Efficacy of Topical Use of Autologous Platelet Rich Plasma in Myringoplasty

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ABSTRACT
Background: Platelet-rich plasma (PRP) is an autologous product derived from whole blood through the process of gradient density centrifugation. Autologous PRP, with growth factors up to 8 times that of normal serum, has been shown to be safe and effective in promoting natural processes of wound healing.
Objective: Assessment of the efficacy and advantage in using autologous platelet-rich plasma during myringoplasty in closure of tympanic membrane perforation improving overall outcome.
Method: Platelet-rich plasma (PRP) is an autologous platelet-rich concentrate prepared from patients' own blood with growth factors up to 8 times that of normal serum. The efficacy of PRP when used during myringoplasty is studied. 40 patients with chronic otitis media inactive mucosal disease were randomly chosen and 20 of them was the study group and other 20 were the control group. Both group patients underwent myringoplasty and PRP was used in the study group and the results were evaluated. Myringoplasty was done and after placement of the cartilage graft, platelet-rich plasma was placed over the myringoplasty site.
Results: In our study among cases that underwent myringoplasty with use of platelet-rich plasma, 90% had complete tympanic membrane closure and only 10% failure has been noticed. In controls 60% out of cases had failure. The graft take up rate in our study is comparable with the reference studies. Use of PRP accelerated graft uptake.
Conclusion: Platelet-rich plasma is a cheap and cost effective platelet concentrate with enriched growth factors. It accelerated the tympanic membrane closure following myringoplasty.
Keywords: Myringoplasty, Tympanic Membrane, Platelet-Rich Plasma, Graft Uptake.

INTRODUCTION
Chronic suppurative otitis media is defined as chronic inflammation of the mucoperiosteal lining of the middle ear cleft. It is associated with persistent or intermittent discharge through a non-intact tympanic membrane [1].

Tympanic membrane perforation may result from acute otitis media (AOM), chronic otitis media, or trauma (injury or surgery). In some instances, a dry, simple perforation results from a single episode of AOM (i.e., necrotizing otitis media) [2].

Myringoplasty is the closure of the perforation of pars tense of the tympanic membrane. When myringoplasty is combined with ossicular reconstruction, it is called tympanoplasty. The graft material most commonly used for the surgery is temporalis fascia. The tragal cartilage and tragal perichondrium are also used as the graft by some surgeons**.** Myringoplasty restores hearing loss in certain cases of tinnitus [3].

Platelet-rich plasma (**PRP**) is a concentrate of platelet-rich plasma protein derived from whole blood. It has a greater concentration of growth factors than whole blood. Platelet-rich plasma is a novel material that is being used more and more frequently in many surgical specialties. Its numerous advantages include safety (because it is an autologous material), increased deposition of platelets and growth factors in the healing area and a short preparation time [4].

The aim of the current study was to assess the efficacy and advantage in using autologous platelet-rich plasma during myringoplasty in closure of tympanic membrane perforation.

PATIENTS AND METHODS
The present study was carried out on 40 patients, 25 female and 15 male aged 15-40 years suffering from chronic suppurative otitis media with tympanic membrane perforation with preserved middle ear anatomy and function.
Ethical approval:
The study protocol and consent forms were approved by the Research Review Committee.
Patients were selected from the Outpatient Clinics of ENT department at Al Zahraa University hospital, Cairo, during the period from January, 2017 to January 2019, all the patients under the study were followed up at the same hospital for a period of 6 to 12 months post-operative.
Patients were classified into two groups: (A) Case group included 20 patients who had undergone myringoplasty with use of autologous PRP and (B) Control group included 20 patients who had undergone myringoplasty without use of autologous PRP.
Exclusion criteria include: Children below 12 years of age, active ear disease, patients with known systemic disorders like uncontrolled diabetes and hypertension, other systemic illness

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like autoimmune disease, active neoplastic disease and patients on immunosuppressant drugs.

All patients were subjected to the following: Complete history taking, (personal history, complaint, present history, past and family history), complete general and E.N.T examination, routine laboratory investigations, pure tone audiogram which is helpful in assessing degree and type of hearing loss and ET function by tympanometry.

