



**CLINICAL ARTICLE**

**MACULAR HOLE RECOVERY SURGERY USING AUTOLOGOUS PLATELET RICH PLASMA**

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**Abstract**

The aim of this study was to evaluate the long-term outcomes of highly concentrated autologous platelet-rich plasma (PRP) used as an adjunct in macular hole surgery.

**Materials and methods:** 11 patients (11 eyes) were selected for surgical treatment, of which 9 patients were female and 2 males. 10 patients (10 eyes) had primary macular tears, of which 8 eyes had grade 4 and 2 eyes had grade 3 macular tears and one patient had post-traumatic macular tear. The age of patients with primary macular tear was 59-75 years, and the patient with traumatic macular tear was 32 years old.

Visiometry, tonometry, ophthalmoscopy, biomicroscopy, echography of the eyeball, and optical coherence tomography of the retina were performed on all patients before the operation and in the postoperative period.

The patients were operated under local anesthesia (2% 2ml Lidocaine and 0.75% 2ml Bupivacaine) in the following way: 25 Gauge standard pars plana vitrectomy with mandatory removal of the posterior hyaloid membrane, after which peeling of the internal limiting membrane of the retina was performed with a large volume. Platelet-rich plasma was separated under sterile conditions in the operating theatre. It was introduced into the macular hole region in the end of surgery and 8% octafluoropropane gas (C3F8) was introduced into the eye.

**Results:** There were no complications during surgery or in postoperative period. Optic coherence tomography of the macula was performed on the 7<sup>th</sup> day after surgery. In all 11 cases there was anatomical closure of the macular holes. Visual acuities were measured on days 14 and 3. On average there was an improvement in visual acuity by 2 lines according to Snellen chart, disappearance of metamorphopsia and image distortion.

During the follow up the patients during 6 month there was no development cataract, retinal tears or detachment, late endophthalmitis or any other complications.

**Conclusion:** During the surgical treatment of patients with primary and secondary macular holes the use of autologous platelet rich plasma promotes the anatomical closure of the holes, as a result of which metamorphopsias and central scotomas disappear and an increase in visual acuity is observed.

**Keywords:** macular hole, platelet rich plasma, vitrectomy

## Introduction

The inner layer of the eyeball is a layer of nerves, located between the choroid and the vitreous body and is called the retina. It includes the macula which is the central part of posterior pole and its responsible for our central vision. The retina lacks sensory innervation and this leaves its mark on the clinical picture of retinal diseases.

Macular hole is a full thickness round tear in the center of the fovea.<sup>1</sup> It is an acquired multifactorial disease that found in developed and developing countries, in people of all races and genders.

There is considerable controversy regarding the pathophysiology, natural history, and treatment of macular holes and antecedent lesions.

The pathogenesis of idiopathic age-related macular holes remains unclear despite many theories. Pseudo-macular holes can be mistaken for macular hole lesions despite careful clinical examination. Vitreous tangential traction may play a role. Cellular components surrounding the edges of the macular holes can also generate tangential traction forces and elevate the edge.

Historically, macular holes have been rare, have been associated with trauma, and have been seen in young adults. Macular hole was first described in ophthalmic literature in 1869 by Herman Knapp as a consequence of eyeball blunt trauma.<sup>2</sup>

Macular hole Due to the accompanying trauma-induced retinal pathologies, such as retinal concussion, vitreous hemorrhage, retinal hemorrhage, choroidal rupture, retinal pigment epithelium (RPE) injury, subretinal choroidal neovascularization, and fibrosis functional prognosis is often uncertain.<sup>3,4</sup>

This pathological condition causes central vision deterioration, metamorphopsia, distortion of images and central scotoma.

