children below 12 years of age, active ear disease, atopic ear conditions, attico antral Type CSOM, Diabetes mellitus, other systemic illness like autoimmune disease, active neoplastic disease, patients on immunosuppressant drugs.

Control group: Patient in whom platelet rich fibrin is not used for myringoplasty during the same study periods are taken as control group.

Sample Size Estimation: 88 patients (44 per group) are required to have a 90% chance of detecting, as significant at the 5% level, a decrease in the failure in tympanic membrane closure from 30% in the control group to 5% in the experimental group. But due this COVID-19 pandemic, the sample size has been reduced to 50 patients.

Statistical Methods Used: For continuous variables, the summary statistics of mean \pm standard deviation (SD) were used. Chi-square (χ^2) test was used for association between two categorical variables. If the p-value was < 0.05 , then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analysed using SPSS software v.23 (IBM Statistics, Chicago, USA) and Microsoft office 2007.

Procedure:

Preparation of Platelet Rich Fibrin: 10ml of venous blood sample was withdrawn from each patient using a syringe and transferred to sterile plastic test tube with lid just before the

surgery. The sample was then centrifuged using a table top centrifuge at 3000 rpm for 13 min. Centrifugation thus resulted in the formation of a fibrin clot (platelet-rich fibrin) in the middle of the tube (between the RBC layer at the bottom and plasma at the top).

The plasma layer is deficient in platelets. Platelet rich fibrin was removed with sterile forceps from the sterile container and stripped from the adjacent red blood cell layer. The blob of PRF was then placed between two glass slides and gently pressed for about three minutes. The exudate (PRF Serum) was carefully collected in another container for further usage in the soaking of temporalis fascia graft. Thus, a thin membrane about the thickness of 1 mm, rich in fibrin from the matrix was obtained. The membrane was then cut according to the required size and used during the procedure.

Steps of Surgery: After harvesting the appropriate graft following steps were followed-Elevation of the periosteal flap. Meatotomy in cases of post-auricular approach. Freshening of the edges of the perforation. Elevation the tympanomeatal flap. Placing the graft by underlay technique. Repositioning the tympanomeatal flap.

Placement of PRF: The Platelet Rich Fibrin membrane which is cut into desired shape is placed over the tympanomeatal flap. Following this, gelfoam pieces soaked with antibiotic are used to pack the ear canal. Suturing of periosteal flap and postauricular skin. Standard mastoid dressing was given in cases operated by post-aural route. Patients were discharged with instruction to continue antibiotics and antihistaminic. Sutures were removed on 7th day. Steroid-antibiotic ear drops for local instillation were started after 7th day.

Visit: 1st follow up (15 OPD), 2nd follow up (21 OPD), 3rd follow up (1 month). Then monthly follow up. PTA done after 6 month of operation.

Results

A total number of 50 patients were enrolled for the study. These patients were randomly divided into two groups, each consisting of 25 individuals. Group I patients underwent myringoplasty with autologous PRF and Group II patients underwent myringoplasty without PRF.

Size of perforation: Majority of patients in cases had subtotal perforation 48 %(n-12) and in controls it was large perforation 44 %(n-11). Overall, most among study had subtotal (40%) and large (40%) perforations. There was not statistical significance between both groups (Table-1).

Size of perforation	Cases		Controls	
	N	%	N	%
Small	1	4	2	8
Medium	3	12	4	16
Large	9	36	11	44
Subtotal	12	48	8	32
Total	25	100	25	100

Degree of hearing loss: Majority of patients [74 %(n-37)] had mild hearing loss on audiogram followed by moderate hearing loss. In mild hearing loss, 32 are having unilateral disease and 1 has bilateral disease. In moderate hearing loss, 9 are having unilateral disease

Procedure done: Majority of patients [84% (n-42)] in both cases and controls underwent cortical mastoidectomy, rest of the patients underwent myringoplasty. There were no significant differences between 2 groups. Myringoplasty alone done for 8patients (3cases and 5control). Cortical mastoidectomy with myringoplasty done for 42patients (22cases and 20control) (Table-2, 3 4).

	Cases		Controls	
No of patients	25		25	
Tympanic membrane closure	Cases	24	Controls	21
	Percent	96%	Percent	84%
Failure	1		4	
Z-2, P value-0.157				

Table-3: Comparison between the cases and control group with regards to preoperative, postoperative audiogram and improvement in hearing

Audiogram	Cases (n=25)	Controls (n=25)	Total (n=50)	P-Value
Pre-operative Audiogram	34.6±7.65	34.28±6.54	34.6±7.04	0.874
Post-operative Audiogram	22.92±9.09	22.64±10.65	22.78±9.80	0.920
Improvement in ABG	11.68±4.96	11.24±6.66	11.46±5.82	0.792

Table-4: Hearing gain more than or less than 10 dB gain in cases and control

Hearing Gain ABG	Cases	Controls
0-10 db	10(40%)	10(40%)
≥10 db	15(60%)	15(60%)
Total	25(100%)	25(100%)
Z-0, P value-1		

Postoperative Hearing Levels: A total of 45 out of 50 patients showed improvement in hearing between 0 to 40 dB (90%). Case group patients showed 96% improvement in hearing. Control group showed 84% improvement in hearing. There is no statistically significant difference in hearing improvement, between 2 groups (Table-5).

