ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 10 | October - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

AUTOLOGOUS PLATELET-RICH PLASMA EYE DROPS FOR THE TREATMENT DRY EYE DISEASE

Ophthalmology

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ABSTRACT

Background: The standard treatment for Dry eye disease is based on reducing inflammation and improving different component of tear film. Autologous serum (AS) has been suggested to be a more efficient treatment for severe DED rather than preservative-free artificial molecules, with varying success rates.

Objective: Present study aimed to assess the role of autologous platelet-rich plasma eye drops for the treatment of dry eye disease.

Patients and Methods: A prospective analysis study was conducted on 50 patients with moderate to severe dry eye disease. Examination included TBUT, Schirmer BCVA and OSDI score. Follow up was done for 1 month.

Results: There was improvement in all parameters and all of them were statistically significant. Symptoms OSDI score decreases to 36.1±14.9 from baseline 62.7±16.1. Similarly, the mean TBUT at the time of baseline measurement was 4.3±1.1 and after follow up of 1 month it was 8.3±2.1;Schirmer at baseline was found to be 8.98±1.6 and after 1 month of follow up it was 14.1±2.5 respectively; and BCVA at baseline was found to be 0.58±0.13and after 1 month of follow up BCVA was 0.84±0.15.

Conclusion: platelet-rich plasma is very potent in treatment of moderate to severe Dry eye disease patients at the level of subjective symptoms, TBUT, CFS, BCVA, and Schirmer test.

KEYWORDS

Dry eye disease, BCVA, OSDI, Schirmer test, TBUT.

INTRODUCTION:

Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles (1).

Dry eye disease (DED) is one of the most popular ocular morbidities. Twenty-five percent of patients who come to Ophthalmic clinics report symptoms of dry eye, making it a growing public health problem and one of the most common conditions seen by ophthalmologists (2).

It has multifactorial etiology which in most cases, is always chronic and progressive. The tear film, cornea, conjunctiva, lacrimal glands and lids work together in a close anatomic and functional relationship as a functional unit to provide an efficient system recognised as the ocular surface. Dry eye is recognized as a consequence of disruption of lacrimal functional unit which consist of lacrimal glands, ocular surface including cornea, conjunctiva, eyelids, meibomian glands, ocular nerves, and goblet cells.(3)

The standard treatment for dry eye is topical use of artificial tears, although the expected results are not satisfying and often ineffective. This has led to the use of other therapeutic methods based on blood derivatives. Autologous serum (AS) has been suggested to be a more efficient treatment for severe DED rather than preservative-free artificial molecules, with varying success rates (4) The idea of using blood-derived topical therapy in treating ocular surface diseases was first presented over 40 years ago by Ralph et al (5).

Platelet rich plasma (PRP) and plasma rich in growth factors (PRGF) have also been reported as successful therapies for moderate to severe dry eye (6). Platelet-rich plasma (PRP) contains more concentrated platelets than whole blood and can be obtained via centrifugation from whole blood mixed with anticoagulant. Platelets are critically important in the wound-healing process. They translocate rapidly to the wound site and adhere to the damaged tissue, initiating a healing reaction that includes the release of a variety of cytokines and growth factors (7).

METHODOLOGY:

A prospective observational study was conducted, it included 50 patients with moderate to severe dry eye disease.

EXCLUSION CRITERIA:

Patient refusal for study
Patient with abnormal platelet count, critical thrombocytopenia
Pregnant and lactating mother

Each patient was subjected to the following:

1- written informed consent
2- Dry eye severity was determined by the Dry Eye Workshop (DEWS) severity scheme. This scheme takes into account the following parameters: ocular discomfort, visual symptoms, conjunctival injection, conjunctival and corneal fluorescein staining (CFS), corneal/ tear signs, lid/meibomian glands, tear film break-up time (TBUT), and Schirmer test score (8).

The study was initiated after approval from the institutional ethical committee.

History includes:

- Demographic data: name, age and gender.
- History of previous ocular or systemic disease.
- History of previous ocular surgery as LASIK surgery.

Ophthalmic examination including:

- Slit lamp examination, evaluation of tear meniscus.
- Schirmer test with anesthesia using a filter paper strip inside the lower eyelid of the two eyes that were tested at the same time.

The patient was asked to close his eyes gently for five minutes. After five minutes, the paper was removed and the moistened strip was measured in millimeters.

- Tear film break up time (TBUT) using fluorescein stain to the cornea and calculating the time between the last blink and the appearance of the first area of break up.
- Best spectacle corrected visual acuity (BCVA) measured by Snellen charts and expressed in decimal.
- Subjective symptoms were evaluated based on the ocular surface disease index (OSDI) self-ad- ministered questionnaire, which was completed once at the time of enrolment in the study (baseline) and again after treatment with E-PRP. OSDI scores range from 0 to 100 according to the severity of the DED symptoms. Patients were also directly asked to report any change in their perception of ocular redness, foreign body sensation, itching, photophobia, dryness, and pain, based on a five-point scale in which 0 = no change, 1 = slight improvement, 2 = moderate improvement, 3 = very good, and 4 = excellent (8).

