# **ORIGINAL ARTICLE**

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# Effect of addition of platelet-rich fibrin to tragal perichondrium graft in the endoscopic trans-canal myringoplasty



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#### **Abstract**

**Background:** Myringoplasty operation is the reconstruction of the tympanic membrane (TM) which is performed to prevent recurrent discharge of the ear and to improve the hearing impairment which is caused by TM perforation. Platelets are the key factors in tissue repair mechanisms. They provide essential growth factors, which stimulate fibroblasts to create extracellular matrix deposition and neovascularization. The aim of this study is the assessment of the topical use of autologous platelet-rich fibrin (PRF) in the improvement of myringoplasty success rate.

**Results:** Patients were divided to two groups, group A included 20 patients who were submitted to myringoplasty operation with adding of PRF from the same patient, and group B included 20 patients who were submitted to myringoplasty operation without adding of PRF. At 6 months postoperatively, the success rate (graft taking) in case group A (95%) was significantly higher than in the control group (70%) (*P* value = 0.037). Success in terms of hearing gain of the air-bone gap was more than 10 dB achieved in 19 patients (95%) in case group A, and 14 patients (70%) in control group B were with a statistically non-significant difference (*P* value = 0.079). There was no effect of PRF use on hearing gain in graft-taken cases because hearing gain is related to the closure of TM.

**Conclusion:** Topical PRF application over tragal perichondreal graft during myringoplasty is successful, safe, and highly efficient with no complications. PRF improves healing of chronic TM perforations and prevents postoperative infection.

**Keywords:** Trans-canal, Endoscopic, Myringoplasty, PRF, Tragal perichondrium

# **Background**

Chronic suppurative otitis media is a chronic inflammation which involves the mucoperiosteal lining of the middle ear cleft characterized by chronic ear discharge due to recurrent middle ear infection through tympanic membrane perforation [1].

There are several trials carried out to close the tympanic membrane (TM) perforations and restore hearing loss. These procedures include the use of different graft materials, such as fat, perichondrium, temporalis fascia, and synthetic materials [2].

Platelets are rich in growth factors which stimulate extracellular matrix deposition and neovascularization. Plasma contains many factors including nutrients, vitamins, hormones, electrolytes, growth factors, and proteins that are essential for cell life and tissue healing [3, 4].

Platelet-rich plasma (PRP) has a major role in current tissue engineering and cellular therapy [5].

Clinical research indicates that PRF (platelet-rich fibrin) is the second generation of platelet concentrates which play an important role to enhance wound healing and homeostasis in both soft and hard tissue wounds [6, 7].

The myringoplasty has success rate which may reach 22% [8] or more up to 40% in adults and 65% in children [9]. Therefore, the search for methods is still needed to

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increase tympanic membrane (TM) healing after myringoplasty and its success rate [10].

#### Aim of the work

The aim of this study is to assess the effectiveness of the addition of PRF to the graft in endoscopic trans-canal myringoplasty to enhance healing and improve the success rate of myringoplasty.

#### Methods

This prospective case control study was conducted on 40 patients, presented with dry central TM perforation caused by tubotympanic chronic suppurative otitis media (CSOM). All of them were submitted to endoscopic trans-canal (trans-perforation) myringoplasty under local anesthesia using a tragal perichondrium graft using a 0° lens (9-cm long, 2.7-mm wide) connected to a camera, cable, light source, and video monitoring system.

#### Inclusion criteria

- 1. Patients had tubotympanic type of CSOM with dry central TM perforation at least for 3 months before surgery.
- 2. Patients with air-bone gap (ABG) of less than or equal to 30 dB to exclude ossicular disruption

# **Exclusion criteria**

- 1. Patients presented with active discharging central perforation
- 2. Patients with atticoantral disease
- 3. Patients with air-bone gap more than 40 dB that suspect presence of ossicular disconnection.
- 4. Recurrent TM perforation

Patients were divided to two groups: group A included 20 patients who were submitted to myringoplasty operation with adding of PRF from the same patient, and group B included 20 patients who were submitted to myringoplasty operation without adding of PRF.

# Preoperative assessment

Full history was taken from all patients; general and local examination, including otoscopy and microscopy to detect the size of perforation, were done for all patients. The sizes of tympanic membrane perforations (TMP) according to the Saliba classification [4] are defined as: "small," which is a perforation less than 25% of the diameter of the TM. Medium is a perforation of more than 25% and less than 50% of the diameter of the TM. Large is a perforation of more than 50% and less than

75% of the diameter of the TM. Total is more than 75% of the diameter of the TMP.

