

# Topical use of Autologous Platelet Rich Fibrin in Tympanoplasty: A Prospective Interventional Study

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## ABSTRACT

**Introduction:** Tympanoplasty is the surgery performed in Chronic Otitis Media (COM) to improve the hearing function and prevent ear discharge. Platelet Rich Fibrin (PRF) is one of the materials that can be used to improve the graft uptake and hearing outcome. It is obtained by centrifugation of blood. The PRF contains leukocytes, cytokines, structural glycoproteins and growth factors which accelerates healing. It has been used in various surgical procedures to improve the outcome.

**Aim:** To determine the efficacy of autologous PRF in closure of tympanic membrane perforation after tympanoplasty and to study the influence of PRF on the hearing outcome in the study population.

**Materials and Methods:** This prospective interventional study was conducted in Department of Ear, Nose and Throat at SDM Medical College, Dharwad, Karnataka, India, from November 2018 to June 2020. The study included 60 patients with safe type of COM, who underwent tympanoplasty. Two group were made, group A consisted of 30 consecutive patients with safe

type COM who underwent tympanoplasty with PRF application and group B, consisted of 30 patients who underwent tympanoplasty without PRF application. The outcome was assessed by endoscopic evaluation every month for 3 months to look for graft uptake. Hearing gain was evaluated by Pure Tone Audiometry (PTA) after 3 months of surgery. Statistical analysis was done using Chi-square test.

**Results:** Group A had 29 cases with complete tympanic membrane closure and only one failure. However in group B, three out of 30 cases had failure. Thus, the overall the success rate was 96.66% in group A and 90% in group B. Postoperative PTA in group A showed that 18 cases (60%) had an improvement of >15 dB whereas in group B, 12 cases (40%) had hearing improvement of >15 dB.

**Conclusion:** Considering the higher success rate of tympanoplasty with group A compared to group B and no noticeable side effects, it is recommended that tympanoplasty with autologous PRF should be preferred.

**Keywords:** Chronic otitis media, Graft uptake, Hearing gain, Myringoplasty, Perforation

## INTRODUCTION

Chronic Otitis Media (COM) is characterized by discharge through a perforated tympanic membrane for a duration of at least 3 months. Other symptoms are decreased hearing and tinnitus. The aim of treatment in mucosal type of COM is to eliminate infection, prevent complications and to restore normal hearing mechanism [1]. Once adequate control of infection is achieved with topical antibiotics, tympanoplasty with cortical mastoidectomy is done with the aim of aerating the middle ear cleft and removal of chronically inflamed tissue.

The success rate of surgery is excellent overall and reperforation after surgical repair is mainly due to secondary infection. Thus it is important to augment the healing process and graft uptake which can be achieved with use of Platelet Rich Fibrin (PRF). It is obtained from patients own blood by centrifugation. The process in turn leads to platelet degranulation and release of growth factors. It plays an important role in cellular process like chemotaxis, mitogenesis, differentiation and metabolism [2]. The secretory proteins released from the platelets namely Platelet Derived Growth Factor (PDGF), Transforming Growth Factor-beta (TGF-beta), Vascular Endothelial Growth Factor (VEGF), Epidermal Growth Factor (EGF), Fibroblast Growth Factors (FGFs), Insulin-like Growth Factor-I (IGF-I) initiates wound healing process. The activated proteins diffuse into the surrounding tissues and binds to transmembrane receptors of target cells. The intracellular signal proteins gets activated and causes the expression of a gene

sequence that directs cellular proliferation, osteoid production and collagen synthesis thus triggering tissue repair [3].

Platelet Rich Plasma (PRP) is similar to blood clot and it initiates a more rapid and complete healing process. A natural blood clot usually contains around 95% Red Blood Cell (RBC), 5% platelets, and less than 1 % of White Blood Count (WBC) and large amount of fibrin strands. A PRP blood clot contains 95% of platelet, 4% of RBCs and 1% of WBCs [4]. The use of PRP has several advantages. The growth factors obtained from platelets are autologous and hence chances of reaction are minimal and it is free from transmissible diseases such as Human Immunodeficiency Virus (HIV), hepatitis [5].

