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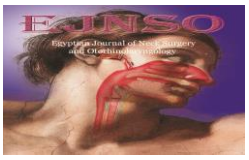

Efficacy of platelet rich plasma on graft uptake in myringoplasty

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Abstract:

Background: The purpose of this research is to compare the effectiveness of platelet-rich plasma (PRP) with conventional temporalis fascia myringoplasty in the treatment of medium-sized central perforations in the central tympanic membrane (TM). This study was designed as a randomized control trial.

Patients and methods: We used a retro-auricular approach underlay graft employing temporalis fascia to perform myringoplasty on fifty-two patients with chronic otitis media (COM) mucosal-type, medium-sized central TM perforation, and conductive hearing loss. We randomly assigned these patients to either with PRP or without PRP procedures.

Results; Graft uptake, or an intact TM, was the main result six weeks after surgery. The analysis includes 52 myringoplasties (control group-26 patients, intervention group-26 patients) performed on 52 patients (34 males and 18 females, ages 25–47). Graft uptake rates were 92.3% in the intervention and 84.6% in control group) six weeks after surgery. Graft uptake did not differ statistically significantly between the two groups (P value = 0.418). Both groups experienced comparable postoperative complications.

Conclusions: Graft-uptake in the intervention group and problems were comparable to those of control group. When it comes to treating TM perforation, intervention group has no advantages over the control group.

Keywords: Platelet-rich plasma, myringoplasty, chronic otitis media, and temporalis fascia

Introduction

Myringoplasty, a surgical treatment to reconstruct the tympanic membrane (TM) perforation, is used to have dry ears and restore hearing loss. [1] Autologous temporalis fascia is the most often utilized graft material. [2] Typically, we use the healing of the perforation and hearing improvement to evaluate the effectiveness of myringoplasty. [1,3]

Using the temporalis fascia for myringoplasty has a failure rate of 26% to 44% in adults and can go as high as 65% in children. The elevated failure rate requires the incorporation of supplementary materials to enhance surgical outcomes. [4-5]

Autologous PRP is one such substance that myringoplasty can use. Tissue engineering and cellular therapy both use PRP, a cutting-edge biotechnology. [6] It is safe to use and somewhat intrusive. Centrifuging whole blood yields PRP, which contains autologous growth factors (GFs) like insulin-like growth factor-I (IGF-I), platelet-derived growth factor (PDGF), and transforming growth factor-b (TGF-b). Speed up the regeneration of platelets and epidermal, epithelial, and endothelial tissues. You can apply it directly over the lesion, as it possesses antinociceptive, anti-inflammatory, and

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regenerative qualities. As a result, it promotes tissue recovery in chronic wounds. Additionally, PRP promotes collagen production, angiogenesis, and soft tissue repair. Additionally, it reduces skin scarring and improves hemostatic response to damage. [7]

Because of the aforementioned benefits, PRP has become more and more popular in biomedical research as well as orthopedic and dermatological treatment.[8-9] In their research, **Erkilet et al.** [10] discovered that PRP helps rats with tympanic membrane perforations mend. However, otolaryngology has restricted its application. Finding out how well PRP works to mend TM perforations and restore hearing in adults with moderate-sized to large-sized central TM perforations was the aim of this study.

The clinical trial aimed, in part, to determine whether platelet-rich plasma or standard myringoplasty was more effective in promoting graft uptake in the temporalis fascia.

The study's hypothesis is that using platelet-rich plasma improves transplant uptake.

Patients and methods:

Design of Trials

We recruited 52 patients with mucosal-type COM who met the inclusion and exclusion criteria for this double-blind, randomized control interventional study between February 2024 and August 2024 after they provided written, informed consent. This study was done after the approval of the Research Ethics Committee of the Faculty of Medicine at Ain Shams University, with registration number FMASU MS274/2024. Informed consent was obtained from the participants regarding the use of the use of PRP in the surgery.

Participants

The Head and Neck Surgery and Otorhinolaryngology Outpatient Clinic served as the recruitment site for the participants.

Criteria for Inclusion

There have been cases of mucosal-type COM with a medium central perforation and conductive hearing loss in both sexes between the ages of 25 and 47.

