Topical Platelet-Rich Plasma in the Treatment of Resistant Corneal Ulcer After Vitrectomy

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Short title: Topical PRP in the Treatment of Resistant Corneal Ulcer After Vitrectomy

Abstract

Objective: To assess the efficacy of topical platelet-rich plasma (PRP) eye drops in promoting corneal epithelial healing in patients with resistant corneal epithelial defects (CED) following vitrectomy.

Methods: In this retrospective study, medical records of patients who underwent 23-gauge pars plana vitrectomy (PPV) from March 2022 to October 2024 were analyzed. Patients with persistent CED post-vitrectomy, either due to spontaneous epithelial breakdown or intraoperative debridement, were treated with PRP eye drops. Data collected included demographics, surgical duration, tamponade type, and intraocular pressure (IOP). Primary outcomes were time to epithelial healing and frequency of delayed healing, defined as requiring >2 weeks for closure.

Results: Among 256 eyes undergoing vitrectomy, 39 (15.2%) developed spontaneous postoperative CED, while 21 (8.2%) required intraoperative debridement. Patients receiving PRP showed a complete epithelium healing without complications, with mean closure times of 4.6 weeks for the intraoperative debridement group and 5.2 weeks for the postoperative CED group. Prolonged surgical time was associated with increased risk of delayed healing.

Conclusion: PRP eye drops are a promising adjunctive therapy for resistant CED following vitrectomy, especially in cases with prolonged surgical duration or high-risk factors like diabetes. PRP's regenerative properties may provide an effective, minimally invasive option for enhancing corneal healing in this population.

Keyword: PRP, Corneal Ulcer, Vitrectomy, CED.

INTRODUCTION

Corneal epithelial defects (CED) are a common complication following vitreoretinal surgeries, arising spontaneously or due to intraoperative corneal debridement required for optimal fundus visualization. Pars plana vitrectomy combined with lensectomy, pan retinal photocoagulation, tamponed use, prolonged surgical duration, and postoperative ocular hypertension (HTN) may contribute to CED risky has been associated with both spontaneous CEDs and the need for intraoperative debridement[1-5]. Postoperative CEDs can lead to increased discomfort, compromised posterior segment visualization, more frequent postoperative visits, and, in some cases, corneal scarring. Although most postoperative CEDs resolve quickly without sequelae, close follow-up and appropriate treatment are crucial to prevent complications. Delayed healing of CEDs increases the risk of corneal scarring, neovascularization, infectious keratitis, corneal melting, and even perforation[4,10].

PRP technology, involving blood-derived products rich in growth factors, supports wound healing and tissue regeneration[6]. These products are processed to concentrate platelets, which release growth factors promoting tissue repair without leukocytes, minimizing inflammation. PRP preparations are created through including blood extraction, centrifugation, and plasma fractionation to yield injectable[7-9]. In ophthalmology, PRP extraction from blood is used for ocular disease as severe dry eye, recurrent corneal erosions, and recently, to improve outcomes in macular hole repair in vitreoretinal surgery[10-14].

Aim and Scope: This study evaluates the impact of topical PRP eye drops on healing outcomes in patients with resistant CED after vitrectomy.

PATIENTS AND METHODS

This retrospective, longitudinal study included patients who underwent 23-gauge PPV for various diagnoses between March 2022 and October 2024 by two surgeons (A.E. and A.A.). In selected cases, phacoemulsification and intraocular lens implantation were performed concurrently. Intraoperative corneal debridement was conducted when corneal epithelial edema hindered fundus visualization, or if pre-existing corneal pathology obstructed clear posterior pole assessment. There was no control group without PRP treatment.

Exclusion criteria included patients with previous history of retinal surgery, history of photocoagulation, history of intravitreal injection, corneal pathology, and poor vision less than PL, glaucoma or ocular surface diseases that could influence epithelial healing and Patients with incomplete follow-up data (<3 months).