Depending on their cell content and fibrin architecture Dohan Ehrenfest DM et al., defined four main families of PRP. Pure Platelet-Rich Plasma (P-PRP) is preparation without leucocytes and with a low-density fibrin network after activation. Leucocyte-PRP (L-PRP) products are preparations with leucocytes and with a low-density fibrin network after activation. Pure Platelet-Rich Fibrin (P-PRF) is without leucocytes and with a high-density fibrin network. The Leucocyte-PRF (L-PRF) or second-generation PRP products are preparations with leucocytes and with a high-density fibrin network [6].

The prerequisites for tympanoplasty are dry ear and healthy middle ear mucosa, patent eustachian tube and good cochlear reserve. The various graft materials used are temporalis fascia, fascialata, tragal or conchal perichondrium, tragal or conchal cartilage, periosteum, vein graft, fat from ear lobule, skin and dura. The graft acts like scaffold supporting the regenerating tympanic membrane

[7,8]. The PRF also protects the graft from infection [9]. The aim of the study was to determine the efficacy of autologous PRF in closure of tympanic membrane perforation after tympanoplasty and to study the influence of PRF on the hearing outcome in the study population.

## MATERIALS AND METHODS

This prospective interventional study was conducted in Department of Ear, Nose and Throat at SDM Medical College, Dharwad, Karnataka, India, from November 2018 to June 2020. The study included 60 patients with safe type of COM, who underwent Tympanoplasty. Patients who gave written informed consent and were willing for regular follow-up were included in this study. The Ethical Committee of the hospital has approved this study (SDMIEC/PG/0179/2018).

**Sample size calculation:** Total 60 patients who met the inclusion and exclusion criteria were divided into two groups. Sample size was estimated using the formula for quantifiable variables.

**Inclusion criteria:** Cases of safe type of COM in inactive stage with hearing loss less than 50 dB between the age of 10 to 60 years were included in the study.

**Exclusion criteria:** Age below 10 years and above 60 years, hearing loss more than 50 dB, unsafe type of COM, only hearing ear, revision surgery, and active infection in paranasal sinuses, throat and nose were excluded from the study. Children below 10 years were excluded from the study due to poor eustachian tube function, frequent upper respiratory tract infection and immature immune system were also excluded.

All eligible patients who met the inclusion criteria were enrolled.

- Group A (n=30): Tympanoplasty with autologous PRF
- Group B (n=30): Tympanoplasty without PRF

## Procedure

Assessment of the patients was done including history, general physical examination, and examination of ear, nose and throat. Perforations were classified according to the size [10]:

- Small: less than 50%
- Medium: 50-75%
- Large: more than 75%

Pure tone audiogram was done to assess the degree and type of hearing loss and average at

- 500 Hz
- 1000 Hz, and
- 2000 Hz frequencies was obtained.

All patients were subjected to otoscopic examination and imaging (bilateral mastoid x-rays). All the cases underwent underlay tympanoplasty with cortical mastoidectomy under general anaesthesia.

## Preparation of PRF

During the surgery, 10 mL of blood was taken in test tubes. No anticoagulant was added to the blood. It was centrifuged using a laboratory centrifuge machine for 12 min at 2,700 rpm. The resultant product consisted of the following three layers:

- Topmost layer contains acellular platelet poor plasma,
- PRF clot is in the middle and
- RBCs at the bottom.

The superficial platelet poor plasma layer was discarded and the middle layer (buffy coat) containing platelet clot was utilised. Blood begins to coagulate as soon as it comes in contact with glass surface. Hence, blood should be drawn and centrifuged just before PRF is needed for application to surgical site [11]. It was applied to the edges of perforation after the graft is placed

and the tympanomeatal flap was repositioned and ear canal packed with gelfoam.

