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Type 1 Tympanoplasty: Conventional Microscopic Technique versus Platelet Gel Technique: A Retrospective Study

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Abstract*— Introduction:** *Type 1 tympanoplasty is indicated to repair tympanic membrane perforation in patients affected by hearing loss. The conventional surgical approach includes endomeatal, endaural and post-auricular routes, using different types of graft. Growth factors are present in platelets and promote physiological healing of damaged tissues. We investigated the outcomes of conventional microscopic technique to type 1 tympanoplasty versus platelet gel technique in tympanic membrane perforations. Considering platelet gel improves soft tissues' healing, the aim of the current study was to evaluate the efficacy of platelet gel application in patients with a damage of a particular soft tissue, as tympanic membrane.* ***Methods*: We retrospectively analyzed record charts of 36 patients with a diagnosis of tympanic membrane perforation and who undergone to a type 1 tympanoplasty between April 2012 and September 2013. During the reconstructive phase 22 patients were treated with a conventional surgical approach, while 14 patients were treated with a platelet gel as an outpatients treatment.* ***Results****: Compared to type 1 conventional tympanoplasty alone, the type 1 tympanoplasty with platelet gel application was no statistically significant in terms of tympanic index closure. Compared to surgery alone, we report a faster recovery for the group treated with platelet gel as outpatients procedure.* ***Conclusions****: Platelet gel application in otosurgery is a non invasive, safe and outpatients technique to restore tympanic perforation. However, further prospective data are needed to confirm these preliminary results.*

***Keywords*—** *Outpatient treatment, Platelet gel, Tympanic membrane perforation, Tympanoplasty.*

I. INTRODUCTION

Tympanic membrane (TM) perforation is the most frequently cause of conductive hearing loss; in such cases, the integrity must be re-established in order to restore hearing and to protect the middle and inner-ear's structures from external harmful (Figure 1). The TM perforations are commonly treated with various surgical approaches as type 1 tympanoplasty, aimed to restore hearing ability as well as to prevent recurrent infections. The conventional surgery includes endomeatal, endaural and post-auricular route, with a different outcome depending on the size and site of perforation (for example, the anterior perforations are characterized by a worse outcome). A surgical technique using either underlay or overlay of grafts over the perforated TM has been employed: the underlay is widely used and relative simple to perform.

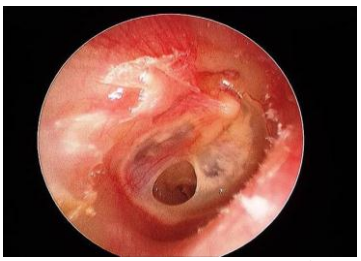

Fig. 1. Small tympanic membrane perforation.

Different TM reconstruction techniques for tympanoplasty using different types of grafts, including *temporalis fascia*, which have better functional outcome with respect to hearing, but contributes to residual perforation following tympanoplasty, particularly in large TM perforations.

In the last few years, new less invasive treatments are developed, as the use of growth factors to promote physiological healing of damaged tissues. This is a process that aim to restore tissue metabolism and function, as the activation of fibroblast's anabolic function by influence of small biologically active proteins, belonging to cytokine's family. This proteins can be produced and stored by multiple tissues and cells, as platelets. The main actors in this process are: PDGF (*platelet-derived growth factor*), VEGF (*vascular endothelial growth factor*), FGF (*fibroblast growth factor*), TGF (*transforming growth factor*), EGF (*epidermal growth factor*), TGF (*transforming growth factor*). PDGF stimulates cell proliferation, collagen synthesis, and fibroblast chemotaxis; VEGF is a prime regulator of angiogenesis and vasculogenesis; EGF promotes keratinocyte's production and matrix formation; TGF controls cell proliferation and differentiation, has intrinsic inflammatory ability and induces extracellular matrix deposition and tissue repair. Platelet gel is obtained by blood extraction and manipulation, with the aim to obtain the platelets' degranulation and proteins release.

This study evaluates the outcome of type 1 tympanoplasty based on TM perforation and hearing improvement using the conventional surgery (type 1 tympanoplasty with *temporalis fascia*) versus type 1 tympanoplasty with application of platelet gel.

