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Evaluation of the use of autologous platelet-rich fibrin in myringoplasty operation

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Abstract

Background: Platelet-rich fibrin (PRF) which is considered a second-generation platelet-rich plasma having a high content of growth factors could be implied as a sealant and adjuvant to grafting materials during tympanoplasty operation. This work aimed to evaluate the role of autologous platelet-rich fibrin as an adjuvant in type 1 tympanoplasty (myringoplasty) for the closure of central tympanic membrane perforations. A prospective comparative study was conducted including one-hundred patients with chronic suppurative otitis media with dry central TM perforations. The patients were classified into two equal groups: group A (case group) was subjected to myringoplasty operation with the use of autologous PRF added to the temporalis fascia graft, and group B (control group) was subjected to myringoplasty operation using graft only without PRF. Both groups were assessed for successful closure of perforation defined as an intact eardrum, success in terms of hearing defined as closure of air-bone gap down to 10 dB or lesser, and hearing gain at 6 months postoperatively.

Results: At 6 months postoperatively, the success rate (graft taking) in group A (90%) was significantly higher than in group B (70%). Success in terms of air-bone gap closure (< 10 dB) revealed that in group A, success was achieved in 39 patients (78%), which was significantly higher than in group B 27 patients (54 %). Air-bone gap at 6 months postoperatively was more in the graft taken cases in the case group than in the control group with a significant difference. There was a nonsignificant correlation between graft uptake and either hemoglobin or platelet concentrations in both groups. In addition, there was a nonsignificant correlation between graft uptake and the size of the perforation in both groups.

Conclusion: Platelet-rich fibrin is a cheap, cost-effective, and completely autologous platelet concentrate with enriched growth factors. It improves the overall success rate of myringoplasty with no noticeable side effects.

Keywords: Myringoplasty, Platelet-rich fibrin, Platelet-rich plasma, Platelet concentrates, Tympanoplasty

Background

The success rate following myringoplasty varies, with an average failure rate of 20% reaching up to 40% in adults in some studies and even up to 65% in children in other studies. Therefore, in order to boost the success rate of myringoplasty, it is necessary to develop methods and materials that would aid in the healing of the tympanic membrane (TM) perforations [1, 2]. Materials including hyaluronic acid, pentoxifylline (Trental), and epidermal and fibroblast growth factors have been suggested in recent years for these uses [3].

Autologous preparations called platelet concentrates are characterized by the condensation of a large number of platelets into a small amount of plasma. In addition to having hemostatic and tissue sealing qualities, platelet concentrates act as a fibrin tissue adhesive. However, in contrast to fibrin glue and other platelet-poor tissue adhesives, platelet concentrates have the special capacity

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to speed up bone formation and improve wound healing. Additionally, they have the benefit of being safe and biocompatible, with little chance of spreading infectious diseases [4].

Platelet-rich plasma (PRP) represents the primary form of platelet concentrates that promotes soft tissue healing, lessens dermal scarring, stimulates angiogenesis, boosts collagen synthesis, accelerates endothelial, epithelial, and epidermal regeneration, and reverses the inhibition of wound healing brought on by glucocorticoids. PRP's high concentration of leukocytes provides an additional antibacterial impact [5].

Platelet-rich fibrin (PRF) which is considered a second-generation platelet-rich plasma having a high content of growth factors could be implied as a sealant and adjuvant to grafting materials during tympanoplasty operation [6]. This work aimed to evaluate the role of autologous platelet-rich fibrin as an adjuvant in type 1 tympanoplasty (myringoplasty) for the closure of central tympanic membrane perforations.

Methods

The current study was a prospective comparative study conducted on patients with chronic suppurative otitis media mucosal type with dry central tympanic membrane perforation spanning the period from July 2017 to December 2021. The study was conducted after the approval of the institutional review board. Informed consent was obtained from every patient before participation in the study.