We classified a perforation as medium-sized if it involved roughly 50% of the tympanic membrane's pars tensa.

Criteria for Exclusion

- Squamous-type COM.
- COM with an ossicular erosion and a small central perforation
- Case history of previous ear surgery or revision.

Interventions

Clinical Assessment and investigations

We recorded tinnitus, vertigo, and hearing impairment during a thorough history of ear discharge.

We inspected TM using the otoscope. We divided the tensa-perforated parts into three sizes: small, medium (50% of the tympanic membrane), and large. The day before surgery, all patients underwent standard investigations (Blood tests, pure tone audiometry **(Figure 1)** and any other anesthesia recommendation).

Operation

Under general anesthesia, the most experienced surgeon performed microscopic myringoplasty in every instance, employing a temporalis fascia graft using the underlay technique and postauricular approach.

Patients in the control group had myringoplasty without the use of PRP, while those in the intervention group had myringoplasty with PRP. PRP-soaked gel foam pieces covered the intervention group's graft-flap assembly,

while ordinary gel foam pieces covered the control groups. We placed pieces of plain gel foam in the middle ear space in both groups.

Blinding and randomization.

We divided the patients into two groups using a straightforward randomization technique, and we used sequentially numbered, sealed, opaque envelopes to hide the allocation. We unsealed the envelopes two hours before the procedure.

Procedure for Making PRP

After tourniqueting the patient, we used an 18-gauge needle to draw 10 ml of peripheral venous blood from the antecubital vein in an ACD A vial, taking all necessary aseptic precautions. We immediately spun the collected blood in the tubes for 15 minutes at 1300 rpm using a tabletop centrifuge. The density of its internal components led to the segregation of blood into three layers: the bottom layer consisted of red blood cells, the middle layer of white blood cells (WBCs; buffy coat), platelet-rich plasma was directly above it, and the top layer contained platelet-deficient plasma Figure (2).

Post-operative Care

Amoxicillin injections were given to every patient. Every patient received clavulanic acid injections on the first day following surgery. We then switched to oral amoxicillin. We discharged the patients on the first or second postoperative day. We conducted the follow-ups six weeks later.

We used otoscopy to assess the main result, which was graft uptake. At six weeks after surgery, an undamaged TM was considered a successful graft uptake.

Analysis of Statistics

We used IBM SPSS Statistics for Windows version 27 (IBM Corp., Armonk, NY, 2020) to analyze the data. We used the Shapiro-Wilk test to determine the normality of the numerical data distribution. The independent-samples t-test is used to assess intergroup differences in continuous numerical data, which are displayed as mean ± SD.

We use Fisher's exact test to compare differences between counts (%) of categorical data. We use the chi-squared test to compare ordinal data for trends. We use multivariable binary logistic regression analysis to investigate the independent impact of PRP on the incidence of full graft uptake after controlling for pertinent baseline factors. A two-sided P value is deemed statistically significant if it is less than .05.

Results

We included fifty-two patients scheduled for myringoplasty from February to August of 2024. The analysis included fifty-two myringoplasties performed on fifty-two patients (n = 26 in the intervention group and another 26 in the control group). Each patient underwent surgery on one side; in cases of bilateral diseased ear, the surgeon selected the ear with the most significant hearing loss for surgery.

We monitored the patients for six weeks following surgery.

Baseline demographics and clinical features

Table 1 displays the baseline demographic and clinical features. There were no statistically significant differences between the two groups.

2. **Analysis of results**

A. Uptake of Graft

We evaluated post-operative graft uptake using an otoscope. The intact neo-tympanic membrane was considered a sign of successful transplant uptake. Remaining perforations were regarded as failures.

Graft uptake rates were 92.3% in the group B and 84.6% in the group A six weeks after surgery. The two groups' graft uptake did not differ statistically significantly (P value = 0.418) (Table 2, Fig. 3, 4).