Macular hole can be primary or idiopathic and secondary.<sup>5</sup> In most cases it is primary as a result of abnormal vitreofoveal traction. The average prevalence of idiopathic macular hole is 3.3 per 1000: usually it is unilateral, only 10% in cases it is bilateral: the female to male ratio for idiopathic macular hole is 3:1.<sup>6,7</sup>

Risk factors macular hole can include older age, female sex, contraction of the premacular cortex of the vitreous, posterior hyaloid detachment, foveal cysts, myopia, eyeball injuries, intraocular inflammations, long term macular edema and etc.<sup>8,9</sup>

Currently optic coherence tomography of the macula is considered the main diagnosis method, which allows evaluating the diameter and height of the macular hole edges.<sup>10-12</sup> The first surgical treatment of macular hole was performed by Neil E Kelly and Robert T. Wendel.<sup>13</sup>

Vitreotomy with gas tamponade is considered an effective treatment method for this pathology, which has been the gold standard of treatment since<sup>14,15</sup> with removal of the epiretinal tissue and internal limiting membrane). Previous studies have shown a decrease in the effectiveness of vitrectomy in LMWH, especially in the absence of additional traction epiretinal components. Thus, treatment recommendations are often delayed, leading to disease progression and possible worse outcome after late initiation of therapy. Therefore, we need safer and more effective therapeutic approaches for LMWH.

Despite continuous improvement in techniques and surgical tools, extremely large and refractory macular holes still have poor surgical outcomes with current treatment standards. PRP is an alternative therapeutic approach for surgical treatment of MH, even in those of difficult management, as with myopic origin.<sup>16</sup>

Since the 1990s, platelet-rich plasma (PRP) has been described as an adjunct to macular surgery for traumatic, persistent, and recurrent full-thickness macular holes or optic disc pit maculopathy.<sup>17</sup>

The surgery using autologous platelet rich plasma technique is one of several techniques that can be used to improve the efficiency of macular hole surgery in eyes in which a previous operation has failed, or which have characteristics that make the hole difficult to close. It facilitates macular hole closure by creating an interface.<sup>18,19</sup>

A prospective method of surgical treatment macular holes is the using of autologous platelet rich plasma during surgery.<sup>20</sup>

Using of autologous platelet rich plasma in treatment of macular holes will significantly improve anatomic and functional outcomes. Platelet rich plasma is believed to enhance glial proliferation, which ensure anatomic closure of macular holes.<sup>21-23</sup>

The main component of PRP are platelets, also called platelets. These cells are a natural reservoir of many growth factors that play an important role in wound healing, such as epidermal growth factor (EGF), nerve growth factor (NGF), platelet-derived growth factor (PDGF), transforming growth factor (TGF), basic

fibroblast growth factor (bFGF) or vascular endothelial growth factor (VEGF).<sup>24</sup>

Autologous platelet rich plasma is easy to obtain and use almost free. It acts as an absorbent plug rather than a tissue glue. It does not cause inflammatory or toxic reactions. Platelet rich plasma acts as a slow-release fibrin matrix containing several growth factors and cytokines, as well as mesenchymal stem cells which promote the healing process.

Considering the prevalence of this disease, the reduction of central vision and the deterioration of quality of life the aim of our research was to develop a surgical treatment system that would allow us to restore the anatomy of the retina thereby improving central vision.

### Materials and methods

11 patients (11 eyes) were selected for surgical treatment, of which 9 patients were female and 2 males. 10 patients (10 eyes) had primary macular tears, of which 8 eyes had grade 4 and 2 eyes had grade 3 macular tears and one patient had post-traumatic macular tear. The age of patients with primary macular tear was 59-75 years, and the patient with traumatic macular tear was 32 years old.

The patients were not taking anticoagulant drugs, nor were they suffering from anemia.

Visiometry, tonometry, ophthalmoscopy, biomicroscopy, echography of the eyeball, and optical coherence tomography of the retina were performed on all patients before the operation and in the postoperative period.