Patients with a 12-week duration of dry central TM perforation with no evidence of otorrhea or active chronic otitis media, cholesteatoma, or retraction pocket were included in this study. Patients with active chronic otitis media with otorrhea, recurrent tympanic membrane perforation, cholesteatoma, or retraction pocket formation and patients with surgical unfitness like bleeding tendency or uncontrolled systemic diseases like hypertension or diabetes mellitus were excluded from the study.

One-hundred patients were included in the study who were randomly and equally distributed among two groups: group A (case group) included 50 patients subjected to myringoplasty operation with the use of autologous PRF, which was added to the temporalis fascia graft, and group B (control group) included 50 patients subjected to myringoplasty operation by using graft only without PRF.

All patients were subjected to a comprehensive history taking and a complete otorhinolaryngology examination to confirm the presence of chronic suppurative otitis media mucosal type with a 12-week duration of dry central tympanic membrane perforation. The size of the perforation was assessed and documented for every patient. A pure tone audiogram was done for all patients to assess the degree and type of hearing loss with the calculation of the air-bone gap which is the average gap at frequencies 500, 1000, 2000, and 4000 Hz. Routine preoperative laboratory investigations were performed for all patients including a complete blood picture and bleeding and coagulation profiles.

Surgical technique

All patients were operated under general anesthesia with endotracheal intubation. Every patient was positioned in a supine position with his face turned to the opposite side of the perforation. The surgical field was scrubbed and draped as usual for otologic surgery. A postauricular incision was done followed by harvesting a temporalis fascia graft. The posterior wall of the external auditory canal (EAC) was opened followed by trimming of the edges of the perforation. Inspection of the middle ear cavity was done followed by raising the tympanomeatal flap with the annulus of the tympanic membrane. A proper-sized graft (1.5 times the size of the perforation) was placed medial to the handle of the malleolus so that its edges extend under the margins of the perforations all around (Fig. 1). In group A, the prepared autologous PRF was inserted into the external auditory canal on the lateral surface of the graft and tympanic membrane remnants (Fig. 2). In group B, gel foam was placed on the lateral surface of the graft and TM remnant in EAC. Finally, the postauricular incision was sutured in layers.

Preparation of the autologous PRF

During induction of anesthesia and under a sterile technique, 10 ml of peripheral venous blood was drawn from every patient with a 16- or 18-gauge butterfly needle or syringe to avoid irritation and damage to the platelets.

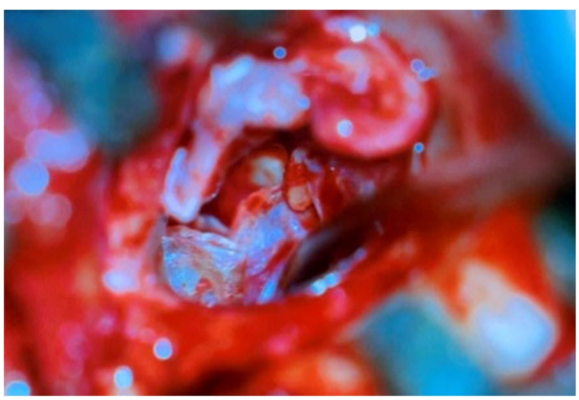

Fig. 1 Placing temporalis fascia graft medial to the handle of malleus and under the tympanic membrane remnants

Fig. 2 Placing PRF membrane lateral to temporalis fascia graft

The blood was collected in two 10 ml plain vacuum tubes (without an anticoagulant) and then immediately centrifuged using a tabletop centrifuge (Zhengji 800 centrifuge) (Jiangsu Zhengji Instruments Co., Ltd., Jintan City, China) for 10 min at 3000 rpm. So, it was separated out into three layers, the bottom layer consisting of red blood cells (specific gravity, 1.09), the middle layer containing PRF, which consisted of platelets and WBCs entangled in fibrin meshwork (buffy coat; specific gravity, 1.06), and the top layer containing PPP (specific gravity, 1.03) [6]. The PRF layer was taken out at the time of use, just before application (Fig. 3).