Data collected: Preoperative Data included Demographics, medical history, and risk factors like diabetes mellitus. Intraoperative Data included Surgery duration, use of intraoperative tamponades, and concurrent phacoemulsification procedures. Postoperative Data included Time to epithelial healing, intraocular pressure (IOP), visual acuity (VA), and complications such as infection or perforation.

Subjects with IOP >21 mm Hg or <7 mm Hg within one week postoperatively were classified as having ocular hypertension or hypotension, respectively. Delayed epithelial healing was defined as CEDs requiring more than two weeks for closure postoperatively.

PRP eye drops Preparation

PRP extraction was performed using double-spin methods described elsewhere[15]. In brief, 30 mL of blood with anticoagulant was collected and centrifuged with 200 g for 10 min. The supernatant was aspirated and re-centrifuged at 300 g for 5 min. Finally, serum was carefully removed while avoiding aspiration of platelet cells and the remaining serum and platelet cells were mixed.

PRP eye drops were added to treatment of Patients with delayed epithelial healing at second week postoperative until complete healing. Patients were advised to use PRP eye drops 4–6 times daily and monitored for tolerance. Follow-up continued daily for the first week, then weekly until epithelialization was complete. Healing was defined as epithelial closure and symptom relief at final follow-up; improvement was indicated by a decrease in ulcer depth or size.

Outcome Measures

The primary outcome was epithelial healing response to PRP eye drops. Secondary outcomes included time to resolution and frequency of delayed healing (healing >2 weeks).

Ethical Approval

The study was approved by the Ethics Committee of Faculty of Medicine, Kafrelsheikh University (no. KFSIRB200-365), adhering to the principles of the Helsinki Declaration. All participants provided informed consent.

Statistical Analysis

Data analysis was performed using SPSS version 18. Continuous data were reported as mean ± standard deviation. Mann-Whitney U and Student’s t-tests compared nonparametric and parametric variables, respectively, while categorical data were assessed with Chi-squared and Fisher’s exact tests. Kaplan-Meier survival curves represented CED resolution over time, and regression analysis identified predictive risk factors. Statistical significance was set at a P value <0.05.

RESULTS:

A total of 256 eyes that underwent vitrectomy were analyzed. Among these, 39 eyes (15.2%) developed spontaneous postoperative CED, while 21 eyes (8.2%) required intraoperative corneal debridement. The mean age of patients was 57.8 years (range: 40–75 years). Gender distribution and key demographic data are summarized in Table 1.

The demographic and clinical characteristics of the subjects are indicated in Table 1.

Table 1: clinical and Demographic data

Parameters	Eyes with spontaneous postop. CED	Eyes requiring intraoperative corneal debridement	P value
No.	39 (15.2%)	21 (8.2%)	
Age (mean±SD), y	56.7±11.5	59.4±17.8	0.479
Gender			
Male	21 (53.8)	12 (57.1)	0.81
Female	18 (46.1)	9 (60.6)	
Diabetes mellitus	26 (27.6)	12 (42.8)	0.465
Lens status			
Pseudophakic	20 (51.3)	9 (42.9)	
Phakic	17 (43.6)	12 (57.1)	0.442
Aphakic	2 (5.1)	0 (0.0)	

Table 2 presents a comparison of CED cases versus matched control eyes without CED. Significant differences were noted in operative times, with longer durations associated with CED development (P < 0.001). However, there were no significant differences in outcomes based on tamponade type or concurrent procedures.

Table 2: Factors associated with postoperative corneal epithelial defect.