The audiological evaluation was done for all patients in the form of pure tone audiometry at the speech frequencies 500, 1000, and 2000 Hz, and the average airbone gap [ABG] in those frequencies was recorded. Also, preoperative laboratory tests including CBC, ESR, and coagulation profile were done to look for any contraindications to PRP use.

# Preparation of the autologous PRF

The required quantity of blood (usually 10–12 ml) was taken from the patient's peripheral vein. The collected blood is transferred into sterile glass tube (without anticoagulants) and immediately centrifuged at 3000 rpm for 10 min in a (Zhengji 800-centrifuge, China). After centrifugation of the blood, it was separated out into 3 layers according to the density of its components. The lower layer consists of red blood cells, the middle layer consists of PRF clot, and the upper one is a thin layer of supernatant plasma (platelet-poor plasma [PPP] (Figs. 1 and 2).

The success of this technique depends on rapidly taking blood and rapidly transferring it to the centrifugation. Also we noticed that without addition of anticoagulant, the blood sample starts to coagulate within few minutes upon contact with the tube glass to concentrate fibrinogen in the upper and the middle part of the tube.

### Operative technique

Under local anesthesia, the endoscopic trans-canal (trans-perforation) myringoplasty was done using a tragal perichondrium graft in all cases.

Pre-operatively, we divided TM perforations into four quadrants according to the Saliba classification (small, moderate, and large perforation). A small tragal skin incision 2 mm was done below the dome of the tragus,



Fig. 1 Separation of the blood into three layers in the test tube



Fig. 2 The PRF clot after centrifugation

and the tragal perichondrium graft was taken carefully for all cases; the edge of TM perforation was refreshed using the needle. The piece of gelfoam was inserted inside the middle ear to prevent medialization of the graft; there was no need for raising of tympanomeatal flap; the tragal perichondrial graft was placed on the undersurface of the TM through the perforation and adjusted in its place under the handle of the malleus (Fig. 3).

In group A after adjustment of the graft in its place, the PRF clot was put on the lateral surface of the graft and TM remnant; then, gelfoam was put into the external auditory canal (EAC) (Fig. 4).

In group B, gelfoam was put on the lateral surface of the graft and TM remnant in EAC without PRF; then, gelfoam was put into the external auditory canal (EAC).

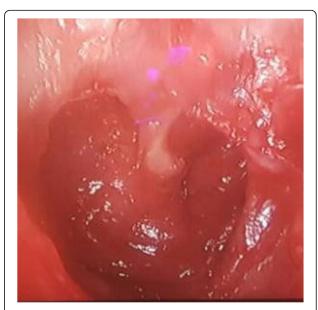
In both groups, an outer EAC pack was left.

All patients were instructed to avoid blowing their nose at 1 month postoperatively at least. Also, they were instructed to avoid wetting of the ear and to keep it dry.

There was no tympanomeatal flap elevation with no risk for granulation tissue formation; also, there was no post-aural incision and therefore no need for postoperative wound care with risk for neither inflammation nor keloid formation.

## Postoperative evaluation

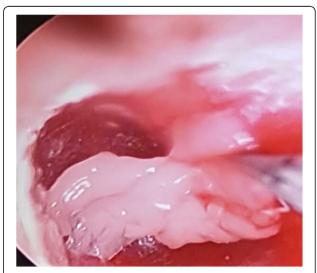
Postoperative evaluation of the graft was performed weekly at the first month and then once monthly until



 ${\bf Fig.~3}$  Adjustment of the graft under handle of the malleus and remnant of TM

the 6th month. The clinical assessment postoperatively included the TM healing, the presence of ear discharge or any granulation tissues, development of complications, and subjective hearing improvement. The closure of TM perforation occurs at 3 weeks to 3 months postoperatively.

Postoperative hearing evaluation by PTA was done by the end of the 3rd and 6th months. We used the postoperative ABG as the parameter for the hearing evaluation. We also calculated the average PTA increase. Success as regard hearing was considered if there was an



**Fig. 4** Putting of PRF clot over the graft after adjustment of the graft in its place under the handle of malleus

improvement in the ABG of 10 dB or more, 6 months postoperatively.

#### Results

Forty patients (18 males and 22 females) involved in this study had central TM perforations and were submitted to endoscopic trans-canal (trans-perforation) myringoplasty, under local anesthesia in all cases. Patients were divided into group A which included 20 patients who underwent endoscopic trans-canal myringoplasty using tragal perichondrium graft and autologous PRF and group B which included 20 patients who underwent endoscopic trans-canal myringoplasty using tragal perichondrium graft alone without the use of autologous PRF.