All the patients received a course of oral antibiotic for the first postoperative week and topical antibiotic thereafter for 2 weeks and regular follow-up was done every 15 days for 3 months. The outcome was measured by endoscopic evaluation every month for at least 3 months to look for graft uptake. Hearing gain was evaluated by Pure Tone Audiometry (PTA) after three months of surgery. The failed cases were taken for the surgical procedure again.

## STATISTICAL ANALYSIS

Statistical analysis for the study was done using Statistical Package for Social Sciences (SPSS) software version 20.0. Chi-square test was used for categorical and independent t-test was used for continuous variable analysis.

## RESULTS

The majority of cases belonged to young adults between 21 to 30 years of age [Table/Fig-1]. Among group A, 11 were males and 19 were females and among group B, 16 were males and 14 were females [Table/Fig-2].

Age groups (years)	Group A		Group B		Total	
	n	%	n	%	n	%
Mean age (years)	31.42±11.04		31.65±11.84		$\chi^2=1.5330$ p-value=0.6750	
11-20	4	12.90	5	16.13	9	14.52
21-30	13	45.16	12	41.94	25	43.55
31-40	8	25.81	5	16.13	13	20.97
≥41	5	16.13	8	25.81	13	20.97
Total	30	100	30	100	60	100

[Table/Fig-1]: Age distribution of COM patients in the study population

Gender	Group A		Group B		Total	
	n	%	n	%	n	%
Male	11	35.48	16	51.61	27	43.55
Female	19	64.52	14	48.39	33	56.45
Total	30	100	30	100	60	100

Chi-square=1.6400, p-value=0.2000

[Table/Fig-2]: Gender distribution in study population.

Almost 53% of the study group had medium sized perforation, 26% had small and 21% had large sized central perforation [Table/Fig-3]. Graft uptake was compared between group A and B at 1, 2 and 3 months.

Size of perforation	Group A		Group B		Total	
	n	%	n	%	n	%
Small	8	25.81	8	25.81	16	25.81
Medium	14	45.16	19	61.29	33	53.23
Large	8	29.03	3	12.90	12	20.97
Total	30	100.00	30	100.00	60	100.00

Chi-square=2.6810, p-value=0.2620

[Table/Fig-3]: Size of perforation in Group A and Group B.

In group A, 96.66 % success rate was seen at 1 month and similar results were noted in Group B. At 2 months, the success rate was 96.66 % and 93.33 % and at 3 months it was 96.66 % and 90 % respectively [Table/Fig-4].

The left side showed large central perforation preoperatively. The endoscopic picture on the right side was of the healed tympanic membrane of patient in group A, 3 months after surgery [Table/Fig-5]. The mean hearing gain in group A and group B was 16.3 dB and 15.5 dB respectively [Table/Fig-6]. Total 60% of the patients in group

A have good hearing gain whereas only 40% in group B have good hearing gain following surgery [Table/Fig-7].

Graft uptake	Group A		Group B		Total	
	n	%	n	%	n	%
<b>At 1 month</b>						
Success	29	96.66	29	96.66	58	96.66
Failures	1	3.33	1	3.33	2	3.33
Total	30	100	30	100	60	100
Fisher's-exact Chi-square, p-value=1						
<b>2 months</b>						
Success	29	96.66	28	93.33	57	95
Failures	1	3.33	2	6.66	3	5
Total	30	100	30	100	60	100
Fisher's-exact Chi-square, p-value=1						
<b>3 months</b>						
Success	29	96.66	27	90	56	93.33
Failures	1	3.33	3	10	4	6.66
Total	30	100	30	100	60	100
Yates $\chi^2=0.2670$ , p-value=0.6050						

**[Table/Fig-4]:** Graft uptake in group A and group B.



**[Table/Fig-5]:** Preoperative and postoperative endoscopic appearance of the tympanic membrane.

Variable	Groups	Mean	Standard deviation	Standard error	t-value	p-value
Preoperative Pure Tone Audiometry (PTA)	A	37.58	8.098	2.05	1.3677	0.1765
	B	38.803	9.43	2.27		
Postoperative PTA	A	21.258	6.2865	1.50	0.4972	0.6209
	B	23.339	8.594	1.68		
Hearing gain	A	16.31	3.39	1.21	1.8501	0.8633
	B	15.481	5.352	1.14		