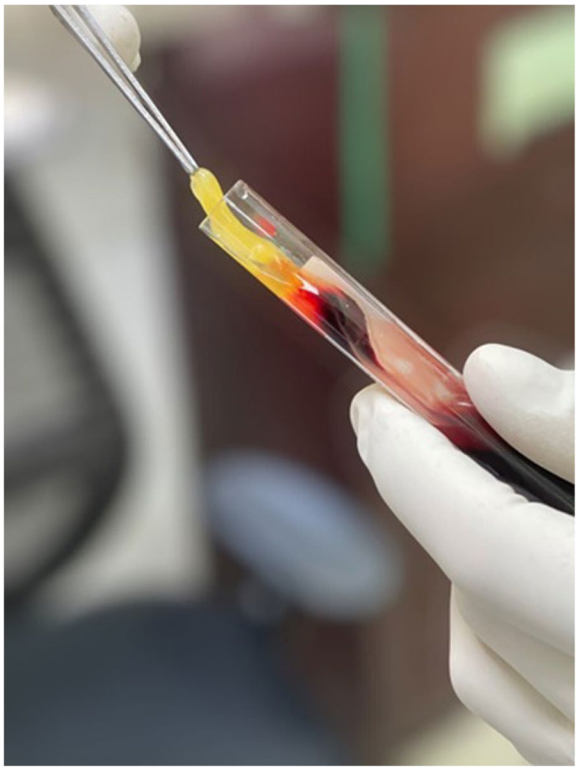

Fig. 3 Platelet-rich fibrin (PRF) extracted for use

Postoperative follow-up

Postoperative follow-up was done by clinical examination weekly at the 1st month and then monthly until 6 months. At every follow-up, patients were examined to check the graft take and complications. Pure tone audiometry was performed at 6 months postoperatively. Hearing results were assessed by comparing preoperative and postoperative pure tone audiograms with an assessment of the closure of the air-bone gap.

Outcomes

The primary outcomes of the study were the assessment of successful closure of perforation defined as an intact eardrum, success in terms of hearing defined as closure of air-bone gap down to 10 dB or lesser, and hearing gain at 6 months postoperative. Secondary outcomes of the study included an assessment of the relationship between aft uptake on one hand and of hemoglobin concentration, platelet count, and perforation size on the other hand.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (IBM Corp., Armonk, NY, USA). Quantitative data were expressed as mean and standard deviation (SD). Qualitative data were expressed as frequency and percentage. The Student *t*-test was used to compare two normally distributed quantitative variables, while the Mann-Whitney *U*-test was used to compare non-normally distributed quantitative variables. Wilcoxon sign-rank test was used to compare preoperative and postoperative quantitative variables. Chi-square and Fisher exact tests were used to compare two qualitative variables. A *p*-value less than 0.05 was considered statistically significant.

Results

In the current study, group A included 50 patients distributed as 21 (42%) males and 29 (58%) females, with an age range from 19 to 40 years and a mean (± SD) of 31.04 ± 6.74 years. Group B included 50 patients distributed as 20 (40%) males and 30 (60%) females with an age range from 19 to 45 years with a mean (± SD) of 32.24 ± 7.39 years. There were nonsignificant differences between the two groups regarding, age, sex, preoperative size of the perforation, hemoglobin concentration, platelet count, and air-bone gap (p = 0.839, 0.398, 0.790, 0.385, 0.388, and 0.452, respectively) (Table 1).