Table-5: Post operative hearing levels among patients

Hearing level (dB)	Cases		Controls		Total	Percentage
	No of patients	Percentage	No of patients	Percentage		
0 TO 10	1	4%	3	12%	4	8%
11 TO 20	14	56%	10	40%	24	48%
21 TO 30	3	12%	7	28%	10	20%
31 TO 40	6	24%	3	12%	9	18%
41 TO 50	1	4%	2	8%	3	6%
Total	25	100%	25	100%	50	100%

Graft Uptake Rate with respect to age of the patients: The graft uptake was highest among <20 years (100%)(15/15patients) followed by 21-30 years (92.8%)(13/14 patients),among 31-40 years (78.58%)(11/14 patients) and >40 years (85.71) (6/7 patients).

Follow up: Patients of both groups were followed up at interval of 3 weeks, 1 month and 3 month post operatively. Both groups of patients were assessed for graft uptake during these intervals. Among cases there was a 96 %(n-24) graft up take starting from 3 weeks, where as in control group it was 56%(n-14) at 3 weeks and 72%(n-18) at 1 month interval. There was statistical significance (P>0.05) in the 2 groups at 3 weeks (p value-0.000929) and 1 month (0.0206). At 3 months interval there was no statistical significance between both the groups.

Discussion

Chronic suppurative otitis media is one of the commonest disease encountered in our daily practice. Myringoplasty is an operation to reconstruct the tympanic membrane (TM) that has been done to prevent recurrent infection of the middle ear and close TM perforation to improve hearing impairment. PRF as a carrier of growth factors which stimulate extra cellular matrix deposition and neovascularization.

PRF along with its plasma contains many factors including nutrients, vitamins, hormones, electrolytes, growth factors, and proteins that are essential for cell life and tissue healing. The autologous PRF is simple and easy to be prepared without reported side

effects. This study was conducted at Al Ameen Medical College, Vijayapura. It included 50 patients presented to the Department of ENT with Chronic suppurative otitis media mucosal type active disease between November 2019 and May 2021. Conservative measures were first tried in all patients, particularly for small to moderately sized perforations.

These included systemic antibiotics, trichloroacetic acid and repeated aural toilet in ears with active infections. Cases with bilateral ear diseases with suspected central septic focus were operated with tonsillectomy, adenoidectomy, septoplasty, etc. as needed. 25 patients were subjected to myringoplasty with autologous PRF and remaining 25 patients under went myringoplasty without PRF. Follow up of postoperative cases were done for 3 months.

The mean age in our study population were 28.54 ± 10.3 years ranging between 14 years and 48 years. The majority of the patients were in the age group of 13-20 years (30%, n=15), followed by 21-30 and 31-40 years (28%, n=14). In majority of study the most common group affected is between 20-30 years of age, which is also same in our case with respect to mean age of our study patients. Among the study population, 62% (n=31) patients were female and 38% (n=19) were male. In majority of studies the percentage of patients are female. The female preponderance was also observed by Sankarnarayanan et. Al [7] and Sharma D et al [8].

In our study only one patient out of 50 patients belong to higher socioeconomic status, whereas about 72 percent of patients were from lower class and 26 percent of patient belongs to middle class, which again reflects the prevalence of this disease in lower class.

These observations were similar to many previous study. The increased incidence of this disease in this lower class is due to overcrowding, poor sanitation, poor nutrition and illiteracy. About 82% (n=41) of people in the study population had unilateral ear disease whereas remaining 18% (n=9) had bilateral disease. In cases 21 patients had unilateral disease and 4 patients had bilateral disease. In controls 20 patients had unilateral disease whereas 5 patients had bilateral disease. Among the unilateral disease in controls 12

patients had right ear disease whereas 8 patients had left ear disease. Among cases 9 patients had right ear disease and 12 patients had left ear disease.

In our study large and subtotal perforation is very common in comparison to other perforations. Among cases 1 patients had small perforation, 3 patients had medium, 9 patients had large and 12 patients had subtotal perforation. In controls 2 small, 4 medium, 11 large and 8 subtotal perforations was seen.