Parameters	Eyes with postop. CED	Matched control eyes without postop. CED	*P*	Odd ratio (95%CI)
No.	60	196		
Age (mean±SD), y	58.7±16.5	60.3±17.8	0.536	-
Gender (M/F)	33/27	104/92	0.792	1.1 (0.6-1.9)
Diabetes mellitus	38 (63.3)	107 (54.6)	0.231	1.4 (0.8-2.6)
Tamponade				
SF_6	16 (26.6)	42 (21.4)	0.396	1.3 (0.7-2.6)
C_3F_8	8 (13.3)	29 (14.8)	0.778	0.88 (0.38-2.1)
Air	11 (18.3)	39 (19.9)	0.789	0.9 (0.43-1.9)
Silicone	25 (41.7)	86 (43.9)	0.762	0.9 (0.51-1.6)
Combined phacoemulsification surgery	17 (28.3)	46 (23.5)	0.44	1.3 (0.67-2.5)
Duration of surgery (min)	115±56	90±41	**<0.001**	-
Postop. ocular hypotension (IOP<7 mm Hg)	16 (26.6)	40 (20.7)	0.304	1.4 (0.72-2.67)
Postop. ocular hypertension (IOP>21 mm Hg)	14 (23.3)	55 (28.1)	0.47	0.78 (0.39-1.5)

CI: confidence interval

Delayed epithelial healing (>2wk) was documented in 10 patients (25.6 %) in the postoperative CED group and 4 patients (19.0 %) in intraoperative debridement group. It is important to note that the patients follow up was usually weekly after the postoperative day 1 visit till epithelium healing and may overestimate time to closure since these eyes were not typically followed daily. Comparative assessment between the intraoperative debridement group and postoperative CED's group was performed (Table 3).

Table 3: Results and comparision of postop. CED group and intraoperative corneal debredment group.

Parameters	Eyes with spontaneous postop. CED	Eyes requiring intraoperative corneal debridement	*P*	Odd ratio (95%CI)
No.	39 (15.2%)	21 (8.2%)		
Duration of surgery (min)	100±59	130±54	0.05	-
Concurrently phacoemulsification	8/19 (20.5)	9/12 (42.9)	0.975	0.98 (0.32-3.1)
Delayed epithelial healing (>2wk)	10 (25.6)	4 (19.0)	0.564	1.5 (0.39-5.4)
Tamponade				
SF_6	9 (23.1)	4 (19.0)	0.717	1.3 (0.3-4.8)
C_3F_8	7 (17.9)	5 (23.8)	0.588	0.59 (0.2-2.6)
Air	3 (7.7)	1 (4.8)	0.664	1.7 (0.2-17)
Silicone	20 (51.3)	11 (52.4)	0.935	0.95 (0.3-2.7)
Postop. ocular hypotension (IOP<7 mm Hg)	9 (23.1)	7 (33.3)	0.39	0.6 (0.18-1.9)
Postop. ocular hypertension (IOP>21 mm Hg)	8 (20.5)	6 (28.6)	0.48	0.6 (0.18-2.2)

n (%

RRD; rhegmatogenous retinal detachment

Diabetic vitrectomy; including vitreous hemorrhage, tractional retinal detachment, resistant macular edema, subhyaloid and subretinal hemorrhage

Macular pathology; including non diabetic epiretinal membrane, macular hole

Complicated ocular surgery; including endophthalmitis, dropped lens, malignant glaucoma

Trauma; including rupture globe, intraocular foreign body, dislocated lens

No occurrences of infectious ulceration, corneal melting or perforation were observed in either group. Delayed epithelial healing occurred in all patients after use of PRP eye drops in persistent epithelium ulcer 2 weeks postoperatively. Delayed epithelial healing occurred in mean 4.6 week in the intraoperative debridement group and mean 5.2 week in the postoperative CED group. The risk factors for delayed healing were analyzed in table 4. The mean size of corneal epithelial defects was 3.1 ± 0.8 mm² in the postoperative group and 2.7 ± 0.5 mm² in the intraoperative group. Larger defects were associated with prolonged healing times (P = 0.02) (figure 1).