### Clinical case

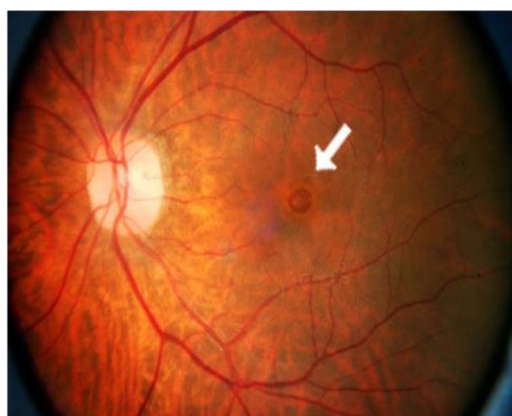


Figure 1. Optic coherence tomography (OCT) picture, posttraumatic macular hole three years old, female 32 years, visual acuity 0.1



Figure 2. Photo of the retina with macular hole

Figure 3. Optic coherence tomography (OCT) picture after surgery of the same patient from figure 1, visual acuity 0.5

### PRP preparation

The preparation of PRP followed the protocol described previously.<sup>25</sup> Whole-blood collected preoperatively (105ml) was anti-coagulated at a ratio of 1:7 and divided into its components by a special closed-circuit centrifugation procedure. In addition to platelet-poor plasma (PPP) and red blood cells (RBC), this method produced a highly concentrated PRP, which, because of the centrifugation mode, had a particularly low proportion of pro-inflammatory leukocytes compared with that obtained by the usual methods.

The patients were operated under local anesthesia (2% 2ml Lidocaine and 0.75% 2ml Bupivacaine) in the following way: 25 Gauge standard pars plana vitrectomy with mandatory removal of the posterior hyaloid membrane, after which peeling of the internal limiting membrane of the retina was performed with a large volume. Platelet-rich plasma was separated under sterile conditions in the operating theatre. It was introduced into the macular hole region in the end of surgery and 8% octafluoropropane gas (C3F8) was introduced into the eye.

To ensure good visibility of the posterior hyaloid membrane and the internal limiting membrane of the retina as stains were used triamcinolone acetonide and 0.05% Brilliant Blue G.

After the operation the patients were left lying on his back for 2 hours, after which they take a face down position for the next 7 days.

**Results**

There were no complications during surgery or in postoperative period.

Optic coherence tomography of the macula was performed on the 7<sup>th</sup> day after surgery. In all 11 cases there was anatomical closure of the macular holes.

Visual acuities were measured on days 14 and 3. On average there was an improvement in visual acuity by 2 lines according to Snellen chart, disappearance of metamorphopsia and image distortion.

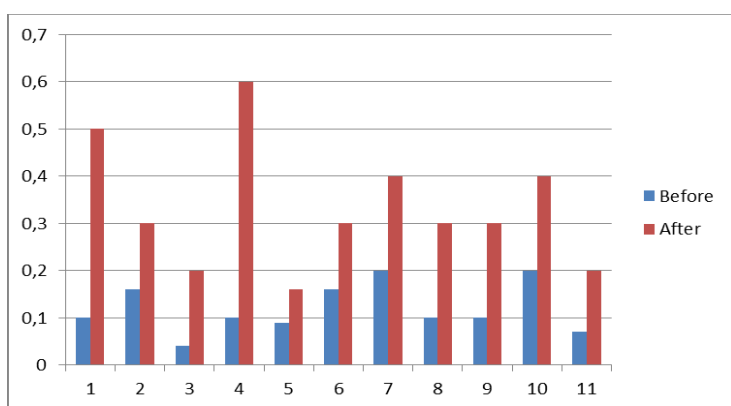


Figure 4. Visual acuity before and after surgery

During the follow up the patients during 6 month there was no development cataract, retinal tears or detachment, late endophthalmitis or any other complications.

**Discussion**

The macular hole is one of the main vitreoretinal disorders causing metamorphopsia and impaired central vision in the elderly.<sup>26</sup> The overall incidence is approximately 3.3% per 1000 people. the prefoveal cortex of the vitreous.<sup>27</sup> It has been suggested that the main factors in spontaneous macular closure are the release of vitreofoveal traction or glia proliferation.<sup>28</sup> The treatment of macular holes has improved over the past 30 years, and improvements in technique allow closure of typical macular holes in more than 90% of cases. Visual acuity improves by at least 2 lines in over 70% of eyes. The challenge of the last decade has been to improve the treatment of eyes with macular holes, in which the prognosis for successful closure of the

macular hole and improvement in visual acuity is less favorable. Although vitreous surgery was first described as a likely treatment for full-thickness macular holes (FTMH), it has become a common surgical procedure. With current surgical techniques, approximately 90% of FTMHs achieve anatomical closure at primary surgery, with nearly half of patients achieving visual acuity of 20/50 or better. The frequency of closure and visual outcome of FTMHs depends on their size and chronic nature.