B. **Complications following surgery**

Intraoperative and postoperative infection, hematoma, sensory neural hearing loss, facial nerve palsy, changed taste perception, vomiting, vertigo, tinnitus, and length of hospital stay did not significantly differ between the two groups (Table 3

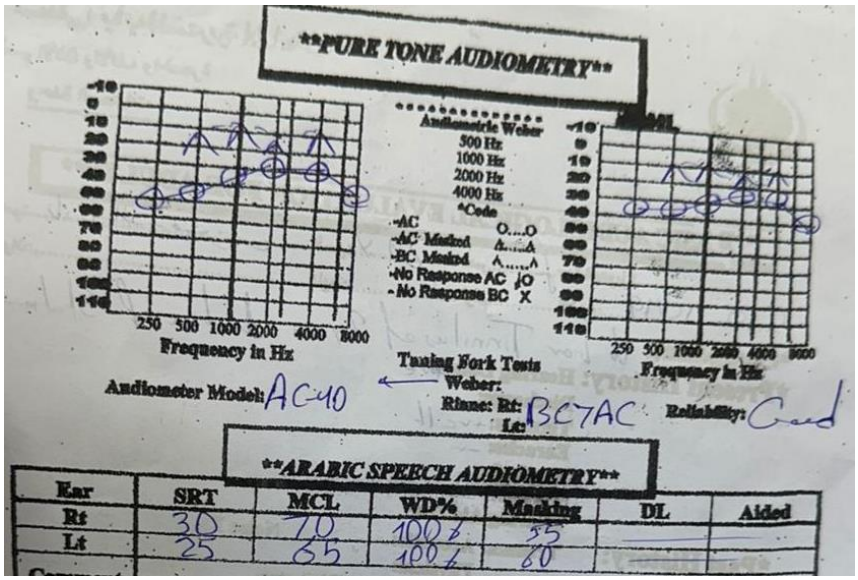

Figure 1: preoperative audiogram for a patient with bilateral COM

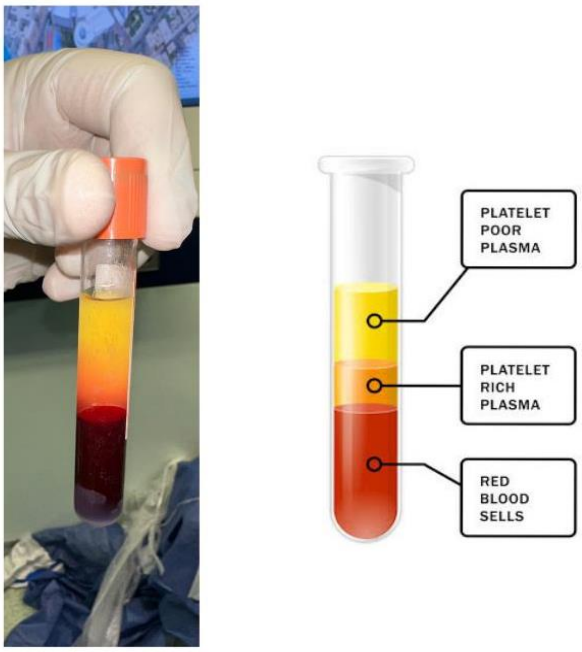

Figure (2) 3 layers of PRP preparation

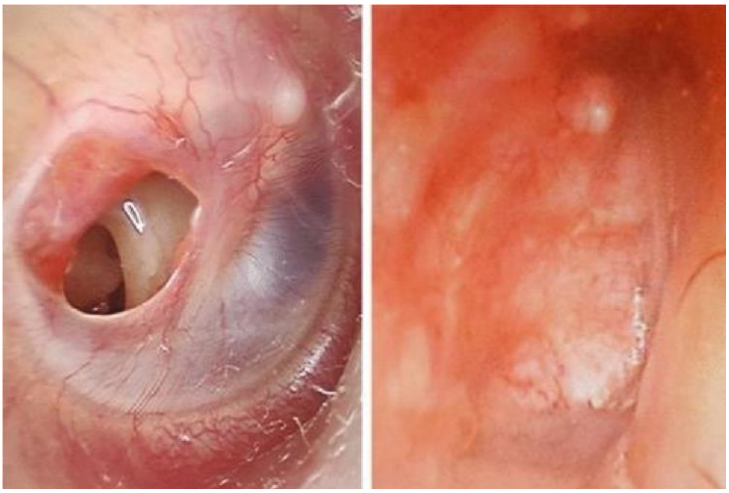

Figure (3): Pre and post myringoplasty of one of the cases in the PRP group

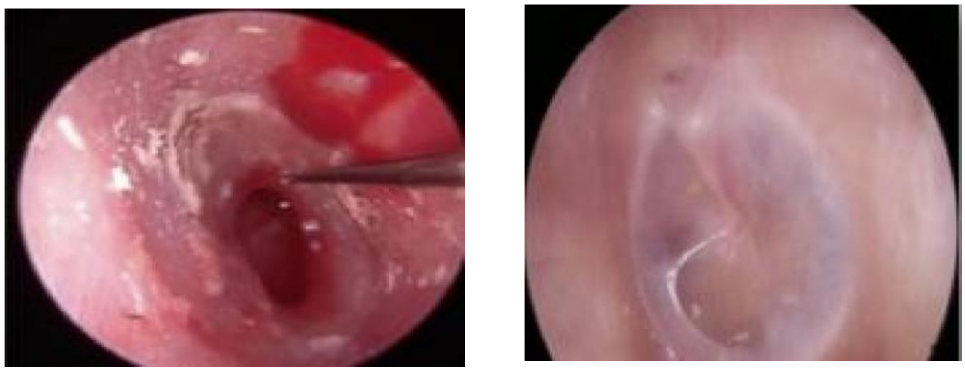

Figure 4: During the operation of myringoplasty and 6 weeks post-operative follow up another case (PRP group)

Table (1): Comparison between PRP vs Control group regarding age, sex, operated side and main presenting symptom

Variable	**PRP group (N=26)**	**Control group (N+26)**	**P value†**
Age (yr)	36.5 ± 11.0	36.0 ± 11.5	.892‡
Sex			.771
F	8 (30.8%)	10 (38.5%)	
M	18 (69.2%)	16 (61.5%)	
Operated side			.782
Left	12 (46.2%)	14 (53.8%)	
Right	14 (53.8%)	12 (46.2%)	
Main presenting symptom			>.999
Hearing loss	14 (53.8%)	14 (53.8%)	
Ear discharge	12 (46.2%)	12 (46.2%)	

Data are mean ± SD or number (%).
†. Fisher's exact test unless otherwise indicated.
‡. Independent-samples t-test.

Table (2): Graft uptake at 6 weeks after surgery in both study groups

Variable	PRP group (N=26)	Control group (N=26)	P value†
Graft uptake at 6 weeks			.418
Failed uptake	1 (3.8%)	2 (7.7%)	
Incomplete uptake	1 (3.8%)	2 (7.7%)	
Complete uptake	24 (92.3%)	22 (84.6%)	

Data are number (%).
†. Chi-squared test for trend.