PRP Preparation

9 ml of whole blood was placed in 10 ml vacutainer tubes containing anticoagulant-citrate-dextrose solution (ACD). Before venipuncture, we use povidone iodine 10% and alcohol swab to scrub. Blood sample was drawn in 10 ml syringe and then transferred 9 ml into ACD tubes. Sample were gently agitated to mix the anticoagulant and centrifugation done at 2000 rpm for 11 min. After centrifugation upper two layer of plasma and buffy coat layer were separated. Around 1-2 ml plasma was collected as final autologous PRP product . The final preparation was stored in 5 ml empty bottle of antibiotic eye drops to avoid any risk of infection and was stored in refrigerator at 4^0C (9).

Patients were instructed to instil the solution 5 times a day and the current bottles were discarded every seven days.

RESULTS:

This study was held on 50 patients with moderate and severe dry eye disease. Average age was (62.1±17.3) range from 36 years to 90 years. They were 44 females (88%) and 6 males (12%). Here, common cause of dry eye was found to be chemical injury (64%) followed by idiopathic cause (14%), Diabetic dry eye and Rheumatoid dry eye (8%) and Recurrent corneal erosion was found in 6% cases.

Table: 1 Etiology of dry eye

Reason of dry eye	Number	%
Chemical injury	32	64%
Idiopathic	7	14%
Diabetic dry eye	4	8%
Recurrent corneal erosion	3	6%
Rheumatoid dry eye	4	8%

Here, the mean OSDI at baseline was found to be 62.7±16.1 at after 15 days it was 50.3±14.2 and after 1 month of follow up OSDI decreases to 36.1±14.9. Similarly, the mean TBUT at the time of baseline measurement was 4.3±1.1, after 15 days it was 6.4±1.7 and after follow up of 1 month it was 8.3±2.1;Schirmer at baseline was found to be 8.98±1.6, after 15 days it was 11.8±2.1 and after 1 month of follow up it was 14.1±2.5 respectively; and BCVA at baseline was found to be 0.58±0.13, after 15 days it was 0.72±0.13 and after 1 month of follow up BCVA was 0.84±0.15 (Table: 1).

Table: 1 Pre and post comparison in patients received PRP regard symptom score, TBUT, Schirmer, and BCVA

	Variable	Baseline	after 15 days	After 1 month	P-value
OSDI	Mean	62.7	50.3	36.1	0.0001
	SD	16.1	14.2	14.9	
TBUT	Mean	4.3	6.4	8.36	0.0042
	SD	1.1	1.7	2.1	
Schirmer	Mean	8.98	11.8	14.1	0.001
	SD	1.6	2.1	2.5	
BCVA	Mean	0.58	0.72	0.84	0.0078
	SD	0.13	0.13	0.15	

Regarding to symptoms of Dry Eye Disease evaluated by OSDI questionnaire there is a great decrease in the score of OSDI, indicating a decrease in dry eye symptoms from (62.7±16.1) pre-treatment to (36.1±14.9) post treatment (P value =0.001) which is statistically significant,. Figure 1.

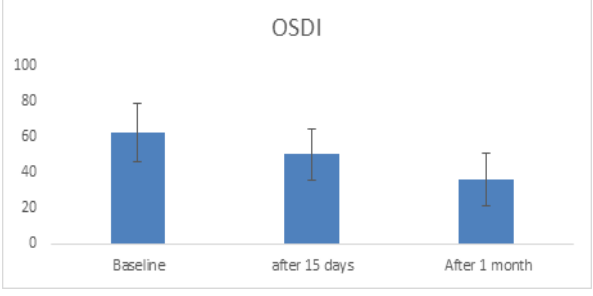

Fig: 1 Pre and post comparison in patients received PRP regard OSDI

Regarding to Schirmer test it also show an improvement from (8.98±1.6) to (14.1±2.5) P value = 0.001 which is statistically significant. Figure 2

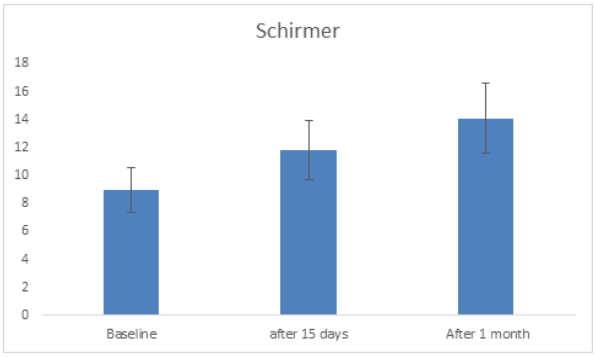

Fig: 2 Pre and post comparison in patients received PRP regard Schirmer

Regarding to TBUT there was an improvement in break up time in seconds from (4.3±1.1) pre-treatment to (8.36±2.1) post treatment, (P value=0.004) which is statistically significant. Figure 3.