In our study population most of the patient had mild conductive hearing loss. Among the unilateral disease patients, 32 had mild conductive hearing loss, 9 had moderate conductive hearing loss. Among bilateral disease both ears having mild conductive hearing loss was seen in 1 patient. Right ear having mild conductive loss is seen in 2 patients, and left ear having mild loss is seen in 2 patients. Moderate conductive hearing loss was seen in right ear in 2 patients and in left ear in 2 patients. The pre operative mean audiogram among cases was 34.6 ± 7.65 dB and controls were 34.28 ± 6.54 dB.

In our study 42 patients underwent cortical mastoidectomy with myringoplasty and 8 patients underwent myringoplasty alone. Among cases 11 were right ears and 14 were left ears. In controls 14 were right ears and 11 were left ears. All the 50 cases were operated under local anesthesia. When compared to other studies is clinically significant in reducing complications related to General anesthesia, helps in intraoperative hearing assessment and early post operative recovery. The graft take up rate in our study is comparable with the reference studies.

According to Sankaranarayanan et al study 96% closure were seen in case group with the use of PRF and 80% closure in control group seen at the end of third month in tympanic membrane perforation during myringoplasty [7]. In Hosamet al study [9] the overall graft take rate was 96% (24 cases) in group A, whereas the graft take rate in group B was 76% (19 cases) with a statistically significant difference between the two groups ($P=0.041$).

In Sharma D et al study [8] in case group, 92% graft uptake was seen and in control groups the graft uptake was 64%. Nithin Prakasan Nair et al the graft uptake success rate was found to be 97.7% in the study group as compared with 81% in control group ($p = 0.012$). [10]. Mohamed Kamelel Awady et al study showed the success rate in PRF group (95%) was significantly higher than in the control group (70%) (P value =0.037) [11].

Sohail Aslam et al in platelet rich fibrin group had successful graft uptake (100%) at 2 months follow-up. In control group with conventional technique 23 out of 30(76%) patients had successful graft uptake [12]. We had overall graft take up rate of 96 % (n=24) in cases and in control group it was 84 % (n=21) which was statistically not significant but clinically important. Our study also have similar outcome with respect to the above references.

At the end of 3 weeks and 1 month on follow up 96% of patient had graft take up rate when compared to controls it was 56% and 72%, which was statistically significant [3 weeks (p -value - 0.000929) and 1 month (p -value - 0.020638)]. At the end of 3 months 96% cases closure was maintained, where as in controls it was 84%. Sankarnarayanan et al observed at the end of first month follow up, 72 percent of cases had closure of tympanic membrane, while only 40 percent of controls had tympanic membrane closure. At the end of second month 92 percent of cases had closure while only 72 percent of control had closure. At the end of 3 months 96percent of cases had closure, whereas only 80 percent of control had closure [7].

One failure among the cases was secondary to bulge in anterior wall of external auditory canal, due to malformed temporomandibular joint. The anterior margin could not be freshened anteroinferiorly, this led to failure due to poor uptake and persistence of small perforation. In controls there were 4 failures, 2 due to graft lateralization and 2 as result of operative site infection. The incidence of no infection in cases group is attributed to the presence of leucocytes with in PRF, which prevent infection. This observations were noted in other studies [7-8]. There was no complications in our case group.

The graft take up with respect to size of perforation was 100% for small, medium and large perforation in cases and 91% in subtotal perforation in case group, were as in control group it was 100% for small perforation, 91% for large perforation and 75% for medium and subtotal perforation. In a study by Sharma D et al case group 100% graft uptake was seen in small perforation 92% uptake in medium size and 80% uptake in large perforation. In control group 77% uptake was seen in small perforation. 72% uptake of graft was seen in medium size perforation and 37% uptake in large size perforation [8]. This shows that in our study the graft take up was high even for large and subtotal perforation.

As regards the postoperative hearing gain we found the following. 0-10 dB hearing gain was recorded in 10 patients in both cases and controls, ≥ 10 dB hearing gain was recorded in 15 patients in cases and control. There was no statistical significance between 2 groups. The overall post operative hearing improvement in audiogram was 11.68 ± 4.96 dB in cases and 11.24 ± 6.66 dB in controls. This was again statistically not significant. With regard to hearing improvement many studies match our observation [12-13].

In a study by Anwar FM et al audiological improvement (>10 dB) was seen in 31 cases (88.57%); whereas in the control group, only 27 (77.1%) had audiological benefits. However, in both studies, it is not statistically significant [14]. S Gökçe Kütük et al found that graft survival rates were significantly higher in the temporal fascia graft plus platelet-rich fibrin therapy group than in the temporal fascia graft alone group at one (100.0 vs 85.5 per cent, $p = 0.020$), three (97.2 vs 80.0 per cent, $p = 0.024$) and six months post-operatively (94.4 vs 74.5 per cent, $p = 0.031$) [15].