II. PATIENTS AND METHODS

This study is a retrospective review of all patients undergoing middle-ear reconstructive surgery (type 1

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tympanoplasty) at S. Maria del Carmine Hospital, Rovereto (TN, Italy) from April 2012 to September 2013, and is promoted by Immunohematology and Transfusion Medicine Service (SITM) and Otolaryngology Department. Thirty-six tympanic membrane perforation were evaluated using medical records. Data were obtained from the clinical records of patients who had been followed-up for a minimum of three months after surgery. Informations retrieved by the investigator from the medical records included site of perforation, sex (female/male), age (18-78 years), medications (antiplatelet drugs) and comorbidity (active neoplastic, autoimmune disease, active infection, coagulopathy, anemia with haemoglobin < 100 g/L or thrombocytopenia with platelet count < 150 x 10^9/L). Patients lost to follow-up before healing was completed, were excluded from the study. The procedure was explained thoroughly to all patients and authorized by a signed informed consent form.

TM were evaluated regarding surgical technique, followed for three months to compare the outcome of different surgical options regarding healing of TM (tympanic index closure, %) and complications (infection) for each group. In addition, we compared recovery time after surgery (days required for removal of surgical dressing).

All patients were allocated into two groups: the first (Group A) included twenty-two patients and was considered as the control group; they were treated according to the best practice guidelines, by surgical microscopic technique type 1 tympanoplasty. The second group (Group B) included fourteen patients, considered the study group and was treated with platelet gel, which was applied during surgery (type 1 tympanoplasty with platelet gel).

Surgical conventional technique: type 1 tympanoplasty.

Behind the ear, a small incision was made after infiltration of the area where the graft was to harvested using Bupivacaine hydrochloride 5 mg/ml with Adrenaline 1 mg/ml. Then, a vascular-strip is prepared. The fat is gently separated by blunt dissection to reveal the *temporalis fascia*, and so the graft is harvested. The fat and loose connective tissues from both sides of the *fascia lata* were then removed: the graft is now ready for final placement. Into the tympanic cavity were placed swabs of modified haemostatic gelatine (*Gelita*®, Braun, Melsungen, Germany). The incision was closed with a 2/0 nylon/silk suture and the dressing was put in place. The stitch was usually removed on the seventh day after surgery and the wound usually healed without any morbidity.

Surgical non conventional technique: type 1 tympanoplasty with platelet gel.

Platelet gel is obtained by extracting 50 mL of autologous peripheral whole blood, that's immediately processed at room temperature in a dedicated device Angel System (*Arthrex, Angel ™ System*, Arthrex Inc., Naples, Florida – USA). Whole blood underwent two consecutive centrifugations as standard protocol (hematocrit 7%) to produce 2 mL of platelet-rich plasma (PRP). The thrombin fraction is then produced from platel-poor plasma (PPP) with another dedicated kit (*Arthrex ActivAT*, Arthrex Inc, Naples, Florida – USA) that enables the extraction of autologous thrombin from PPP: when added to the harvested PRP, thrombin activates the coagulation's cascade inducing platelets' degranulation; finally, the supernatant containing thrombin precursor, was ready to activate PRP into platelet gel at the patient's bedside by adding the platelet concentrate to 2 mL of activated thrombin and initiating the formation of the fibrin matrix. The solution thus obtained was mixed gently and left to rest for 10-15 minutes at room temperature until the platelet gel was formed, appeared as a gelatinous disc in a sterile 3.5-cm plastic dish. Use of the platelet gel may improve the release of growth factors at the application site over a period of several days. Then a cotton soaked in anesthetic was placed on TM and into the external ear canal for a time of 25-30 minutes. Finally, some swabs of modified hemostatic gelatine (*Gelita*®, Braun, Melsungen, Germany) were dipped into the PRP for 3 minutes and then placed into tympanic cavity with a membrane of bovine collagen (*Tutopatch*®, Tutogen Medical, Bavaria, Germany). The cotton was usually removed on the fifth day after surgery and the wound usually healed without any morbidity.

Statistical Analysis

A statistical analysis was performed using the Fisher exact test to evaluate the statistical value of different surgical technique on tympanic index closure (% of closure).

III. RESULTS

Over a period of seventeen months we retrospectively analized all patients with tympanic membrane perforation (thirty-six patients), allocated into two different groups based on surgical technique (conventional microscopic versus platelet gel technique). In Table I we describe clinical baseline characteristics of all patients.

A not statistically significant difference between conventional treatment and platelet gel technique was observed using Fisher exact test (p value = 0.0637). Compared to type 1 conventional tympanoplasty (surgery, Group A), the type 1 tympanoplasty with platelet gel (outpatient treatment, Group B) was not statistically significant in term of tympanic index closure. In the group A we obtained 21/22 total closures of tympanic membrane perforation (95.4%), while in the group B we obtained 10/14 closures (71.4%).

However, compared to surgery alone (Group A) we reported a faster recovery for the group treated with platelet gel as an outpatient procedure (Group B): a complete closure was achieved after 7 days in the control group (Group A) versus 5 days in the platelet gel group (Group B).

No adverse reactions to used platelet gel were observed.

TABLE I. Clinical baseline characteristics of included patients.

	Clinical baseline characteristic of patients. N=36.	
	Group A (N=22)	**Group B (N=14)**
1. Age (years), mean (SD)	52.4 ± 16.61 (19-78)	47.4 = 11.35 (30-68)
2. Sex (F/M)	F 10/22 M 12/22	F 7/14 M 7/14
3. Site of TM perforation	Right 8/22 Left 14/22	Right 7/14 Left 7/14

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The data of outcomes of both groups were presented in Table II.

TABLE II. Data of outcomes in type 1 tympanoplasty with surgical conventional technique (Group A) and type 1 tympanoplasty with platelet gel technique (Group B).

Group	**Data of outcomes in both groups. N=36.**	
	Tympanic index closure (% of total)	**Recovery time after surgery (days)**
A (Surgery) N=22	21/22 (95.4%)	7 days
B (Platelet Gel) N=14	10/14 (71.4%)	5 days

IV. DISCUSSION

We used freshly prepared autologous platelet gel activated by thrombin from PRP, which provide > 5 folds of platelet level in the patient's circulating blood. The used technique for PRP and platelet gel preparation takes from 30 to 60 minutes and is simple, so it can be practically carried out as an outpatient procedure. The gel preparation procedure with a dedicated kit (*Arthrex ActivAT*, Arthrex Inc, Naples, Florida – USA) ensures a faster autologous final graft for surgeon. This can be done through separating the PRP from a whole blood donated in one session, 1 hour before surgery: fresh gel can be prepared by activating PRP bedside, in a "one time" surgery.

In the present study, by the end of three months 71.4% of the platelet gel group (Group B) showed complete healing and closure compared with 95.4% of the conventional surgery group (Group A). We observed a significant slower rate of tympanic membrane closure and healing by conventional surgery (7 days) compared to 5 days of platelet gel (Group B). This may be explained by concentration of growth factors that lead to soft tissue recovery.

In addition, we have any infections in platelet gel group (Group B) and this may suggest that the PRP concentrate may also contain other immune factors, as previously suggested by Drik Jan et al.

V. CONCLUSION

Autologous platelet-rich plasma (PRP) is the processed liquid fraction of autologous peripheral whole blood with a platelet concentration above the baseline [1]. PRP therapies have been used in almost all fields of surgery for the treatment of a variety of soft-tissue defects, most notably in the management of chronic foot ulcers and musculoskeletal disorders, with promising results for the healing capacity of the biological active proteins.

Activated platelets release many anti-inflammatory mediators that are able to modulate the microenvironment and induce anabolic/catabolic processes as cell proliferation and differentiation, with a remodeling of tissues.

These PRP characteristics have led us to evaluate the implementation of a surgical technique as type 1 tympanoplasty with platelet gel: our rationale for platelet gel application is that an injection of concentrated platelets at sites of injury as tympanic membrane perforation may initiate tissue repair by the release of many biologically active factors (growth factors, cytokines). The main advantages of platelet gel surgery include its safety and feasibility; most importantly, platelet gel is an autologous product with no known adverse effects, in contrast to the commonly used medicaments.

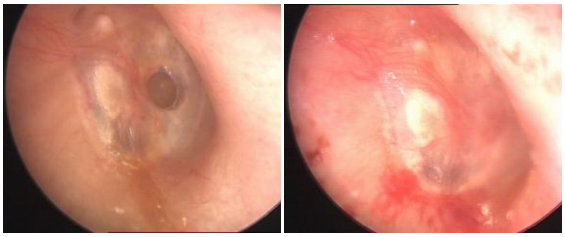

Fig. 2. Tympanic membrane closure after type 1 tympanoplasty with platelet gel.

In conclusion, this surgical technique of type 1 tympanoplasty with platelet gel is a non-invasive, safe and easy method to restore integrity of tympanic membrane after perforation, also present for more than 6 months. According to the proposed hypothesis of healing capacity of platelet gel if apposed on soft tissues, we described this effect in 10 of 14 patients (Group B). Finally, we report a faster recovery for the group treated with platelet gel as an outpatient procedure (Group B) as 5 days after surgery versus 7 days after surgery with a conventional technique (Group A).

Limitation of the study

In this study, we faced many limitations. First: the sample size was relatively small. Second: Selection of patient based on co-morbidity was performed only for Group B. Third: the study in not blinded and the surgeons decided a specific surgery; thus, this may affect the outcome.

Conflict of Interest

There are no conflict of interest.

Financial support and sponsorship

This study did not received any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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