In the present study, at 6 months postoperatively, the success rate (graft taking) in group A (90%) was

Table 1 Comparison between the two studied groups regarding the demographic and preoperative clinical data

Variable	Cases (group A) ($n = 50$)		Control (group B) ($n = 50$)		Test of sig.	*p*
	No.	%	No.	%		
Sex						
Male	21	42.0	20	40.0	$\chi^2 = 0.041$	0.839
Female	29	58.0	30	60.0		
Age (years)						
Min.–max.	19.0–40.0		19.0–45.0		$t = 0.848$	0.398
Mean ± SD.	31.04 ± 6.74		32.24 ± 7.39			
Median (IQR)	33.0 (25.0–37.0)		35.0 (26.0–38.0)			
Size of perforation					$\chi^2 = 0.071$	0.790
Medium	41	82.0	42	84.0		
Large	9	18.0	8	16.0		
Hemoglobin concentration						
Min.–max.	10.10–13.90		10.40–14.70		$t = 0.873$	0.385
Mean ± SD.	12.12 ± 0.79		12.28 ± 0.99			
Median (IQR)	12.20 (11.40–12.60)		12.20 (11.60–13.0)			
Platelet count						
Min.–max.	172.0–453.0		177.0–447.0		$t = 0.867$	0.388
Mean ± SD.	295.6 ± 72.34		283.6 ± 66.67			
Median (IQR)	280.5 (244.0–342.0)		264.0 (245.0–309.0)			
Preoperative ABG					$t = 1142.50$	0.452
Min.–max.	21.0–37.0		26.0–40.0			
Mean ± SD	31.56 ± 5.12		32.68 ± 3.94			
Median (IQR)	32.0 (27.0–36.0)		32.0 (27.0–36.0)			

SD standard déviation, *IQR* interquartile range, χ^2 chi-square test, *t* Student *t*-test, *p p*-value. *ABG* air-bone gap

significantly higher than in group B (70%) ($p = 0.012$). Success in terms of air-bone gap closure (< 10 dB) revealed that in group A, success was achieved in 39 patients (78%), which was significantly higher than in group B (27 patients, 54%) ($p = 0.011$) (Table 2).

Comparing graft taken cases in both study groups, there was a nonsignificant difference between the preoperative ABG in both groups, while there was a significant difference between the ABG at 6 months postoperatively in both groups favoring the case group ($p = 0.965$ and $p = 0.014$, respectively). Longitudinal follow-up showed a highly significant improvement of ABG 6 months postoperatively compared with preoperative ABG in graft-taken cases in both groups ($p < 0.001$ for both) (Table 3).

In the current study, there was a nonsignificant correlation between graft uptake and either hemoglobin

Table 2 Comparison between the two studied groups regarding graft uptake take and air-bone gap closure and hearing gain at 6 months postoperatively

Variable		Case group (group A) ($n = 50$)		Control group (group B) ($n = 50$)		Test of sig.	*p*
		No.	%	No.	%		
Graft uptake						$\chi^2 = 6.250$*	0.012*
	Failure	5	10.0	15	30.0		
	Success	45	90.0	35	70.0		
Air-bone gap closure						$\chi^2 = 6.417$*	0.011*
	> 10 dB ABG (failure)	11	22.0	23	46.0		
	< 10 dB ABG (success)	39	78.0	27	54.0		

χ^2 chi-square test, *p p*-value. *Statistically significant at $p \leq 0.05$

Table 3 Comparison between the graft taken cases among the two studied groups regarding ABG preoperative, and 6 months postoperatively, along with a comparison between preoperative and postoperative ABG in both groups

ABG	Cases ($n = 45$)	Control ($n = 35$)	*U*	*p*
Preoperative				
Min.–max.	21.0–37.0	26.0–40.0	783.0	0.965
Mean ± SD	31.60 ± 5.27	32.09 ± 4.02		
Median (IQR)	32.0 (27.0–36.0)	32.0 (31.0–36.0)		
After 6 months				
Min.–max.	0.0–22.0	0.0–21.0	538.50*	0.014*
Mean ± SD	6.49 ± 5.11	8.86 ± 5.72		
Median (IQR)	6.0 (5.0–7.0)	7.0 (6.0–12.0)		
Z	5.864*	5.174*		
p_1	< 0.001*	< 0.001*		

SD standard deviation, *IQR* interquartile range, *U* Mann-Whitney test, *Z* Wilcoxon signed-rank test, *p* *p*-value for comparing between the studied groups, p_1 *p*-value for comparing between preoperative and after 6 months. *Statistically significant at $p \leq 0.05$

concentration or platelet count in both groups (Table 4). In addition, there was a nonsignificant correlation between graft uptake and size of the perforation in both groups (Table 5).