Table (3): Complications seen in control group and intervention group

Variable	PRP group (N=26)	Control group (N=26)	P value†
SNHL	0	0	
Vertigo, vomiting, tinnitus	0	0	
Haematoma	0	0	
Alteration of taste	0	0	
Infection	1 (3.8%)	2 (7.7%)	>.999

Data are number (%).
†. Fisher's exact test.

Discussion:

By eliminating inflammation and restoring a healthy middle ear and undamaged TM, myringoplasty primarily attempts to restore the inner ear's ability to transmit sound. The goal of numerous studies has been to find ways to increase myringoplasty success rates.

Several authors have outlined various strategies to enhance the success rate of myringoplasty, such as the choice of graft material, the surgeon's training and expertise, among others. [11-13] This is the second randomized clinical trial that focuses on the topical application of autologous PRP in temporalis fascia myringoplasty, utilizing the underlay method via the retro-aural approach. Nonetheless, the exploration of PRP in myringoplasty for medium-sized to large-sized central tympanic membrane perforations has been addressed in a limited number of studies. [14]

Our study aimed to examine the rate of graft uptake and complications during myringoplasty with and without the use of PRP.

Myringoplasty with PRP had a success rate of 92.3%, whereas myringoplasty without PRP had a success rate of 84.6%. These findings were in line with the success rates that other authors reported in their PRP studies. [15-19] At six weeks after surgery, the intervention group's graft uptake rate was higher than the control group's (92.3% vs. 84.6%), although the difference was not statistically significant (P value = 0.418).