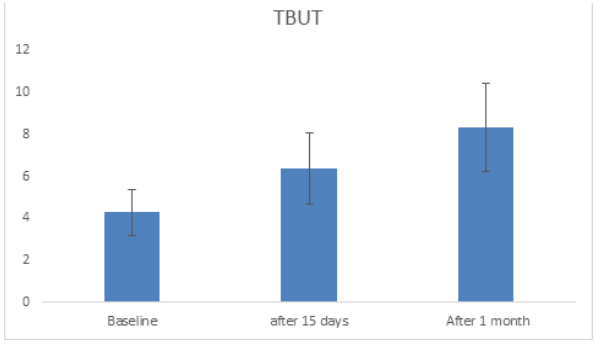

Fig: 3 Pre and post comparison in patients received PRP regard TBUT

Regarding to BCVA there was an improvement from (0.58±0.13) to (0.84±0.15) P value=0.0078 which is statistically significant. Figure 4

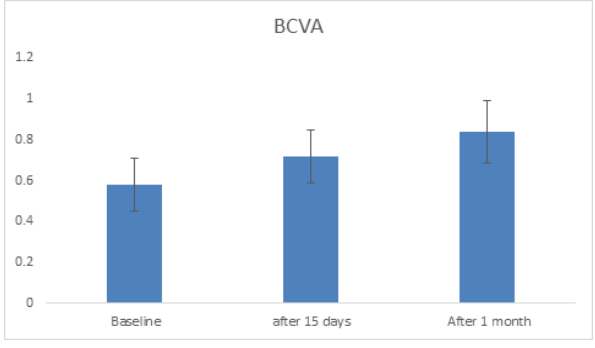

Fig: 4 Pre and post comparison in patients received PRP regard BCVA

DISCUSSION:

Dry eye disease is a group of entities with an ocular surface disorder with varying degrees of severity. Some patients experience mild symptoms and some experienced advanced symptoms like complications of keratoconjunctivitis sicca such as infection, epithelial metaplasia, glandular dysfunction, and neurotrophic damage. The frequently accounted problem in patients with dry eye disease was sandy-gritty eye irritation, burning, intermittent sharp pain (10). DED can also affect visual acuity due to tear film instability and induction of corneal irregularity. (8)

The use of artificial tears still remains the most commonly used option of treatment in dry eye (11). However, an artificial tear is a pharmaceutical product that tries to simulate the properties of the true tears of our eyes in terms of water composition, fluidity, osmolarity, pH and surface tension, being far from resembling them (12).

As a new alternative, plasma rich in growth factors (PRGF) is a hemoderivative product, which is different from AS, and has been proposed for the treatment of DED. An experimental study showed that PRGF exerts more potent proliferative and anti-inflammatory

effects than AS on a cell culture inflammatory model. Similar to PRGF, autologous PRP has been proposed for the treatment of dry eye syndrome with some theoretical advantages. Autologous PRP is a preservative-free biological product from the patient's own blood and due to the presence of platelets and many biological active agents, PRP assists in the healing process. Autologous PRP has been successfully implemented in ophthalmology and can be stored at -20 °C for up to 3 months maintaining constant or slight variations in the concentration of the most important growth factors (8)

Present study was conducted on 50 patients with mean age 62.1±17.1 years. There were 44 females and 6 males. Here, the mean OSDI at baseline was found to be 62.7±16.1 at after 15 days it was 50.3±14.2 and after 1 month of follow up OSDI increases to 36.1±14.9. Similarly, the mean TBUT at the time of baseline measurement was 4.3±1.1, after 15 days it was 6.4±1.7 and after follow up of 1 month it was 8.3±2.1;Schirmer was 8.98±1.6, 11.8±2.1 and 14.1±2.5 respectively; and BCVA was 0.58±0.13, 0.72±0.13 and 0.84±0.15 respectively. Thus in our study OSDI score decreased indicating improvement of 58% from baseline. TBUT improved 93%, of cases. Schirmer test improved 57.1% and BCVA improved 44.8% from baseline values. In a study by Wahdan et al found Symptoms OSDI score decreased indicating improvement in 86.6% of patients (6).

TBUT improved in 66.6% of cases. CFS improved up to disappearance of staining in 33% of cases and fair improvement in 53.3%, total improvement was 86.6%. Schirmer test improved in (40%) of cases. BCVA improved in (26.6%) of patients, improvement was not more than one line.