Discussion

While tympanoplasty is a typically beneficial and safe treatment for closing tympanic membrane perforations, it is possible for problems to arise, including injury to the middle ear ossicles, tympanic annulus, or chorda tympani [7]. Different options have been investigated over the past few decades to improve the results of tympanoplasty, including the use of scaffold materials, bioactive molecules, and cells. These new technologies outperformed traditional tympanoplasty, with platelet concentrations showing great potential for TM repair and efficacy as an adjuvant for wound healing [8].

The effect of PRF on human keratinocytes and preadipocytes' in vitro proliferation was examined by Choukroun et al. in 2007 [9]. They discovered that with the aid of PRF, the number of cells in culture rose by more than 60% at the 7th day and by over 150% at the 14th day, reaching a peak for daily proliferation around day 14. The two studied cellular types responded similarly. They proposed PRF as a healing biomaterial to enhance the therapeutic outcomes of tympanic and facial lipostructure operations.

The current study evaluated the therapeutic role of platelet-rich fibrin in the operation of myringoplasty and found a statistically significant effect of PRF on the success of myringoplasty in terms of intact tympanic membrane and closure of air-bone gap to less than 10 and postoperative ABG with no correlation between graft uptake and either hemoglobin concentration, platelet count, or perforation size. These findings match the results of previous studies investigating such a role for PRF. Platelet-rich fibrin (PRF) was evaluated by Garin et al. [10] as autologous packing material for middle ear

Table 4 Correlation between the graft uptake, on one hand, and hemoglobin concentration and platelet count on the other hand in each group

	Variable	Graft uptake		*t*	*p*
		Failed	Taken		
Cases ($n = 50$)	**Hemoglobin concentration**	**($n = 5$)**	**($n = 45$)**		
	Min.–max.	11.10–13.20	10.10–13.90	0.898	0.374
	Mean ± SD	11.82 ± 0.84	12.15 ± 0.78		
	Median	11.40	12.30		
	Platelet count	**($n = 5$)**	**($n = 45$)**		
	Min.–max.	224.0–323.0	172.0–453.0	1.051	0.299
	Mean ± SD	263.4 ± 37.58	299.20 ± 74.62		
	Median	260.0	284.0		
Control ($n = 50$)	**Hemoglobin concentration**	**($n = 15$)**	**($n = 35$)**		
	Min.–max.	10.40–14.70	10.40–13.60	0.036	0.972
	Mean ± SD	12.27 ± 1.33	12.28 ± 0.82		
	Median	12.10	12.30		
	Platelet count	**($n = 15$)**	**($n = 35$)**		
	Min.–max.	192.0–442.0	177.0–447.0	0.913	0.366
	Mean ± SD	296.73 ± 79.39	277.91 ± 60.84		
	Median	273.0	263.0		

SD standard deviation, *IQR* interquartile range, *t* Student *t*-test, *p* *p*-value. *Statistically significant at $p \leq 0.05$

Table 5 Correlation between graft taking and size of the perforation in each group

Perforation size	Graft taking				χ^2	^{FE}p
	Failed		Taken			
	No.	%	No.	%		
Cases (50)	**(*n* = 5)**		**(*n* = 45)**			
Medium	4	80.0	37	82.2	0.015	1.000
Large	1	20.0	8	17.8		
Control (50)	**(*n* = 15)**		**(*n* = 35)**			
Medium	12	80.0	30	85.70	0.255	0.683
Large	3	20.0	5	14.3		

χ^2 chi-square test, *FE* Fisher exact test, *p p*-value

microsurgery. They conducted a retrospective study on 108 individuals in whom only optimized PRF was employed to pack the middle ear or external auditory canal. One year following surgery, 45/48 patients had intact tympanic membrane.

Nair et al. [11] assessed the safety and efficacy of autologous platelet-rich fibrin on graft uptake in myringoplasty in eighty-six patients distributed equally among two groups, a case group with the application of PRF during myringoplasty and a control group without PRF application. The patients were observed for 3 months postoperatively by a blinded observer. They reported that when platelet-rich fibrin was employed, there was a higher incidence of postoperative graft uptake with a reduction of the postoperative infection rate.

By contrasting 55 patients who received a temporalis fascia graft alone with 36 patients who received a temporalis fascia graft plus platelet-rich fibrin, Gökçe and Zdaş [12] evaluated the effects of platelet-rich fibrin in tympanoplasty type 1 surgery on graft survival and frequency-specific hearing outcomes. According to their research, using a platelet-rich fibrin and temporalis fascia graft was associated with better postoperative results both in terms of tympanic membrane healing and graft survival, while hearing restoration outcomes were comparable in both groups.

In prospective research comprising 41 patients, Shukla et al. [13] evaluated the utilization of platelet-rich fibrin membrane in transcanal myringoplasty. Tympanic membrane perforations were repaired using PRF membrane, and 85.4% of the patients in this study experienced a good outcome. In a prospective single-blinded randomized controlled experiment with 50 patients, Riaz et al. [14] evaluated the effectiveness of topical drops of platelet-rich fibrin in 25 patients subjected to myringoplasty with an underlay technique via a postauricular approach. They reported that this topical application enhanced graft uptake with better hearing, significantly lower infection rates, and significantly higher perforation closure rates.

A systematic review with meta-analysis was performed by Huang et al. in 2022 [15] to evaluate the regeneration of the tympanic membrane utilizing platelet-rich fibrin. Seven of the ten papers eligible for the qualitative evaluation were included in the final quantitative comparison. The study concluded that PRF can lower the occurrence of infections, improve the survival rate of autografts in TM operations, and boost the closure rate of acute perforations, but with no effect on hearing outcomes. The study supported the use of PRF as a healing agent for tympanic membrane surgeries.

Platelet rich has a healing-promoting impact because it is abundant in platelets, cytokines, growth factors, and leukocytes that are retained and released gradually over time. It acts as a resorbable barrier that shields the tympanic membrane from mechanical and inflammatory harm. It hastens matrix remodeling and cell growth. Being an autologous biomaterial, it has no adverse effects on the tissue. It may also be easily handled during surgical operations and is simple, rapid, and inexpensive to create. It is regarded as the best patch material for perforations in the tympanic membrane due to its strong elastic fibers and plenty of growth ingredients. Leukocytes implanted in the fibrin scaffold rich in platelets are also involved in the remodeling of the matrix during wound healing, the release of growth factors, immunological control, and antimicrobial response [16].

Conclusion

Platelet-rich fibrin is a cheap, cost-effective, and completely autologous platelet concentrate with enriched growth factors. It improves the overall success rate of myringoplasty with no noticeable side effects.

Abbreviations
ABG: Air bone gap; EAC: External auditory canal; Hz: Hertz; PRF: Platelet-rich fibrin; PRP: Platelet-rich plasma; TM: Tympanic membrane.

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Authors' contributions
ME provided the concept, with the definition of intellectual content; HA provided the study plan and conducted clinical studies and data analysis; AA and TE conducted clinical studies and data collection; and TA conducted clinical studies, data analysis, and manuscript editing. The authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Approval was obtained from Institutional Review Boards (IRB) of the Menoufia Faculty of Medicine and following the Declaration of Helsinki. After an explanation of all aspects of the study and being given the right to withdraw at any time, written consent was taken from all the patients.

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

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