Platelet-derived growth factor (PDGF), transforming growth factor alpha (TGF-a), transforming growth factor beta (TGF-b), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor, and

platelet-derived angiogenesis factors are among the growth factors that may also be present in PRP.

Angiogenesis, endothelial and epithelial regeneration, collagen production, and soft tissue repair are all accelerated by these growth factors. [7] Because of all these reasons, PRP treatment may improve the healing of TM perforation. In our investigation, however, there was no statistically significant difference in the graft absorption rate between the intervention and control groups. For the closure of minor to large central TM holes, investigators have employed PRP either by itself or in combination with fat (from ear lobules), temporalis fascia, and conchal perichondrium. [15-19] According to some studies, the success rate for myringoplasty with PRP is 95% to 100%, while the control group's success rate is between 81 and 85%. [15-16,19] Additionally, they discovered that the PRP group's graft absorption rate was noticeably higher than that of the control group. [15-16,19]

Nevertheless, our study did not find a statistically significant difference in success rates between the intervention and control groups.

After myringoplasty, the stated percentage of re-perforation ranges from 26 to 44%. [4-5] Monitoring patients for a longer period of time (10 years) makes re-perforation more noticeable. [20] For myringoplasty to be successful, good surgical technique is necessary.

For myringoplasty to be successful, the surgical procedure must be flawless and followed precisely at every stage. [21] We should use better surgical techniques to increase the success rate, as a technical error could lead to a failed myringoplasty in the immediate postoperative period. [22]

Several studies linked infection to delayed graft failure in 10.5% to 13% of cases, but did not link it to early failures. [22-23] Three individuals (11.5%) in our study had postoperative discharge and infection. Upon follow-up six weeks later, all of them displayed persistent perforations. Research by **MacKinnon**, [24] found that recurrent suppurative otitis media that failed myringoplasty was not related to an inadequate eustachian tube function or a long time without discharge before myringoplasty.

Otoscopically, several patients showed discharge with an intact graft. This could be the result of a minor defect in the repaired neotympanum that is not clinically detectable. [25] Another condition that could contribute to graft failure is avascular necrosis of the graft, which can result from a decline in the vascular supply from the neotympanum's perimeter. [25] Numerous studies have demonstrated that this type of graft atrophy, which lowers the success rate, accounts for 32–40% of transplant failures. [22,24]

Bilateral disease may also impact the success of graft uptake. Clinical examination revealed bilateral illness in one intervention group case and one control group case with residual perforation. It is possible that this observation indicates the presence of bilateral eustachian tube dysfunction.

It is believed that myringoplasty is a safe operation. One of the many problems that can happen after myringoplasty is infections, loss of sensorineural hearing, damage to the chorda tympani nerve, facial nerve paresis, external auditory canal stenosis, perichondritis, neotympanic membrane retraction, and tinnitus.

In our study, two patients (7.7%) in the control group and one patient (3.8%) in the study group had infection and postoperative ear discharge. Because PRP has a larger concentration of WBCs, which makes it bactericidal, the infection rate was lower in the PRP group. According to **El-Anwar et al.** [19] ,

the control group had a noticeably greater infection rate (12.5%) than the PRP group.

Conclusion

Although autologous PRP has no serious side effects when used for myringoplasty, our investigation showed that its impact on graft uptake was not statistically different from that of the group without PRP.

When compared to the control group, the PRP group's low postoperative infection prevalence was not statistically significant. It might take a large multicentric randomized controlled trial with a longer follow-up period to prove that PRP has a positive impact on myringoplasty.

Limitations and Suggestions

The current investigation involved 52 patients, with 26 in each group, and monitored the cases for six weeks. As a result, there was no statistically significant way to determine the impact of PRP use in myringoplasty on graft uptake rate (healing of the TM), complications, or any potential advantages of PRP. Therefore, we recommend a large-scale trial with a lengthy follow-up period to illustrate the advantages and disadvantages of employing PRP in myringoplasty.

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Conflicts of interest: No

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