Table 4: Results and comparision of Delayed epithelial healing (>2wk)

Parameters	Eyes with spontaneous postop. CED	Eyes requiring intraoperative corneal debridement	*P*	Odd ratio (95%CI)
No. of Delayed epithelial healing (>2wk)	10 (25.6)	4 (19.0)	0.564	1.5 (0.39-5.4)
Type of surgery				
RRD	2 (20)	1 (25)	0.83	0.7 (0.04-11.6)
Diabetic vitrectomy	6 (60)	1 (25)	0.23	4.5 (0.3-60)
Giant retinal tear	1 (10)	-		
Macular pathology	-	-		-
Complicated ocular surgery	1 (10)	2 (50)	0.09	0.1 (0.01-1.9)
Trauma	-	-		
Tamponade				
SF_6	3 (30)	1 (25)	0.85	1.3 (0.1-17.9)
C_3F_8	1 (10)	-		-
Air	1 (10)	-		-
Silicone	5 (50)	3 (75)	0.39	0.33 (0.02-4.4)
Postop. ocular hypotension (IOP<7 mm Hg)	4(40)	2 (50)	0.73	0.67 (0.1-6.8)
Postop. ocular hypertension (IOP>21 mm Hg)	2 (20)	1 (25)	0.83	0.7 (0.04-11.6)

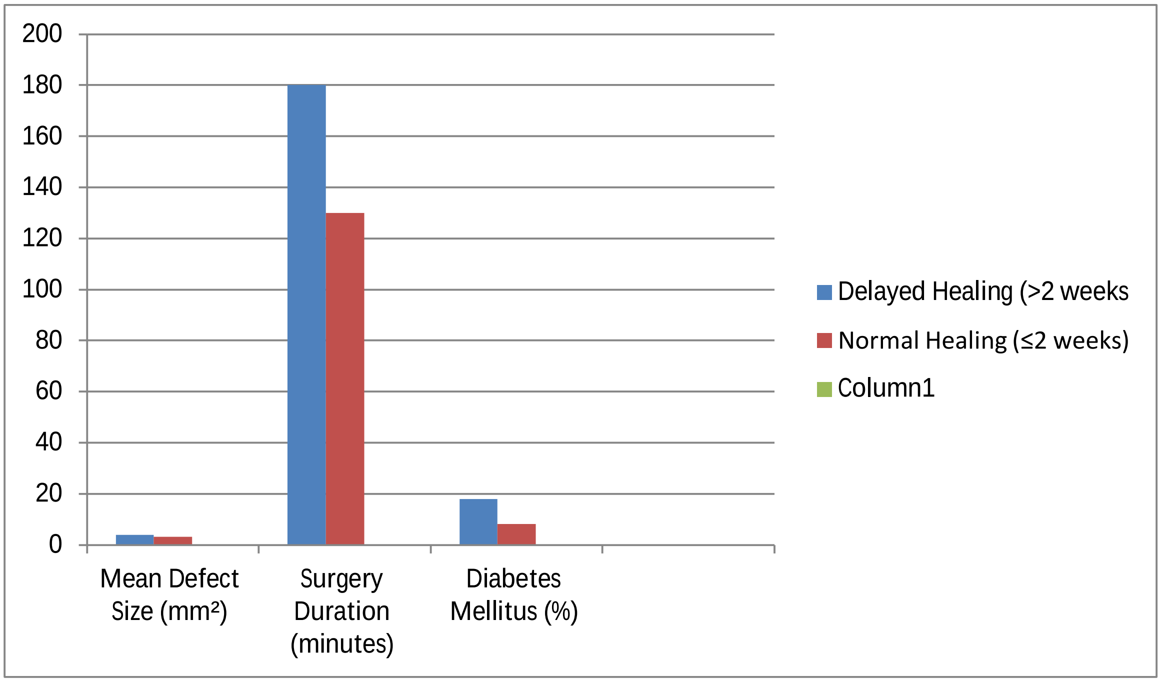

Figure 1: comparing key parameters between delayed healing (>2 weeks) and normal healing (≤2 weeks).

DISCUSSION

This study demonstrates the potential benefits of using topical platelet-rich plasma (PRP) eye drops to promote corneal epithelial healing in patients with persistent corneal epithelial defects (CED) following vitrectomy. PRP eye drops help in healing in these cases, supporting their utility as an adjunctive treatment in patients with resistant corneal ulcers. Notably, delayed healing occurred in some cases, with longer surgery durations identified as a risk factor. These findings align with previous research and highlight areas for further investigation to refine postoperative care protocols in high-risk populations[16,18,22].

PRP has emerged as a valuable treatment for ocular surface diseases due to its high concentration of growth factors, which are known to enhance epithelial cell proliferation, migration, and adhesion. Previous studies have demonstrated PRP's efficacy in treating conditions like severe dry eye, recurrent corneal erosions, and neurotrophic keratitis, where traditional therapies may fall short[16,17]. By promoting tissue regeneration and reducing inflammation, PRP offers a biologically compatible option that supports the corneal healing process without adverse effects[16].

The efficacy of PRP in resistant corneal ulcers following vitrectomy underscores the broader therapeutic potential of PRP beyond anterior segment conditions. In cases where prolonged surgical time, diabetes, or ocular hypertension are present, the regenerative properties of PRP may counteract delayed healing and reduce complications like scarring and neovascularization[18]. This study contributes to the existing body of literature by extending the potential indications for PRP to cases with intraoperative corneal debridement, where epithelial recovery can be particularly challenging[19].

Corneal epithelial defects following vitrectomy can arise spontaneously or require intervention when pre-existing pathology limits posterior segment visualization. Risk factors, such as prolonged surgery time, diabetes mellitus, and use of intraoperative corneal debridement, have been widely recognized in previous studies[20,21]. Our findings corroborate these associations, as surgery duration was significantly longer in eyes with postoperative CED compared to those without CED ($p<0.01$). This supports the hypothesis that extended surgical exposure, particularly in complex cases, may compromise corneal integrity, necessitating additional treatments to aid healing[22].

While we found no significant association between tamponade type and CED incidence or delayed healing, previous studies suggest that tamponades like silicone oil can impact corneal health by elevating IOP or causing direct corneal toxicity over time [23]. Further research could clarify these potential correlations by examining a larger sample size or by isolating tamponade effects more rigorously. The lack of significant associations in our study may be due to sample size limitations or follow-up protocols.

Several therapeutic options, including artificial tears, bandage contact lenses, and amniotic membrane transplantation, have been explored for CED management. Although these treatments provide symptomatic relief and temporary protection, they often fail to promote robust epithelial regeneration, particularly in resistant cases[17]. Amniotic membrane transplantation, while effective in certain scenarios, requires a surgical approach and may carry the risk of immunogenic reactions[24]. PRP, on the other hand, is minimally invasive, cost-effective, and can be easily applied as topical eye drops, making it a practical option for outpatient use. The present study supports PRP as a viable alternative for patients with delayed healing after vitrectomy, particularly in cases where conventional treatments are ineffective.

However, our study did not compare PRP to a control group without PRP treatment, limiting definitive conclusions about its relative efficacy. Future randomized controlled trials are warranted to address this limitation and optimize PRP protocols.

Study Limitations

This study is limited by its retrospective design and reliance on medical records, which may introduce selection bias. The follow-up intervals, typically weekly rather than daily, could overestimate healing times. Additionally, variations in PRP preparation methods may influence treatment outcomes. Standardized protocols for PRP concentration and application frequency are needed to ensure reproducibility and maximize therapeutic benefits.

Future Directions

Exploring PRP's effects in larger, prospective cohorts and comparing its efficacy to alternative treatments could further validate its role in corneal healing. Investigations into the impact of varying PRP concentrations and delivery methods (e.g., sustained-release formulations) could also optimize its clinical application. Moreover, exploring the impact of different PRP concentrations or treatment frequencies could optimize its therapeutic effects[19].

CONCLUSION

Topical PRP eye drops represent a viable adjunctive therapy for resistant CED following vitrectomy, particularly in patients with prolonged surgical durations or underlying risk factors. PRP may reduces the risk of complications, accelerating corneal epithelialization, and enhances postoperative outcomes. Further research is essential to refine PRP protocols and establish its role in broader clinical contexts.

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Data Availability: The authors declare that all data supporting the findings of this study are available within the article.

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Conflict of interest

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