The mean age of the patients in group A was 33.15  $\pm$  6.459 years and 29.90  $\pm$  6.648 years in group B, with a statistically non-significant difference (P = 0.125) (Table 1).

The size of TM perforation in group A (with PRF) was small in 8 cases (40%), medium in 7 cases (35%), and large in 5 cases (25%) while the size of TM perforation in group B (without PRF) was small in 5 cases (25%), medium in 8 cases (40%), and large in 7 cases (35%) with a statistically non-significant difference (P = 0.579, Table 2).

The criteria of success are based on the complete closure of the TM. There was a statistically significant success rate achieved in patients of group A (with PRF) where 19 cases (95.0%) showed healed graft and one case (5%) showed a residual TM perforation, while in group B (without PRF), 14 cases (70%) showed healed graft and 6 cases (30.0%) showed residual TM perforation with statistically significant difference (P = 0.037, Table 3).

In group A, the unsuccessful case was a large size, and the cause of failure was on the second week postoperatively due to upper respiratory tract infection and severe irritative cough that led to dislodgment of the graft from its place and non-touching the edge of perforation, and lastly, on the fourth week, medialization of a part of the graft despite gelfoam inserted inside the middle ear and the healing occurred in a part of the perforation and failed in the other part, so the perforation was changed from large size to medium size but not closed.

In group B, the unsuccessful cases were 6 cases, two cases had medium-sized perforations, and four cases had large-sized perforations. The cause of failure in these six cases was in the second week postoperatively due to infection of the graft followed by otitis media and ear discharge not responding to medical treatment. In the third week, medialization of the graft occurred in all patients, so the healing occurred in a part of the perforation and failed in the other part. So the perforation was changed from large size to medium and small size but not closed.

As regards the postoperative hearing gain, it found the following.

The preoperative mean  $\pm$  SD of air-bone gap (ABG) in group A was 28  $\pm$  8.335 and 25.05  $\pm$  6.143 in group B without significant difference (P = .210), while the post-operative mean  $\pm$  SD of ABG was 12.22  $\pm$  3.524 in group A and 12.31  $\pm$  4.837 in group B without statistical significant difference between the 2 groups (P = 0.955). The mean  $\pm$  SD hearing gain was 14.44  $\pm$  4.501 in group A and was 11.69  $\pm$  3.119 in group B (Table 4).

There was no statistically significant difference between the two groups regarding the pre-operative and post-operative A-B gap and hearing gain. So, the hearing gain in graft-taken cases was not affected by PRF use as the hearing gain is related to closure of TM.

As regards complications, there was no graft lateralization or retraction pocket observed during the period of follow-up. Also, the postoperative complications as SNHL, tympano-sclerosis, or chalky patches were not observed. In case group, no infection was reported while in control group, six cases developed postoperative otorrhea that was caused by middle ear infection, these six cases were given local and systemic antibiotics, and the infection was controlled by medical treatment; the rate of infection in control group (12.5%) was significantly higher than in the case group (P < 0.037).

#### **Discussion**

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 [11, 12]. PRF as a carrier of growth factors which stimulate

Table 1 Comparison between the study groups regarding demographic data

			Group A (graft with PRF)	Group B (graft without PRF)	χ²	P value
Sex	Male	No.	8	10	.404	.525
		%	40.0%	50.0%		
	Female	No.	12	10		
		%	60.0%	50.0%		
Age (years)	Mean ± SD		33.15 ± 6.459	29.90 ± 6.648	1.568	0.125

Table 2 Comparison between group A and group B regarding the size of perforation

			Group A (graft with PRF)	Group B (graft without PRF)	χ²	P value
Size of perforation	Small	No.	8	5	1.092	.579
		%	40.0%	25.0%		
	Medium	No.	7	8		
		%	35.0%	40.0%		
	Large	No.	5	7		
		%	25.0%	35.0%		

There was no statistically significant difference between group A and group B regarding the size of the perforation.

extracellular matrix deposition and neovascularization. Plasma contains many factors including nutrients, vitamins, hormones, electrolytes, growth factors, and proteins that are essential for cell life and tissue healing [13]. The autologous PRF is simple and easy to be prepared without reported side effects [14, 15].

In the present study, it was found that the application of PRF makes chronic TM perforation heal more efficiently than the use of gelfoam alone. This is evident in this study; no postoperative infection was observed in the case group (with PRF). Bielecki et al. [16] and Tate and Crane [17] proved that high concentrations of WBCs in PRF make it act as a bactericidal.

In 2009, Erkilet et al. reported that PRF is effective in speeding up the healing of the perforated TMs in rats and making the healing period shorter. Therefore, they suggested that PRF might be effective in humans as it is an autologous material [18].

In the study of El-Anwar et al., success rate of closure of tympanic membrane was 100% with PRP in 32 patients while in control group, success rate of tympanic membrane with gelfoam was 32 (81%) patients. Also, El-Anwar et al., described a myringoplasty under general anesthesia using autologous platelet-rich plasma (PRP) with perichondrium graft. They do tympanoplasty operation under general anesthesia using autologous platelet-rich plasma (PRP) and gelfoam for 64 patients using perichondrium graft; then, they used the PRP as dressing lateral to perforated tympanic membrane and they compared it with another group where they used gelfoam as dressing [19].

In 2016, Gur et al. published a study to assess the effects of using PRF membrane in repairing the traumatic

TM perforations and to compare the results of using a PRF membrane with the paper patch technique. The closure was achieved in 28 (93%) perforations in group 1 and 25 (83%) perforations in group 2 which is consistent with this study [20].

Kaur reported that PRF aids in the initial stability of the grafted tissue at the recipient sites. PRF allows rapid vascularization of the healing tissue by delivering growth factors that induce regeneration. The regeneration occurred due to super-saturation of the wound with PRF, growth factors [21].

Autologous PRF is safe and effective in promoting natural processes of wound healing and graft taking. So, topical application of autologous PRF during myringoplasty is safe, more efficient, and successful. Autologous PRF not only improves the healing of chronic TM perforations but also avoids infection in EAC and postoperative discharge. Therefore, it is recommended to use the topical PRF during myringoplasty, and further studies will be needed to prove its healing effect especially in immunecompromised patients as in patients with diabetes mellitus. Also, at the cellular level, healing effect of PRF on different layers of the TM is needed to be studied.

# **Conclusion**

Platelet-rich fibrin (PRF) application during myringoplasty is safe and has high success rate with no complications. PRF increased healing rate of chronic TM perforations and also prevent infection of the graft with good results.

Topical autologous PRF application during myringoplasty is highly successful with no reported postoperative infections and minimal morbidity. It accelerates TM

Table 3 Comparison between group A and group B regarding the healing of the graft

			Group A (graft with PRF	Group B (graft without PRF)	X <sup>2</sup>	P value
Healing of graft	Healed	No.	19	14	4.32	.037
		%	95.0%	70.0%		
	Not healed	No.	1	6		
		%	5.0%	30.0%		

Table 4 Comparison between group A and group B regarding preoperative ABG, postoperative ABG, and A-B gain

		Group A (graft with PRF)	Group B (graft without PRF)	t test	P value
Pre-operation A-B gap	$\textbf{Mean} \pm \textbf{SD}$	28 ± 8.335	25.05 ± 6.143	1.274	.210
Post-operation A-B gap	$\textbf{Mean} \pm \textbf{SD}$	12.22 ± 3.524	12.31 ± 4.837	057-	.955
A-B gain	$\textbf{Mean} \pm \textbf{SD}$	14.44 ± 4.501	11.69 ± 3.119	1.890	.068

closure following myringoplasty and prevents graft displacement. It not only enhances the healing of the graft but also protects it from infection.

Therefore, it is recommended to use topical PRF during myringoplasty, and further studies will be needed to prove its healing effect especially in immune-compromised patients as with diabetes mellitus. Also, at the cellular level, healing effect of PRF on different layers of the TM is needed to be studied.

#### Abbreviations

TM: Tympanic membrane; PRP: Platelet-rich plasma; CSOM: Chronic suppurative otitis media; PRF: Platelet-rich fibrin; ABG: Air-bone gap; PPP: Platelet poor plasma; TMP: Tympanic membrane perforation; EAC: External auditory canal

#### Acknowledgements

Not applicable

#### Authors' contributions

All authors contributed to the study conception and design. Material preparation and data collection and analysis were performed by MK and M EL. The centrifugation of blood was separated out into three layers; this laboratory part of the study was performed by NA. The surgical operation was done by MK and M EL. The first draft of the manuscript was written by MK and all authors commented on the previous versions of the manuscript. The authors read and approved the final manuscript.

#### **Funding**

None

#### Availability of data and materials

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

#### Ethics approval and consent to participate

The ethical committee of Faculty of Medicine, Alazhar University, Cairo Egypt, approved this work, and informed written consent was obtained from all participants (reference committee number is not available).

#### Consent for publication

Not applicable.

#### **Competing interests**

The authors declare that they have no competing interests.

Received: 24 July 2020 Accepted: 5 January 2021 Published online: 05 February 2021

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