In a study by Alio et al. (9) on 368 cases of moderate and severe DED, 297(80.7%) patients were women, and 71 (19.3%) were men. 232(63%) patients had EDED, while136 (37%) had ADDED. After 6 weeks of monotherapy treatment with autologous PRP, Dry eye symptoms improved in 322 (87.5%) cases. a decrease of CFS was observed in 280 (76.1%) patients. 106(28.8%) patients improved at least 1 line of BCVA. The scores in the ocular Surface Disease Index and the Oxford scale of corneal fluorescein staining decreased statistically after the treatment (p value <0.05). Results at this study were near our study, but CFS improved more in our study, may be due to the more enriched PRP (1.90) we used and the fresh plasma used as mentioned before.

Another study by Alio et al. (13) a prospective, nonrandomized, observational consecutive pilot study that included 36 eyes of 18 patients with moderate to severe dry eye disease. E-PRP was given topically as eye drops (4-6 times a day per eye) to patients suffering from moderate to severe dry eye symptoms. After 1 month of treatment with PRP eye drops 89% of the patients came with improvement of subjective symptoms. BCVA improved in the 2 studies one line or more, but in our study just one line, may be due to insufficient PRP frequency (4 times per day).

In another study; Ribeiro et al. (14) on treatment of DED in diabetic patients, a prospective interventional study; 12 patients were treated with autologous PRP eye drops four times a day for a month. Resulted in: 100% of patients had symptomatic improvement regarding dryness, itching, burning and redness (p=0.002). Five patients, 41.66% (5/12) had improvement of 1 or more lines of visual acuity in both eyes, Schirmer test improved in 66.66% (8/12) of patients,25% (3/12) had no alteration in this test value and 8.33% (1/12) had a reduced value the value of BUT test 58.33% (7/12) had improvement in the test value and 41.66% (5/12) had no alteration in this test value (p=0.018) symptoms and Schirmer values improved in this study more than our study, may be due to using two spin methods of PRP preparation which give an enrichment more than one spin method but less plasma volume.

CONCLUSION:

Monotherapy with autologous PRP eye drops has shown to be a very good option for the treatment of moderate to severe chronic DED. Significant advantages are ease of preparation, absence of preservatives, its autologous origin, safety, and minimal or no intolerance. A significant clinical improvement after treatment with PRGF eye drops, in signs and symptoms were found. Although more clinical studies are needed, treatment with PRGF eye drops could be considered a possible therapeutic option.

REFERENCES

1. Craig JP, Nelson JD, Azar DT, Belmonte C, Bron AJ, Chauhan SK, et al. TFOS DEWS II Report Executive Summary. Ocul Surf. 2017 Oct;15(4):802-812.
2. O'Brien PD and Collum LM. Dry eye: diagnosis and current treatment strategies. Curr Allergy Asthma Rep. 2004 Jul;4(4):314-9.
3. Lang JC and Roehrs RE, Ophthalmic preparations in Remington: The Science and Practise of Pharmacy, Troy DB, (Ed.), vol 1, pp 850-854, Lippincott Williaims Wilkins, Philadelphia, 21st edition, 2005.
4. Hussain M, Shtein RM, Sugar A, Soong HK, Woodward MA, DeLoss K et al. Long-term use of autologous serum 50% eye drops for the treatment of dry eye disease. Cornea. 2014 Dec;33(12):1245-51.
5. Ralph RA, Doane MG, Dohlman CH. Clinical experience with a mobile ocular perfusion pump. Arch Ophthalmol 1975; 93: 1039-43.
6. Wahdan, M., Ibrahim, M., Elaraby, M. Assessment of Autologous (Platelet-Rich-Plasma) as A Monotherapy for Treatment of Dry Eye Disease. The Egyptian Journal of Hospital Medicine, 2019; 76(5): 4092-4098.
7. Lee JH, Kim MJ, Ha SW, Kim HK. Autologous Platelet-rich Plasma Eye Drops in the Treatment of Recurrent Corneal Erosions. Korean J Ophthalmol. 2016 Apr;30(2):101-7.
8. Alio JL, Rodriguez AE, Ferreira-Oliveira R, Wróbel-Dudzińska D, Abdelghany AA. Treatment of Dry Eye Disease with Autologous Platelet-Rich Plasma: A Prospective, Interventional, Non-Randomized Study. Ophthalmol Ther. 2017 Dec;6(2):285-293.
9. Boehlen F, Clemetson KJ Platelet chemokines and their receptors: what is their relevance to platelet storage and transfusion practice Transfus Med. 2001: 11:403-417.
10. Nichols KK, Nichols JJ, Mitchell GL. The lack of association between signs and symptoms in patients with dry eye disease. Cornea. 2004;23(8):762–70.
11. Thulasi P, Djalilian AR2. Update in Current Diagnostics and Therapeutics of Dry Eye Disease. