Original Article

Comparison of 20% Autologous Platelet-Rich Plasma Versus Conventional Treatment in Moderate to Severe Dry Eye Patients

Shubhi Sachan, Kshama Dwivedi, Satya Prakash Singh, Santosh Kumar, Vinod Kumar Singh

Regional Institute of Ophthalmology, MLN Medical College, Department of Ophthalmology, Prayagraj, India

Abstract

Objectives: To evaluate the effectiveness of conventional therapy and 20% autologous platelet-rich plasma (aPRP) eye drops for moderate to severe dry eye disease (DED).

Materials and Methods: In this prospective interventional study, 40 individuals (80 eyes) with moderate to severe DED were analyzed. Twenty patients each were randomly assigned to the study and control groups. The study group was given 20% aPRP eye drops; the control group was given artificial tears as per conventional treatment. Comprehensive eye examinations including evaluation of best corrected visual acuity (BCVA), tear meniscus height, tear break-up time (TBUT), Schirmer's test, corneal fluorescein staining, conjunctival impression cytology, and Ocular Surface Disease Index (OSDI) were conducted in both groups for 3 months. Pre- and posttreatment results were compared.

Results: The average age of patients in the study group was 51±14 years (range, 37-65 years), whereas that of the control group was 50±17 years (range, 33-67 years). After 3 months, there was a more significant decrease in OSDI score in the study group than in the control group ($p<0.01$). The BCVA data demonstrated no statistically significant difference ($p>0.05$). Measurements of tear meniscus height, Schirmer's value, and TBUT at 3 months showed statistically significant differences ($p<0.01$). The posttreatment improvements in fluorescein staining and impression cytology scores in the study group were markedly superior to those in the control group ($p<0.01$).

Conclusion: aPRP is both safe and more effective than conventional treatments for moderate to severe symptomatic DED.

Keywords: Autologous platelet-rich plasma (aPRP), dry eye disease, OSDI, autologous serum, impression cytology

Cite this article as: Sachan S, Dwivedi K, Singh SP, Kumar S, Singh VK. Comparison of 20% Autologous Platelet-Rich Plasma Versus Conventional Treatment in Moderate to Severe Dry Eye Patients. Turk J Ophthalmol. 2025;55:112-119

Address for Correspondence: Kshama Dwivedi, Regional Institute of Ophthalmology, MLN Medical College, Department of Ophthalmology, Prayagraj, India
E-mail: drdkshama@gmail.com **ORCID-ID:** orcid.org/0000-0003-0568-4096
Received: 03.09.2024 **Accepted:** 28.02.2025

DOI: 10.4274/tjo.galenos.2025.47717

Introduction

Dry eye disease (DED) is a prevalent and multifactorial condition of the ocular surface marked by disruption of tear film homeostasis and accompanied by ocular symptoms. The etiology of this disease includes inflammation and damage to the ocular surface, abnormalities in the neurosensory system, and tear film instability and hyperosmolarity.[1] Burning, photophobia, tearing, and foreign body sensation are symptoms of this disorder that can greatly impair a patient's quality of life. The estimated global prevalence of DED varies greatly (4%-50%) depending on the diagnostic criteria used and the population under consideration.[2,3,4] Smoking, contact lens wear, and prolonged use of digital screens are all contributing factors.[5]

The topical use of artificial tears is the primary conventional treatment for dry eye, despite the fact that the outcomes are frequently unsatisfactory. This has prompted the use of other hemoderivative-based treatment approaches. Autologous platelet-rich plasma (aPRP) has been proposed as a more suitable therapy for severe DED than artificial tears without preservatives. aPRP is a hemoderivative that contains a high concentration of platelets and is used to stimulate corneal epithelial cell migration, proliferation, and differentiation. The platelets in aPRP adhere to injured tissues and release growth factors and cytokines that promote healing.[6]

There are several benefits of aPRP over conventional therapies. Being homologous, it lowers the possibility of immunological problems or allergic responses that may occur with other therapies. Research indicates that aPRP is more effective than conventional therapies in improving tear film stability, increasing tear output, and decreasing ocular surface damage. aPRP has great promise, but it also has certain limitations, such as the need for specific handling and preparation, the possibility of infection and contamination, limited availability, and the lack of standard protocols. According to a recent meta-analysis assessing the

effect of PRP on dry eye, only 19 studies were eligible for inclusion. Of these, 10 were comparative (6 randomized and 4 nonrandomized studies).[7] Investigating the efficacy of this treatment approach, especially in comparison to conventional treatment, is important because the frequency of DED is increasing worldwide. This increase is particularly pronounced in younger populations, which may be a result of greater use of digital devices or other unidentified reasons. With its capacity for regeneration and low risk of side effects, aPRP may be a valuable development in the treatment of moderate to severe DED.

Materials and Methods

This prospective interventional comparative research was undertaken at the Regional Institute of Ophthalmology (MD Eye Hospital) in Prayagraj, Uttar Pradesh, over one year, from July 2023 to June 2024. The study was initiated after approval from the ethics council of MLN Medical College, Prayagraj (ECR/922/Inst/UP/RR-22 on 5/7/2023). Patients of either sex between 18 to 70 years of age were included in the study. Based on their Ocular Surface Disease Index (OSDI) score, the patients' symptoms were categorized, and those diagnosed with DED were randomly allocated to the study group (n=20) or control group (n=20). After explaining the procedures, all participants signed an informed consent form.

The study assessed OSDI score, best corrected visual acuity (BCVA), tear meniscus height, tear break-up time (TBUT), Schirmer's test, and corneal fluorescein staining before treatment and after 1 week, 1 month, and 3 months of treatment, as well as conjunctival impression cytology in both groups before and after 3 months of treatment. The study group received 20% aPRP eye drops, while the control group received conventional treatment consisting of Systane Complete lubricant eye drops (active ingredient: propylene glycol 0.6%; Alcon, Nagpur, India). As per the Dry Eye Workshop II recommendation, artificial tears are the first line of management in mild to severe cases of both evaporative and aqueous-deficient dry eye.[4]

Sample size was calculated using the following formula:

$$n = \frac{2(Z\alpha/_2 + Z_{(1-\beta)})^2 \times \sigma^2}{(\mu 1 - \mu 2)^2}$$

Assuming a 0.05 level of significance, n was calculated as 79.8. Therefore, 80 eyes were included in the study.

Inclusion and Exclusion Criteria

Patients aged 18-70 years with ODSI scores above 23 were eligible for the 12-week study. If the patient was already using topical lubricant eye drops, they were stopped 48 hours before starting the study intervention.

Patients meeting any of the following criteria were excluded from the study: being younger than 18 or older than 70 years of age or having advanced cancer, active infection, uncontrolled illness, pregnancy, contraindication for blood donation (e.g., recent anticoagulants or antiplatelets use, surgical interventions, positive HIV, hepatitis B or C, syphilis, or anemia), severe meibomian gland dysfunction, aberrant eyelid function, or ongoing ocular infection or inflammation. Patients with intolerable ocular side effects or allergic reactions to the topical therapies were also excluded during follow-up. Follow-up examinations were performed on day 0 and at 1 week, 1 month, and 3 months.

Method of Autologous Platelet-Rich Plasma Preparation

Ten milliliters of blood was collected from each patient in a blood collection tube coated with sodium citrate. The samples were centrifuged at soft spin (2400 rpm). The upper two-thirds was transferred to a separate tube which was subjected to hard spin (3600 rpm). The upper layer was removed and 3-5 mL of buffy coat/PRP was extracted. This was diluted with balanced salt solution to obtain a 20% concentration of aPRP. The aPRP eye drops were stored in sterile amber glass vials with eye drop applicators. The 20% aPRP drops were dispensed in 5 mL eye drop vials to the patient. The currently used vial was stored at 2-8 °C between instillations, while the remaining vials were stored at -20 °C until needed (Figure 1). Patients were advised to wash their hands before administering eye drops.

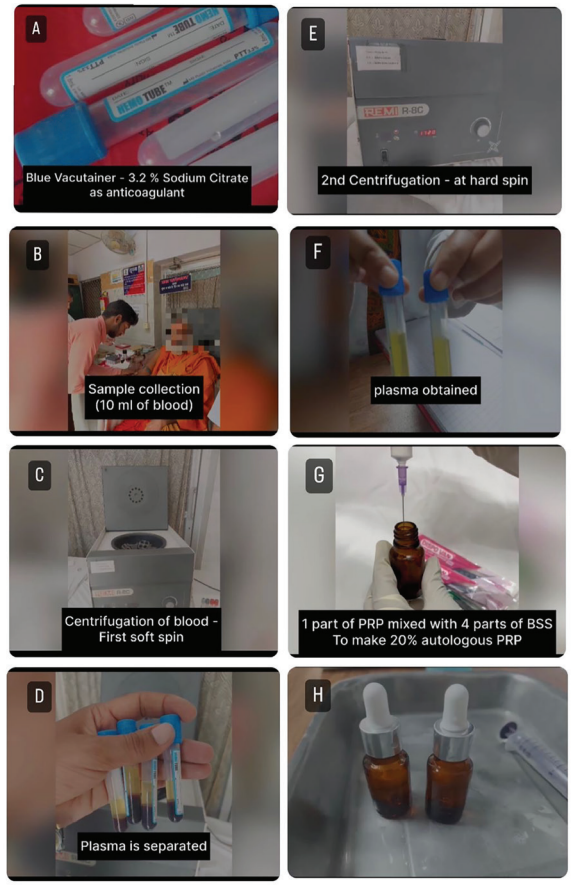

Figure 1. Method of preparing 20% autologous platelet-rich plasma eye drops
BSS: Balanced salt solution, PRP: Platelet-rich plasma

Statistical Analysis

We utilized Microsoft Excel 2016 and IBM SPSS Statistics for Windows version 29.0 (IBM Corp., Armonk, NY) for data analysis. Frequency and percentage were used for categorical variables and mean and standard deviation for continuous variables. Comparisons between the groups were made using independent-samples t-test for continuous variables and chi-square test for qualitative categorical data. The significance threshold was set at 0.05 for all statistical tests.

Results

OSDI scores in the study group ranged from 57 to 88, whereas those in the control group ranged from 54 to 88. There was no statistically significant difference in OSDI between the two groups at day 0 ($p>0.05$). However, there were statistically significant differences at 1 week ($p<0.05$), 1 month ($p<0.01$), and 3 months ($p<0.01$). The study group had lower mean OSDI values at these time points compared to the control group (Table 1).

The differences in BCVA between the study and control groups were not statistically significant at any time interval (Table 2).

Tear meniscus height did not differ significantly between the groups on day 0 or at 1 week ($p>0.05$). However, it was significantly higher in the study group than the control group at 1 month ($p<0.05$) and 3 months ($p<0.001$) (Table 3).

Table 1. Comparison of Ocular Surface Disease Index (OSDI) values between the groups

OSDI	Group	n	Mean	SD	t	p
Day 0	Study	20	71.95	9.10	0.018	0.986
	Control	20	72.00	8.91		
Week 1	Study	20	61.25	10.11	2.304	0.027*
	Control	20	68.35	9.37		
Month 1	Study	20	50.55	11.36	4.415	0.0005**
	Control	20	64.90	9.07		
Month 3	Study	20	38.90	9.00	7.473	0.0005**
	Control	20	61.55	10.14		

Independent-samples t-test, *Statistically significant ($p<0.05$), **Highly statistically significant ($p<0.01$). n: Number of patients, SD: Standard deviation

Table 2. Comparison of best corrected visual acuity (BCVA) between the groups

BCVA (logMAR)	Group	n	Mean	SD	t	p
Day 0	Study	40	0.123	0.11	0.090	0.929
	Control	40	0.120	0.14		
Week 1	Study	40	0.113	0.11	0.267	0.790
	Control	40	0.120	0.14		
Month 1	Study	40	0.108	0.11	0.445	0.658
	Control	40	0.120	0.14		
Month 3	Study	40	0.098	0.11	0.991	0.325
	Control	40	0.128	0.16		

Independent-samples t-test. logMAR: Logarithm of the minimum angle of resolution, n: Number of eyes, SD: Standard deviation

Table 3. Comparison of tear meniscus height between the groups

Tear meniscus height (µm)	Group	n	Mean	SD	t	p
Day 0	Study	40	188.38	56.37	0.861	0.392
	Control	40	199.13	55.31		
Week 1	Study	40	196.85	58.80	0.704	0.484
	Control	40	205.90	56.21		
Month 1	Study	40	234.58	48.65	2.259	0.027*
	Control	40	208.40	54.79		
Month 3	Study	40	262.20	48.74	4.576	0.0005**
	Control	40	208.18	56.57		

Independent-samples t-test, *Statistically significant ($p<0.05$), **Highly statistically significant ($p<0.01$). n: Number of eyes, SD: Standard deviation

TBUT improved with duration of aPRP therapy. There was no statistical difference between the groups on day 0 or at 1 week ($p>0.05$), whereas highly significant differences favoring the study group were observed at 1 month and 3 months ($p<0.01$) (Table 4).

Comparisons of Schirmer's test between the two groups revealed statistically significant differences at the $p<0.01$ level on day 0 and at 1 week, 1 month, and 3 months. At all time points, Schirmer's test values were significantly higher in the study group (Table 5).

Fluorescein staining also showed highly significant differences between the two groups at all time points ($p<0.01$). Staining was more extensive in the control group on day 0 and at 1 week, 1 month, and 3 months (Figure 2, Table 6).

The comparison of impression cytology between the groups showed that there was no statistically significant difference on day 0 ($p>0.05$), whereas at 3 months there was a highly significant difference (Figures 3 and 4, Table 7).

Refer to Table 8 for summarized results and Table 9 for main outcomes.

Table 4. Comparison of tear film break-up time (TBUT) between the groups

TBUT (s)	Group	n	Mean	SD	t	p
Day 0	Study	40	3.63	0.84	0.502	0.617
	Control	40	3.75	1.33		
Week 1	Study	40	4.13	0.91	0.466	0.643
	Control	40	4.00	1.43		
Month 1	Study	40	5.30	0.91	2.873	0.005**
	Control	40	4.55	1.38		
Month 3	Study	40	7.28	1.66	6.823	0.0005**
	Control	40	5.05	1.22		

Independent-samples t-test, **Highly statistically significant ($p<0.01$). n: Number of eyes, SD: Standard deviation

Table 5. Comparison of Schirmer's test results between the groups

Schirmer's test (mm)	Group	n	Mean	SD	t	p
Day 0	Study	40	4.3	2.1	2.867	0.005**
	Control	40	3.2	1.0		
Week 1	Study	40	5.9	2.1	6.631	0.0005**
	Control	40	3.5	0.9		
Month 1	Study	40	7.5	1.9	9.391	0.0005**
	Control	40	4.4	0.8		
Month 3	Study	40	9.7	1.1	20.093	0.0005**
	Control	40	5.2	0.9		

Independent-samples t-test, **Highly statistically significant ($p<0.01$). n: Number of eyes, SD: Standard deviation

Table 6. Comparison of corneal fluorescein staining between the groups

Fluorescein staining score	Group	n	Mean	SD	t	p
Day 0	Study	40	3.23	0.89	3.826	0.0005**
	Control	40	3.98	0.86		
Week 1	Study	40	3.03	1.03	3.051	0.003**
	Control	40	3.63	0.70		
Month 1	Study	40	2.45	0.78	4.787	0.0005**
	Control	40	3.20	0.61		
Month 3	Study	40	1.33	0.66	8.589	0.0005**
	Control	40	2.60	0.67		

Independent-samples t-test, **Highly statistically significant ($p<0.01$). n: Number of eyes, SD: Standard deviation

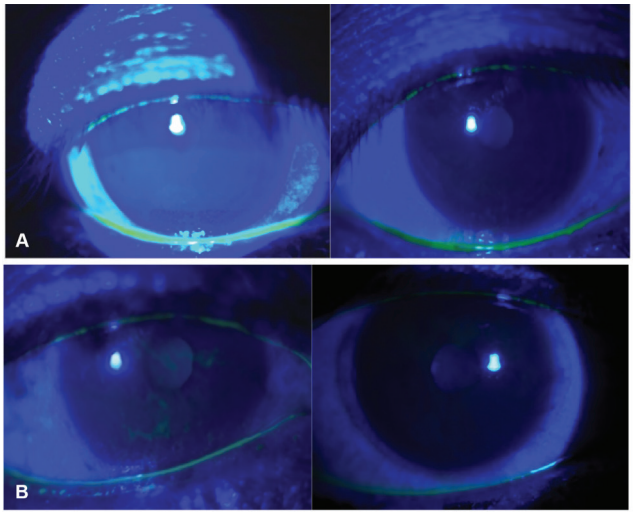

Figure 2. Pre- and posttreatment corneal fluorescein staining in the study group (A) and control group (B)

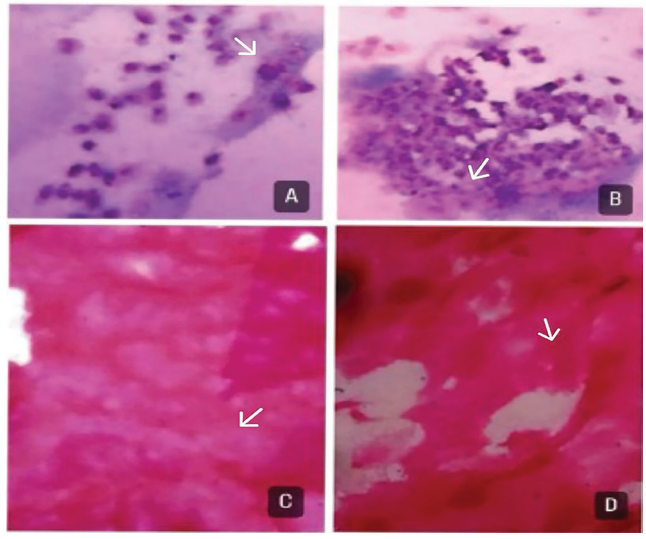

Figure 3. Pre- and posttreatment conjunctival impression cytology images from the study group. A) Complete loss of cohesion with enucleated cells and severe keratinization (grade 3) on day 0 (Papanicolaou stain, 40x). B) Loss of cohesion in the form of clusters with a nucleus-to-cytoplasm ratio of 1:3 to 1:4 (grade 1) after 3 months of treatment (Papanicolaou stain, 40x). C) Mucin spot/occasional goblet cells (grade 3) on day 0 (periodic acid-Schiff stain, 40x). D) Mild reduction of goblet cells (grade 1) after 3 months of treatment (periodic acid-Schiff stain, 40x)

Table 7. Comparison of impression cytology scores between the groups

Impression cytology score	Group	n	Mean	SD	t	p
Day 0	Study	40	1.98	0.83	0.291	0.772
	Control	40	2.03	0.70		
Month 3	Study	40	0.98	0.83	5.039	0.0005**
	Control	40	1.90	0.81		

Independent-samples t-test, **Highly statistically significant (p<0.01). n: Number of eyes, SD: Standard deviation

Table 8. Summarized results

Main outcome measures	Study group (mean±SD)		Control group (mean±SD)		p*
	Day 0	Month 3	Day 0	Month 3	
OSDI	71.95±9.10	38.90±9.00	72.00±8.91	61.55±10.14	0.0005
BCVA (logMAR)	0.12±0.11	0.10±0.11	0.12±0.14	0.13±0.16	0.325
TMH (µm)	188.38±.56.37	262.20±48.74	199.13±.55.31	208.18±56.57	0.0005
TBUT (s)	3.63±0.84	7.28±1.66	3.75±1.33	5.05±1.22	0.0005
Schirmer's (mm)	4.3±2.1	9.7±1.1	3.2±1.0	5.2±0.9	0.0005
CFS score	3.23±0.89	1.33±0.66	3.98±0.86	2.60±0.67	0.0005
CIC score	1.98±0.83	0.98±0.83	2.03±0.70	1.90±0.81	0.0005

*p values for intergroup comparison of month-3 values. OSDI: Ocular Surface Disease Index, BCVA: Best corrected visual acuity, logMAR: Logarithm of the minimum angle of resolution, TMH: Tear meniscus height, TBUT: Tear break-up time, CFS: Corneal fluorescein staining, CIC: Conjunctival impression cytology, SD: Standard deviation

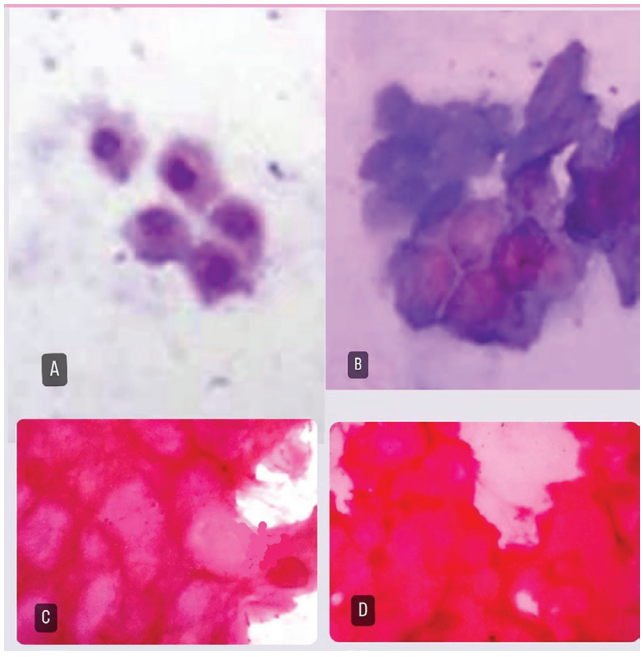

Figure 4. Pre- and posttreatment conjunctival impression cytology images from the control group. A) Scattered cells with a nucleus-to-cytoplasm (N:C) ratio ≥ 1:5 (grade 2) on day 0 (Papanicolaou stain, 40x). B) Loss of cohesion in the form of clusters with N:C of 1:3 to 1:4 (grade 1) after 3 months (Papanicolaou stain, 40x). C) Moderate reduction of goblet cells (grade 2) on day 0 (periodic acid-Schiff stain, 40x). D) Moderate reduction of goblet cells (grade 2) after 3 months (periodic acid-Schiff stain, 40x)

Table 9. Main outcomes after 3 months of autologous platelet-rich plasma treatment

Main outcome measures	Result	Study group (n=20)	Control group (n=20)
OSDI	Severe dry eye	0 (0%)	11 (55%)
	Moderate dry eye	5 (25%)	9 (45%)
	Mild dry eye	13 (65%)	1 (5%)
	Normal	2 (10%)	0 (0%)
BCVA	≥1 line gain	5 (25%)	1 (5%)
	No gain	15 (75%)	14 (70%)
	Loss	0 (0%)	5 (25%)
CIC	Improvement	20 (100%)	0.5 (2.5%)
	No change	0 (0%)	16 (80%)
	Worsening	0 (0%)	3.5 (17.5%)
CFS	Stain negative	9 (45%)	0 (0%)
	Improvement	11 (55%)	9 (45%)
	No change	0 (0%)	8 (40%)
	Worsening	0 (0%)	3 (15%)

n: Number of patients, OSDI: Ocular Surface Disease Index, BCVA: Best corrected visual acuity, CIC: Conjunctival impression cytology, CFS: Corneal fluorescein staining

Discussion

DED is a major problem that affects millions of people globally and is currently one of the leading reasons individuals see an ophthalmologist.[5] It lowers quality of life with incapacitating symptoms and frequent lubricant instillations.

The most commonly used therapy for dry eye is still the conventional approach, such as using artificial tears.[8] According to Drew et al.[9], there is a notable resemblance between tears and plasma since they originate from the same source and may have similar effects on the ocular surface. In an observational study by Alio et al.[10], improvements were noted in corneal staining, conjunctival impression cytology, conjunctival hyperemia, and symptoms in individuals with symptomatic dry eye treated with aPRP. These differences in impression cytology and corneal staining have been associated with tissue regeneration, which may be linked to the superior regenerative capacity of aPRP over autologous serum. According to a study by López-Plandolit et al.[11], Schirmer's test results and clinical symptoms also improved, but the degree of conjunctival metaplasia did not change significantly.

A decrease in OSDI score was seen with both treatment modalities in our group. By 3 months, the mean OSDI improved to 38.90 in the study group versus 61.55 in the controls (p=0.0005). The substantial improvement in symptomatology we observed with aPRP is similar to that reported in other studies.[10,11] Numerous studies have demonstrated a significant decrease in OSDI scores when using plasma rich in growth factors in dry eyes.[11,12,13,14,15]

Regarding visual changes, the improvements in BCVA in the study group, while potentially clinically relevant, did not reach statistical significance when compared to the control group over the study duration. In their study, Alio et al.[10] discovered that only 28% of patients receiving aPRP had a visual improvement of one line or more. In contrast, studies by Emam et al.[16], García-Concha et al.[12], and Rawat et al.[13] showed statistically significant improvement in BCVA in the aPRP-treated groups. Epithelial damage and tear film instability are factors contributing to visual deterioration in dry eye. Improvement in these factors with treatment leads to improved visual acuity.[17,18]

The study group exhibited a substantial increase in tear meniscus height from 188.38 µm at baseline to 262.20 µm at 3 months. This was significantly greater than the change from 199.13 µm to 208.18 µm seen in controls (p=0.0005). The progressive increase in tear meniscus height in the study group suggests that aPRP treatment may be effective in enhancing tear film stability over time, which could be beneficial for patients with tear film-related eye conditions. Similar results were also reported by Alio et al.[10] and observed in a retrospective study by Murtaza et al.[19] in eyes with evaporative dry eye secondary to meibomian gland disease.

In our study, significant changes in TBUT from baseline were observed at 1 month. The improvement in the study group was even more pronounced at 3 months (7.28 s vs. 5.05 s

in the control group, p=0.0005). This suggests enhanced ocular surface health and may reflect the therapeutic benefits of aPRP in maintaining a stable tear film. Emam et al.[16] reported that aPRP as a monotherapy led to a significant increase in TBUT when compared to artificial tears (hyaluronic acid). After aPRP therapy, Alio et al.[10] observed that 46% of the subjects showed an improvement in TBUT of more than 2 seconds. Rawat et al.[13] also reported that TBUT increased by more than 2 seconds in 42.6% and 1-2 seconds in 57.4% of cases in their aPRP group.

We assessed the effect of therapies on tear film volume in our sample by examining Schirmer's test results. Schirmer's test shows high variability, both in repeated measurements and between examiners. Hence, it is advised to perform all tear parameter testing is the same room conditions (temperature, humidity, and air flow). These environmental factors are important in all dry eye investigations, but especially during Schirmer's test. In our sample, the study group showed a marked increase in tear production by 1 week. This trend continued, with mean Schirmer's test results increasing to 7.5 mm at 1 month and 9.7 mm at 3 months. Both of these values were significantly higher than those in the control group (4.4 mm and 5.20 mm, respectively; p=0.0005). These treatment outcomes may also be attributable to the greater capacity of aPRP for ocular surface regeneration and its impact on acinar cells in the lacrimal glands. Indeed, Avila et al.[20] discovered that Schirmer's test findings were much enhanced by aPRP injections administered in close proximity to the lacrimal gland. According to García-Conca et al.[12], Schirmer's values after using aPRP increased significantly when compared to artificial tears (p<0.05). However, Rawat et al.[13] found no appreciable differences in Schirmer's values in their comparison of aPRP and artificial tears.

The present study revealed a substantial decrease in corneal fluorescein staining scores in both groups. By 3 months, the study group achieved a remarkable mean score of 1.33, significantly lower than the controls' score of 2.60 (p=0.0005). Alio et al.[10] reported similar outcomes, and Rawat et al.[13] also found that aPRP treatment significantly reduced corneal fluorescein staining grade according to the Oxford scale in severe dry eye cases.

Nelson and Wright[21] stated that there is a notable decrease in the quantity of goblet cells in DED. This reduction has been found to have an impact on the stability of the tear film. According to Amparo et al.[22], there was a 17% decrease in cell counts over the interpalpebral region in individuals with dry eyes. We observed in our sample that there was significant improvement in conjunctival impression cytology grade after aPRP therapy. While no difference between the groups was observed on day 0, the grade of conjunctival metaplasia was highly significantly lower in the study group at 3 months. Similar results were reported by Alio et al.[10] and García-Conca et al.[12] for the use of aPRP eye drops in DED and diabetic patients, respectively.

Study Limitations

Our study has some limitations. This is a single-center study; hence the results cannot be generalized to all populations. Secondly, we used 20% aPRP in this study, but 100% aPRP may be more beneficial and can be used in severe to very severe cases.[1] Determining the platelet concentration in the prepared eye drop (which was not performed in this study) may demonstrate a clearer correlation with treatment response.

Conclusion

aPRP eye drops have a distinct edge over conventional treatments when it comes to treating ocular surface illnesses. Rich in cytokines and growth factors, the regenerative qualities of aPRP facilitate a more efficient and natural healing process, accelerating recovery and improving tissue regeneration. This research will add to the literature because it shows that even 20% aPRP is better than conventional treatment. The dry eye parameters are also supported by impression cytology findings, which has not been done in previous studies of aPRP.

Ethics

Ethics Committee Approval: The study was initiated after approval from the ethics council of MLN Medical College, Prayagraj (ECR/922/Inst/UP/RR-22 on 5/7/2023).

Informed Consent: Informed consent was obtained from all individuals who participated in the study.

Declarations

Authorship Contributions

Surgical and Medical Practices: K.D., S.S., S.P.S., Concept: K.D., S.S., S.K., Design: S.P.S., S.K., V.K.S., Data Collection or Processing: K.D., S.S., S.P.S., Analysis or Interpretation: K.D., S.S., S.K., V.K.S., Literature Search: K.D., S.S., S.K., V.K.S., Writing: S.K.S., S.K., V.K.S.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Behrens A, Doyle JJ, Stern L, Chuck RS, McDonnell PJ, Azar DT, Dua HS, Hom M, Karpecki PM, Laibson PR, Lemp MA, Meisler DM, Del Castillo JM, O'Brien TP, Pflugfelder SC, Rolando M, Schein OD, Seitz B, Tseng SC, van Setten G, Wilson SE, Yiu SC; Dysfunctional tear syndrome study group. Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. Cornea. 2006;25:900-907.
2. Gupta N, Prasad I, Jain R, D'Souza P. Estimating the prevalence of dry eye among Indian patients attending a tertiary ophthalmology clinic. Ann Trop Med Parasitol. 2010;104:247-255.
3. Shah S, Jani H. Prevalence and associated factors of dry eye: our experience in patients above 40 years of age at a Tertiary Care Center. Oman J Ophthalmol. 2015;8:151-156.
4. Craig JP, Nelson JD, Azar DT, Belmonte C, Bron AJ, Chauhan SK, de Paiva CS, Gomes JAP, Hammitt KM, Jones L, Nichols JJ, Nichols KK, Novack GD, Stapleton FJ, Willcox MDP, Wolffsohn JS, Sullivan DA. TFOS DEWS II report executive summary. Ocul Surf. 2017;15:802-812.

5. Titiyal JS, Falera RC, Kaur M, Sharma V, Sharma N. Prevalence and risk factors of dry eye disease in North India: ocular surface disease index-based cross-sectional hospital study. Indian J Ophthalmol. 2018;66:207-211.
6. Anitua E, Andia I, Ardanza B, Nurden P, Nurden AT. Autologous platelets as a source of proteins for healing and tissue regeneration. Thromb Haemost. 2004;91:4-15.
7. Kwaku Akowuah P, Junior Obinwanne C, Owusu E, Kyeremeh S, Bonsu K, Karikari LAA, Akyaa Akomeah F, Kyei Nkansah E, Kobia-Acquah E. Platelet-rich plasma for treating dry eye disease - a systematic review and meta-analysis. Cont Lens Anterior Eye. 2024;47:102091.
8. Thulasi P, Djalilian AR. Update in current diagnostics and therapeutics of dry eye disease. Ophthalmology. 2017;124:S27-S33.
9. Drew VJ, Tseng CL, Seghatchian J, Burnouf T. Reflections on dry eye syndrome treatment: therapeutic role of blood products. Front Med (Lausanne). 2018;5:33.
10. Alio JL, Colecha JR, Pastor S, Rodriguez A, Artola A. Symptomatic dry eye treatment with autologous platelet-rich plasma. Ophthalmic Res. 2007;39:124-129.
11. López-Plandolit S, Morales MC, Freire V, Grau AE, Durán JA. Efficacy of plasma rich in growth factors for the treatment of dry eye. Cornea. 2011;30:1312-1317.
12. García-Conca V, Abad-Collado M, Hueso-Abancens JR, Mengual-Verdú E, Piñero DP, Aguirre-Balsalobre F, Molina JC. Efficacy and safety of treatment of hyposecretory dry eye with platelet-rich plasma. Acta Ophthalmol. 2019;97:e170-e178.
13. Rawat P, Agrawal R, Bhaisare V, Walia S, Kori N, Gupta R. Autologous platelet-rich plasma eye drop versus artificial tear eye drop for symptomatic dry eye disease: a prospective comparative interventional study. Indian J Ophthalmol. 2022;70:1549-1553.
14. Sanchez-Avila RM, Merayo-Lloves J, Riestra AC, Anitua E, Muruzabal F, Orive G, Fernández-Vega L. The effect of immunologically safe plasma rich in growth factor eye drops in patients with Sjögren syndrome. J Ocul Pharmacol Ther. 2017;33:391-399.
15. Merayo-Lloves J, Sanchez-Avila RM, Riestra AC, Anitua E, Begoña L, Orive G, Fernandez-Vega L. Safety and efficacy of autologous plasma rich in growth factors eye drops for the treatment of evaporative dry eye. Ophthalmic Res. 2016;56:68-73.
16. Emam DHF, El Mashad GY, Alkawas A, El Deen SMS. Evaluating the role of autologous platelet-¬rich-plasma in the treatment of dry eye disease. Egypt J Hosp Med. 2021;84:2065-2070.
17. Kaido M, Matsumoto Y, Shigeno Y, Ishida R, Dogru M, Tsubota K. Corneal fluorescein staining correlates with visual function in dry eye patients. Invest Ophthalmol Vis Sci. 2011;52:9516-9522.
18. Benítez-Del-Castillo J, Labetoulle M, Baudouin C, Rolando M, Akova YA, Aragona P, Geerling G, Merayo-Lloves J, Messmer EM, Boboridis K. Visual acuity and quality of life in dry eye disease: proceedings of the OCEAN group meeting. Ocul Surf. 2017;15:169-178.
19. Murtaza F, Toameh D, Chiu HH, Tam ES, Somani S. Autologous platelet-rich plasma drops for evaporative dry eye disease from meibomian gland dysfunction: a pilot study. Clin Ophthalmol. 2022;16:2199-2208.
20. Avila MY, Igua AM, Mora AM. Randomised, prospective clinical trial of platelet-rich plasma injection in the management of severe dry eye. Br J Ophthalmol. 2018:bjophthalmol-2018-312072.
21. Nelson JD, Wright JC. Conjunctival goblet cell densities in ocular surface disease. Arch Ophthalmol. 1984;102:1049-1051.
22. Amparo F, Wang H, Emami-Naeini P, Karimian P, Dana R. The Ocular Redness Index: a novel automated method for measuring ocular injection. Invest Ophthalmol Vis Sci. 2013;54:4821-4826.