**[Table/Fig-6]:** Comparison of hearing gain in group A and B (dB) by independent t-test.

Hearing gain	Group A	Group B
<5 dB None	0	0
5-10 dB Minimal	1	0
>10-15 dB satisfactory	11	18
≥15 dB good	18	12

**[Table/Fig-7]:** Postoperative hearing gain in Group A and Group B.

## DISCUSSION

Choukroun JI et al., was the first to develop PRF and since then it is popular as second generation platelet rich plasma [12]. This study was done to evaluate whether PRF augments the healing of tympanic membrane perforation following Tympanoplasty. The etiology for perforation was safe type of chronic otitis media. The age of distribution of chronic otitis media in the present study

population was compared to the study conducted by Taneja MK [13]. The disease is common in 20 to 30 years of age group in the present study population. Total 44% of the study group were males and 56% females. The perforation was classified as small (<50%), medium (50-75%) and large (>75%) based on the size. In this study, majority (53%) of the patients had medium sized perforation. Outcomes were not compared with the size of the perforation in each group which could be a shortcoming of the study.

Erkilet E et al., studied the effect of PRP in healing of traumatic membrane perforations in 44 rats. They noticed a statistically significant (p-value <0.001) decrease in the mean healing time in the study group compared to the control group [14]. Similar outcome in humans was reported by Habesoglu M et al., with 64.3% closure of perforation in study group compared to 22.2% in control group at the end of 1 month [15]. Both these studies were on acute or traumatic tympanic membrane perforation whereas the present study was on perforation of chronic middle ear disease.

In the present study, the success of graft uptake was 96.66% in group A. Regular follow-up and endoscopic examination was done for atleast 3 months postoperatively. The success rate in group B was 96.66% at the end of 1 month which dropped to 90% at the end of 3 months. Similar results of 96% success rate with use of PRF have been achieved in other studies too [16,17]. Taneja MK, randomised controlled trial on 82 patients also had a success rate of 95% in PRP group which was comparable to the current study [13]. Nair NP et al., had a higher success rate of 98% in the study group [18]. The success rate in control group was 80 to 85% in various studies whereas it was 90% in the current study [17,18].

Sharma D et al., achieved 100% graft uptake rate in small perforation, 92% in medium size and 80% in large perforation in the case group [19]. Though the study had results comparable to the present study, the correlation of graft uptake rate to the size of perforation has not been done in the present study.

In the present study, the postoperative hearing gain among cases shows that 18 cases (60%) had an improvement of >15 dB whereas among controls 12 cases (40%) had hearing improvement of >15 dB. The p-value=0.3804 which was statistically not significant. Similar study conducted by Sharma D et al., on 100 patients showed significant improvement in air-bone gap at speech frequencies [19].

The present have achieved a mean hearing gain of 16.3 dB in the PRF group compared to 15.5 dB in the control group. The p-value was 0.86 was not statistically significant. A similar study by Anwar FM et al., with 70 patients showed an audiological improvement of >10 dB in 88.6% of cases and 77% of the controls [20].

This study showed improved outcomes in terms of graft uptake and hearing gain with use of PRF. It encourages routine use to prevent tympanoplasty failure. However, the present study observed no statistically significant outcomes in terms of graft uptake or hearing gain as the p-value was >0.05.

## Limitation(s)

The association of outcome of surgery with other factors like the size and location of perforation and status of middle ear mucosa was not ascertained which could also be a shortfall of this study. Diabetic status and blood group of the patient should be considered in future studies.

## CONCLUSION(S)

Newer advances are necessary to prevent graft rejection and improve functional outcomes of tympanoplasty In our study population, the success in PRP group in terms of postoperative hearing gain and graft uptake was encouraging, though not statistically significant. Authors concluded that tympanoplasty with PRF has a higher success rate.

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