This comparison proves the graft take up rate was very early (3 weeks) in PRF group. In Hosamet al study noticed that hearing gain (≥ 10 dB) was achieved in 20 (80%) patients of group A, which is better than the hearing gain achieved in group B (15 patients;60%), with a statistically no significant difference [9] ($P=0.217$).

Conclusion

To conclude, myringoplasty is the most effective method for control of the disease and hearing improvement. Platelet-rich fibrin (PRF) application during myringoplasty is safe, cost effective and has high success rate with no side effects. PRF increased healing rate of chronic TM

perforations and also prevent infection of the graft with good results. It accelerates TM closure following myringoplasty and prevents graft displacement. It improves overall success rate in myringoplasty. There was not much to suggest regarding improvement in hearing with PRF use, it was similar to control.

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References

- World Health Organization. Child and Adolescent Health and Development Prevention of Blindness and Deafness. Global burden of disease due to chronic suppurative otitis media: Introduction. *Jose Acuin : The Organization*; 2004; 9.
- Saluja H, Dehane V, Mahindra U. Platelet-Rich fibrin: A second generation platelet concentrate and a new friend of oral and maxillofacial surgeons. *Ann Maxillofac Surg*. 2011; 1(1):53-57.
- Jameson C. Autologous platelet concentrate for the production of platelet gel. *Lab Med*. 2007; 38:39-42.
- Choukroun JI, Braccini F, Diss A, Giordano G, Doglioli P, Dohan DM. Influence of platelet rich fibrin (PRF) on proliferation of human preadipocytes and tympanic keratinocytes: A new opportunity in facial liposuction (Coleman's technique) and tympanoplasty. *Rev Laryngol Otol Rhinol (Bord)*, 2007; 128(1-2):27-32.
- Miron RJ, Choukroun J, editors. Platelet Rich Fibrin in Regenerative Dentistry: Biological Background and Clinical Indications. 1st ed. Hoboken, NJ 07030, USA: *John Wiley and Sons*, 2017; 1-14.
- Fujioka-Kobayashi M, Miron RJ. Biological components of platelet rich fibrin: growth factor release and cellular activity. Platelet rich fibrin in regenerative dentistry: biological background and clinical indications. *Oxford: John Wiley and Sons Ltd*, 2017; 15-31.
- Sankarnarayanan G, Prithviraj V, Kumar RV. A Study on efficacy of autologous platelet rich plasma in myringoplasty. *Otolaryngology Online Journal*, 2013; 3(3):2250-2359.
- Sharma D, Mohindroo S, Azad RK. Efficacy of platelet rich fibrin in myringoplasty. *Int J Otorhinolaryngol Head Neck Surg*. 2018; 4(3):67781.
- Hosam M, Shaker M and Aboulwafa A. Effect of topical use of platelet rich fibrin in repairing central tympanic membrane perforation using the endoscopic inlay butterfly cartilage myringoplasty technique. *The Egyptian Journal of Otolaryngology Ola S. ElShimi*, 2017; 33:557-563.
- Nair NP, Alexander A, Abhishekh B, Hegde JS, Ganesan S, Saxena SK. Safety and Efficacy of Autologous Platelet-rich Fibrin on Graft Uptake in Myringoplasty: A Randomized Controlled Trial. *Int Arch Otorhinolaryngol*, 2019; 23(1):77-82.
- eAwady M.K, Sharkawy MEL and abo Mohamed NM. Effect of addition of Platelet-rich fibrin to tragal perichondrium graft in the endoscopic trans-canal myringoplasty. *Egypt J Otolaryngol*, 2021; 37:11.
- Aslam S, Asghar A, Bukhari SMAS, Akhtar S, Mumtaz H, Wasim NF. Role of Fibrin Glue for Better Success Rate In Myringoplasty. *Pak Armed Forces Med J*. 2021; 71(Suppl-3):S603-606.
- Huang J, Teh BM, Zhou C, Shi Y, Shen Y. Tympanic membrane regeneration using platelet-rich fibrin: a systematic review and meta-analysis. *Eur Arch Otorhinolaryngol*. 2022; 279(2):557-565.
- Anwar FM, Shenoy VS, Kamath PM, Deviprasad SSD, Domah HA. Study on Use of Platelet-Rich Plasma in Myringoplasty. *Indian Journal of Otolaryngology*, 2020; 26(2):71-74.
- Gökçe Kütük S, Özdaş T. Impact of platelet-rich fibrin therapy in tympanoplasty type 1 surgery on graft survival and frequency-specific hearing outcomes: a retrospective analysis in patients with tympanic membrane perforation due to chronic otitis media. *J Laryngol Otol*. 2019; 133(12):1068-1073.

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