Modern surgical interventions effectively treat macular holes (MR) in more than 90%.<sup>29-30</sup> The current surgical treatment for MH is epiretinal squamous vitrectomy, internal limiting membrane peeling (ILM). However, a small subset of MH creates problems for surgeons and is frustrating for patients. Several surgical techniques are developed and tried for the management of refractory macular holes. These include relaxing retinotomy, free and inverted ILM flaps, posterior lens capsular flap, autologous neurosensory retinal flap, and foveal hydrodissection.

Two new alternative methods for closing atypical macular holes have been described, including amniotic membrane transplantation (AMT) and autologous retinal transplantation (ART).<sup>31</sup> They differ from the various ILM flap techniques in that tissue is placed in the macular hole to help occlude the macular dehiscence. In AMT, the amniotic membrane is cut and inserted into the vitreous. When the amniotic membrane is placed inside the opening, it could theoretically release some of the growth factors that promote closure.<sup>32</sup> Further research is needed to determine long-term outcomes and determine when this procedure is most appropriate.

So far, neither national nor international guidelines have been developed for the treatment of incomplete macular holes. Thus, the correct approach - to treat or not to treat lamellar macular holes - is still a matter of debate.

Platelet-rich plasma (PRP), whose therapeutic value is equal to that of stem cells, is currently one of the most promising therapy agents in regenerative medicine. It is increasingly being used in different areas of medicine including aesthetic dermatology, orthopedics, sports medicine and surgery. One possibility is the use of highly concentrated autologous platelet-rich plasma for macular hole surgery. Autologous blood products such as simple

blood clot and platelet rich plasma,<sup>33-35</sup> as well as several tissue glues comprising nonautologous blood products and synthetic molecules are also tried for facilitating hole closure.<sup>36-39</sup>

The article reports recovery surgery using autologous platelet rich plasma to treat these complex macular holes.

In this clinical study of 11 macular hole patients underwent recovery surgery using autologous platelet rich plasma (PRP), we could observe morphological and functional improvement in the long-term follow-up. Thus, preventing further progression even at stages that are more visually limiting also seems to be an argument in favor of earlier surgical intervention. When considering the results of our study, two different outcomes need to be taken into account. On the one hand, there was a morphological improvement in the foveal structure and prevention of progression. On the other hand, measurements show that visual acuity improves functionally.

The use of autologous PRF appears to be a safe and effective alternative treatment for macular holes. Our study is limited by its small sample size, lack of control group, and inhomogeneous lens status. Further studies are needed to compare the advantages of the different techniques and approaches and to determine the most efficient method.

## Conclusion

During the surgical treatment of patients with primary and secondary macular holes the use of autologous platelet rich plasma promotes the anatomical closure of the holes, as a result of which metamorphopsias and central scotomas disappear and an increase in visual acuity is observed.

## Funding

This research received no external funding.

## Institutional Review Board Statement

The study was conducted by the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee).

## Informed Consent Statement

Informed consent was obtained from patient involved in the study.

## Data Availability Statement

Not applicable.

## Conflicts of Interest

The authors declare no conflict of interest.