Procedure:

At the start of operation, PRP is prepared as 5 ml of peripheral venous blood is drawn from patient and placed in a tube (with sodium citrate) and immediately centrifuged for 10 minutes with speed 900 rpm using digital centrifuge (HERMLE z 326 k centrifuge, maximum speed 18000 rpm). The centrifugation cause the blood to separate into three layers of different density. The bottom layer consisted of red blood cells, the middle layer consist of platelet-rich plasma (about 1.5 ml), and the top layer contain platelet-poor plasma. The platelet-rich plasma is extracted just before application.

Myringoplasty was done and after placement of the cartilage graft, the prepared autologous PRP was inserted into external auditory canal [EAC] on the lateral surface of the graft and TM remnant. Gel foam were inserted filling the medial part of EAC to support the PRP. Meatal pack soaked in gentamycin ointment was placed for one week.

The first follow up of patients was one month after surgery and the second follow up was at end of third month and the third one was performed at end of 6 months. The patients were observed for closure and healing of tymbanic membrane. Pure tone audiogram and tympanogram were done.

Statistical analysis

All data were gathered, tabulated and statistically analysed using Statistical Program for Social Sciences (SPSS) soft wear program version 20. Numerical data was expressed as mean and standard deviation while non-numerical data was expressed as number and percentage. Comparison between groups was done using chi-square test. Person correlation analysis was done to determine the correlation between the studied variables. A P value less than 0.05 was considered statistically significant.

RESULTS

The current study included 40 patients (63% females & 37% males) ranged between 15-47 years old, with the mean age of (26.73 ± 8.58), who were admitted to the Department of Otolaryngology at Al-Zahraa university Hospital. The patients were divided into two groups: **Group**

(A) included 20 patients (10 male & 10 female) with mean age 26.00 ± 8.58, ranged between 15-38 years. In this group myringoplasty was done with the use of PRP, which was added to the graft using gel foam that was soaked with PRP. **Group (B)** included 20 patients (5 male & 15 female) with mean age 30.90 ± 10.03, ranged between 18-47 years. In this group myringoplasty was done by using cartilage graft without PRP.

In our study among 20 cases that underwent myringoplasty with use of platelet-rich plasma, 18 had complete tympanic membrane closure and only 2 cases of failure were recorded. In controls 12 out of 20 cases had failure due to superinfection, irregular attendance of patients to follow up, not following postoperative instructions as lifting heavy objects, straining and recurrent upper respiratory tract infections.

The distribution of cases according to their sex and age revealed no statistical significant difference (P > 0.05) as shown in table (1).

In our study large perforation is very common in comparison to other perforations. Among cases 10 patients had large perforation, 8 patients had medium, and 2 patients had subtotal perforation. In controls, 8 large, 8 medium and 4 subtotal perforations were seen (table 1). In our study population, most of the patients had mild conductive hearing loss. Among the patients, 23 had mild conductive hearing loss, 15 had moderate conductive hearing loss, whereas 2 cases had moderately sever conductive hearing loss (table 2).

In the present study, tympanic membrane perforation was treated using PRP in combination with graft in group (A), & the graft uptake occurred in 90% of the patients (P = 0.001).

In our current study, it was found that pure tone average (PTA) was statistically significant at 6 months postoperatively in PRPM group. The air-bone gab (ABG) was improved at 6 months postoperatively in group A (PRPM) (P = 0.000). However in group B, PTA was not statistically significant at 6 months postoperatively while, the ABG of group B was not statistically significantly improved postoperatively (P = 0.225).

- As regards the age, sex, side of affection and size of perforation between the two studied groups, there was no statistical significant difference (p value > 0.05) as shown in table (1).
- There was no statistically significant difference found between the two groups regarding preoperative assessment of TM status, grade of hearing and air-bone gap as shown in table (2).
- There was highly statistical significant difference between the two groups regarding post-operative T.M status follow up after 1

month, 3 months and 6 months as shown in table (3).

- There was no statistical significant difference found between the two groups regarding post-operative 6 months hearing grade and air-bone gap as shown in table (4).
- There was highly statistically significant difference found between preoperative and post-operative 6 months regarding air-bone gap in group A as shown in table (5).
- There was no statistically significant difference found between preoperative and post-operative 6 months regarding hearing grade and air-bone gap in group B as shown in table (6).

Table (1): Comparison between group A and group B regarding demographic data and side of affection.

		Group A	Group B	Test value	P-value	Sig.
		No. = 20	No. = 20			
Age (years)	Mean ± SD	26.00 ± 8.58	30.90 ± 10.03	1.660	0.105	NS
	Range	15 – 38	18 – 47			
Sex	Female	10 (50.0%)	15 (75.0%)	2.667	0.102	NS
	Male	10 (50.0%)	5 (25.0%)			
Side affected	Right ear	15 (75.0%)	10 (50.0%)	2.667	0.102	NS
	Left ear	5 (25.0%)	10 (50.0%)			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) *: Chi-square test; •: Independent t-test

The Previous table showed that there was no statistically significant difference found between the two groups regarding demographic data and side of affection.

Table (2): Comparison between group A and group B regarding preoperative assessment of TM status, grade of hearing and air-bone gap

Preoperative		Group A	Group B	Test value	P-value	Sig.
		No. = 20	No. = 20			
T.M status	Large central perforation	10 (50.0%)	8 (40.0%)	0.889	0.641	NS
	Medium sized perforation	8 (40.0%)	8 (40.0%)			
	Subtotal perforation	2 (10.0%)	4 (20.0%)			
Grade of hearing loss	Mild CHL	13 (65.0%)	10 (50.0%)	4.058	0.131	NS
	Moderate CHL	5 (25.0%)	10 (50.0%)			
	Moderately severe CHL	2 (10.0%)	0 (0.0%)			
Air-bone gap	Mean ± SD	19.80 ± 8.30	20.10 ± 7.58	0.119	0.906	NS
	Range	10 – 39	10 – 30			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) *: Chi-square test; •: Independent t-test

The Previous table showed that there was no statistically significant difference found between two groups regarding preoperative assessment of TM status, grade of hearing and air-bone gap.

Table (3): Comparison between Group A and Group B regarding post-operative T.M status follow up after 1 month, 3 months and 6 months

Post-operative T.M status		Group A		Group B		Test value	P-value	Sig.
		No.	%	No.	%			
1 month	Healed	15	75.0%	2	10.0%	17.289	0.000	HS
	Perforated	5	25.0%	18	90.0%			
3 months	Healed	18	90.0%	8	40.0%	10.989	0.001	HS
	Perforated	2	10.0%	12	60.0%			
6 months	Healed	18	90.0%	8	40.0%	10.989	0.001	HS
	Perforated	2	10.0%	12	60.0%			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) *: Chi-square test

Table (4): Comparison between Group A and Group B regarding post-operative 6 months hearing grade and air-bone gap

Post-operative 6 months		Group A	Group B	Test value*	P-value	Sig.
		No. = 20	No. = 20			
Hearing grade	Normal	2 (10.0%)	0 (0.0%)	8.821	0.066	NS
	Minimal	4 (20.0%)	0 (0.0%)			
	Mild	12 (60.0%)	14 (70.0%)			
	Moderate	2 (10.0%)	4 (20.0%)			
	Severe	0 (0.0%)	2 (10.0%)			
Air bone gap	Mean ± SD	11.20 ± 9.98	17.40 ± 9.88	1.974	0.056	NS
	Range	0 – 29	10 – 40			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) *: Chi-square test; •: Independent t-test

Table (5): Comparison between preoperative and post-operative 6 months regarding hearing grade and air-bone gap in group A

Group A		Preoperative	Post-operative 6 months	Test value*	P-value	Sig.
		No. = 20	No. = 20			
Hearing grade	Normal	0 (0.0%)	2 (10.0%)	9.326	0.053	NS
	Minimal	0 (0.0%)	4 (20.0%)			
	Mild	13 (65.0%)	12 (60.0%)			
	Moderate	5 (25.0%)	2 (10.0%)			
	Severe	2 (10.0%)	0 (0.0%)			
Air bone gap	Mean ± SD	19.80 ± 8.30	11.20 ± 9.98	-3.537	0.000	HS
	Range	10 – 39	0 – 29			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) *: Chi-square test; •: Paired t-test

The Previous table showed that there was high statistically significant difference found between preoperative and postoperative 6 months regarding air-bone gap in group A.

Table (6): Comparison between preoperative and postoperative 6 months regarding hearing grade and air-bone gap in group B

Group B		Preoperative	Postoperative 6 months	Test value*	P-value	Sig.
		No. = 20	No. = 20			
Hearing grade	Mild	10 (50.0%)	14 (70.0%)	5.238*	0.073	NS
	Moderate	10 (50.0%)	4 (20.0%)			
	Severe	0 (0.0%)	2 (10.0%)			
Air bone gap	Mean ± SD	20.10 ± 7.58	17.40 ± 9.88	-1.970•	0.225	NS
	Range	10 – 30	10 – 40			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) *: Chi-square test; •: Paired t-test

The previous table showed that there was no statistically significant difference found between preoperative and postoperative 6 months regarding hearing grade and air-bone gap in group B.

DISCUSSION

In the present study, tympanic membrane perforation was treated using PRP in combination with graft in group (A) & the graft uptake occurred in 90% of the patients (P = 0.001).

This is similar to **El-Anwar et al.** [5] who studied 64 patients with large dry central tympanic membrane perforations. Patients were classified into two groups: case group included 32 patients who underwent myringoplasty with use of autologous PRP and control group included 32 patients who underwent myringoplasty without use of autologous PRP. In their study, at 6 months was found that pure tone average (PTA) was statistically highly significant at 6 months postoperatively in PRPM group and the air-bone gab (ABG) was improved at 6 months postoperatively in group A (PRPM) (P = 0.000). However, in group B pure tone average (PTA) was not statistically significant at 6 months postoperatively and the ABG was not statistically significantly improved postoperatively (P = 0.225).

This matches with **Yadav et al.** [6] study that included 40 patients. Autologous platelet-rich plasma was applied in-between temporalis fascia graft and tympanic membrane remnant during underlay myringoplasty in group 1 (n = 20). The outcome was evaluated after three months and compared to group 2 (n = 20 control group) that underwent routine underlay tympanoplasty.

Results of this study showed that after three months' follow up, graft uptake was 95 per cent in group 1 and 85 per cent in group 2 (p < 0.03). Mean hearing threshold gain was 18.62 dB in group 1 and 13.15 dB in group 2. This difference was statistically significant (p < 0.01).

Yadav et al. [6] proved that platelet-rich plasma, with its ease of preparation technique, availability, low cost, autologous nature and good graft uptake rate, justifies its use in tympanoplasty type I procedures.

Our study also matches with **Bajpai** [7], that carried out on patients were diagnosed as cases of chronic suppurative otitis media tubotympanic type who were divided into two groups of 35 each. Patients in first group underwent myringoplasty with PRP, while those in second group underwent myringoplasty without PRP. Results of this study showed that out of 35 patients in each group, four in the study group and eight in the control group had residual perforation. Graft uptake in case group was 88.57% and graft uptake in the control group was 77.1%. Results were better in cases that underwent myringoplasty with PRP. Out of 35 patients in case group, audiological improvement (> 10 dB) was seen in 31 patients (88.57%) while in the control group out of 35 patients, 27 (77.1%) had

postoperatively, success rate (graft taking) in case group (100%) was significantly higher than in control group (81.25%) (P = 0.02). Success in terms of hearing gain (≥10 dB) was achieved in 21 patients (65.6%) in case group and 11 patients (34.4%) in control group with statistically non-significant difference (P = 0.079).

El-Anwar et al. [5] proved that topical autologous PRP application during myringolpasty is safe and highly efficient and successful with no reported complications.

In our current study, It

audiological benefits. **Bajpai** [7] study showed that there was definite benefit by using PRP in myringoplasty which agrees with our study.

Gopalakrishnan et al. [8], in their study found that platelet-rich plasma is a cheap and cost effective platelet concentrate with enriched growth factors. It accelerates the tympanic membrane closure following myringoplasty. This study included 50 patients with chronic otitis media inactive mucosal disease were randomly chosen and 25 of them was the study group and other 25 were the control group. All patients underwent myringoplasty and PRP was used in the study group and the results were evaluated. Results of this study showed that among 25 cases of study group, 24 cases had complete tympanic membrane closure and only one failure has been noticed. In controls 5 out of 25 cases had failure. So, they concluded that use of PRP accelerates graft uptake which is matching with our study. Our results also matches with **Saeedi et al.** [9], who used PRP-enriched gelfoam to evaluate the effect on the healing of chronic TM perforation in comparison with gelfoam alone. In their study, complete TM healing was seen in 66.67% patients of intervention group and in 25% patients of control group three months after intervention. So, this study concluded that addition of PRP to conventional gelfoams used in TM perforation repair increased the complete healing rate of TM perforation with less morbidity and complications.

We also agree with **Fawzy et al.** [10] in their study, 90% cases of study group significantly showed an intact tympanic membrane, while eleven cases (55%) cases were successful in control group (P=0.044). So this study concluded that topical autologous PRP application during fat plug myringoplasty was highly successful with no reported postoperative infections and minimal morbidity, which match with our results.

Our results also match with **Ahmed et al.** [11] study that included twenty patients with small to medium-sized tympanic membrane perforations. The PRP was applied over the fat graft. Results of

this study showed 100% success rate was obtained in small perforation and 79.3% in medium sized perforation. There was significant postoperative improvement in the mean air bone gap [p = 0.0016]. **Ahmed et al.** [11], concluded that adding PRP to fat myringoplasty is a safe, effective, cost saving and minimally invasive procedure. It is suitable to repair small as well as moderate sized TM perforations.

We also agree with **Fouad et al.** [12] where successful TM perforation repair was achieved in 85.7% with using PRP with FGM and in 87% with using HA with FGM and in 60% with pure FGM. So, this study proved that FGM with adding PRP or HA is more successful in closure of TM perforation than pure FGM in case of medium sized central TM perforation.

CONCLUSION

Our study concluded that platelet-rich plasma is a cheap and cost effective platelet concentrate with enriched growth factors. It accelerated the tympanic membrane closure following myringoplasty, it prevented graft migration, it improved the overall success rate of myringoplasty and it had no noticeable side effects.

REFERENCES

1. **Anil K L (2011):** Current diagnosis and treatment in otolaryngology – Head and Neck surgery, Third Edition. Front Cover. Anil Lalwani. McGraw Hill Professional, Pp: 1008.
2. **Gleeson M, Browning GG, Burton MJ et al. (2011):** Otorhinolaryngology head and neck surgery, 7th edition. Ann R Coll Surg Engl., 93 (7): 559.
3. **Watson G (2012):** Myringoplasty repairs a hole in the tympanic membrane. https://web.archive.org/web/20121221014726/ http://www.glennwatson. com.au/Myringoplasty.html
4. **Alvaro MLN, Ortiz N, Rodriguez L et al. (2011):** Research Article on Pilot Study on the Efficiency of the Biostimulation with Autologous Plasma Rich in Platelet Growth Factors in Otorhinolaryngology: Otologic Surgery (Tympanoplasty Type I). ISRN Surg., 2011: 451020.
5. **El-Anwar MW, El-Ahl MA, Zidan AA et al. (2015):** Topical use of autologous platelet rich plasma in myringoplasty. Auris Nasus Larynx, 5: 365-8.
6. **Yadav SPS, Malik JS, Malik P et al. (2018):** Studying the result of underlay myringoplasty using platelet-rich plasma. J Laryngol Otol., 132 (11): 990-994.
7. **Bajpai S (2019):** Study on Use of Platelet-Rich Plasma in Myringoplasty. Annals of Otology and Neurotology, 2 (1): 14-15.
8. **Gopalakrishnan S, Venkatasamy P, Vivekanandamurthy KA (2014):** study on efficacy of autologous platelet rich plasma in myringoplasty. Online J Otolaryngol., 3: 36–51.
9. **Saeedi M, Ajalloueian M, Zare E et al. (2017):** The Effect of PRP-enriched Gelfoam on Chronic Tympanic Membrane Perforation: A Double-blind. Int Tinnitus J., 21 (2): 108-111.
10. **Fawzy T, Hussein M, Eid S et al. (2018):** Effect of adding platelet- rich plasma to fat grafts in myringoplasty. Egypt J Otolaryngol., 34: 224-228.
11. **Ahmed RE, Yasser AF, Magdy BA et al. (2018):** Myringoplasty of Central Tympanic Membrane perforation with fat graft from the ear lobule and platelet rich plasma. ZUMJ., 24: 143-149.
12. **Fouad YA, Abdelhady M, El-Anwar M et al. (2018):** Topical platelet rich plasma versus hyaluronic acid during fat graft myringoplasty. Am J Otolaryngol., 39 (6):741-745.