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ՄԵՓԱԿԱՆ ԱՐՅԱՆ ԹՐՈՄԲՈՑԻՏԵՆԵՐՈՎ ՀԱՐՈՒՍՏ ՊԼԱՁՄԱՅԻ ԿԻՐԱՌՄԱՆ ԱՐԴՅՈՒՆՔՆԵՐԸ ՄԱԿՈՒԼՅԱՐ ՊԱՏՈՎԱԾՔՆԵՐԻ ՎԻՐԱԲՈՒԺԱԿԱՆ ԲՈՒԺՄԱՆ ԺԱՄԱՆԱԿ

Լիլիթ Ոսկանյան,<sup>1</sup> Աղաբեկյան Էդգար <sup>2</sup>

<sup>1</sup> Ակնաբուժության ամբիոնի վարիչ Մ. Հերացու անվան Պետական բժշկական, համալսարան, Հայաստան, Ս.Վ. Մալայանի անվան ակնաբուժական կենտրոն, Երևան, Հայաստան

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**Ամփոփում**

**Հետազոտության նպատակն էր** գնահատել բարձր խտացված թրոմբոցիտներով հարուստ աուտոպլազմայի (PRP) կիրառման երկարաժամկետ արդյունքները, որն օգտագործվել էր մակուլային անցքի պատվածքների վիրաբուժական բուժման ժամանակ:

**Նյութեր և մեթոդներ.** Վիրահատական բուժման համար ընտրվել է 11 հիվանդ (11 աչք), որից 9-ը իզոկան սեռի և 2-ը տղամարդ: 10 հիվանդ (10 աչք) ունեցել է դեղին բծի պատվածք, որից 8-ը՝ 4-րդ աստիճանի, իսկ 2-ը՝ 3-րդ աստիճանի դեղին բծի պատվածք ք, իսկ մեկ հիվանդ՝ հետտրավմատիկ դեղին բծի պատվածք: Առաջնային մակուլայի պատվածքով հիվանդների տարիքը եղել է 59-75 տարեկան, իսկ տրավմատիկ մակուլայի պատվածքով հիվանդը՝ 32 տարեկան:

Բոլոր հիվանդների մոտ վիրահատությունից առաջ և հետվիրահատական շրջանում կատարվել է վիզուալիզացիա, տոնոմետրիա, օֆտալմոսկոպիա, բիոմիկրոսկոպիա, ակնագնդի էխոգրաֆիա, ցանցաթաղանթի օպտիկական համակցված տոմոգրաֆիա:

Թրոմբոցիտներով հարուստ պլազման վիրահատարանում առանձնացվել է ստերիլ պայմաններում: Հիվանդներին վիրահատել են տեղային անզգայացմամբ (2% 2մլ Լիդոկաին և 0,75% 2մլ բուպիվակաին), ինչը ներառել է պարս պլանա վիտրեկոմիա, հետին հիալոիդային մեմբրանի պարտադիր հեռացում, ցանցենու ներքին սահմանային մեմբրանի փիլինգ, թրոմբոցիտներով հարուստ արյան պլազմայի ներմուծում պատվածքի շրջան և 8% օկտաֆտորոպրոպան (C3F8) գազային էնդոտամպոնադա:

**Արդյունքներ.** Վիրահատության ընթացքում և հետվիրահատական շրջանում որևէ բարդություն չի եղել: Վիրահատությունից հետո 7-րդ օրը կատարվել է մակուլայի օպտիկական համակցված տոմոգրաֆիա: Բոլոր 11 դեպքերում եղել է մակուլայի անցքերի անատոմիական փակում: Տեսողության սրությունը չափվել է 3-րդ և 14-րդ օրերին: Միջինում կար տեսողության սրության բարելավում 2 տողով՝ ըստ Մնելենի գծապատկերի, մետամորֆոպսիայի անհետացում և պատկերի աղավաղում:

Հետազոտության ընթացքում հիվանդների մոտ 6 ամսվա ընթացքում կատարակտի զարգացում, ցանցաթաղանթի պատվածք կամ անջատում, ուշ էնդոֆթալմիտ կամ որևէ այլ բարդություն չի եղել:

Մեր դիտարկումները ցույց են տվել, որ առաջնային կամ երկրորդային մակուլյար պատվածքների վիրաբուժական բուժման ժամանակ թրոմբոցիտներով հարուստ արյան պլազմայի կիրառումը հանդիսանում է անվտանգ և էֆեկտիվ մեթոդ: Տվյալ մեթոդի շնորհիվ կարելի է հասնել մակուլյար պատվածքների անատոմիական փակման և տեսողության սրության բարձրացման:

**Եզրակացություն.** Առաջնային և երկրորդային մակուլյար անցքերով հիվանդների վիրաբուժական բուժման ընթացքում աուտոլոգ թրոմբոցիտներով հարուստ պլազմայի օգտագործումը նպաստում է մակուլյար պատվածքների անատոմիական փակմանը, ինչի հետևանքով անհետանում են մետամորֆոպսիաները և կենտրոնական սկոտոմաները և նկատվում է տեսողության սրության բարձրացում:

**РЕЗУЛЬТАТЫ ИСПОЛЬЗОВАНИЯ СОБСТВЕННОЙ БОГАТОЙ ТРОМБОЦИТАМИ ПЛАЗМЫ КРОВИ ПРИ ХИРУРГИЧЕСКОМ ЛЕЧЕНИИ МАКУЛЯРНЫХ РАЗРЫВОВ**

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**Абстракт**

**Цель** этого исследования состояла в том, чтобы оценить долгосрочные результаты высококонцентрированной богатой тромбоцитами аутоплазмы (PRP), используемой в качестве дополнительной операции на макулярном отверстии.

**Материалы и методы:** Для оперативного лечения включены 11 пациентов (11 глаз), из них 9 женщин и 2 мужчины. У 10 пациентов (10 глаз) были первичные разрывы желтого пятна, из которых 8 глаз имели разрывы желтого пятна 4 степени и 2 глаза имели разрывы желтого пятна 3 степени и один пациент имел посттравматический разрыв желтого пятна. Возраст пациентов с первичным макулярным разрывом составлял 59-75 лет, с травматическим макулярным разрывом — 32 года.

Всем пациентам до операции и в послеоперационном периоде выполняли визиометрию, тонометрию, офтальмоскопию, биомикроскопию, эхографию глазного яблока, оптическую когерентную томографию сетчатки. Пациенты были оперированы под местной анестезией (2% 2мл лидокаина и 0,75% 2мл бупивакаина) следующим образом: витрэктомия 25 Калибр стандартной паре плоскость с обязательным удалением задней гиалоидной мембраны, после чего производили отслоение внутренней пограничной мембраны сетчатки, выполняется с большим объемом. Обогащенную тромбоцитами плазму отделяли в стерильных условиях в операционной и вводили в область макулярного отверстия в конце операции, а в глаз вводили 8% газ октафторпропан (C3F8).

**Результаты:** Осложнений во время операции и в послеоперационном периоде не было. Оптическую когерентную томографию макулы выполняли на 7-е сутки после операции. Во всех 11 случаях произошло анатомическое закрытие макулярных отверстий. Остроту зрения измеряли на 3-й и 14-й день. В среднем отмечалось улучшение остроты зрения на 2 строки по таблице Снеллена, исчезновение метаморфопсии и искажения изображения.

При наблюдении за больными в течение 6 мес развития катаракты, разрывов или отслойки сетчатки, позднего эндофтальмита и других осложнений не отмечено. Наши наблюдения показали, что использование обогащенной тромбоцитами плазмы крови при хирургическом лечении первичных или вторичных макулярных разрывов, включающий в себя паре плана витрэктомию, обязательное удаление задней гиалоидной мембраны, пиллинг внутренней пограничной мембраны сетчатки, введение богатой тромбоцитами плазма крови в область разрыва и газовая эндотампонада, является безопасным и эффективным методом. Благодаря этому методу удается добиться анатомического закрытия макулярных разрывов и повышения остроты зрения.

**Заключение:** При хирургическом лечении больных с первичными и вторичными макулярными разрывами применение аутологичной обогащенной тромбоцитами плазмы способствует анатомическому закрытию отверстий, в результате чего исчезают метаморфопсии и центральные скотомы и наблюдается повышение остроты зрения.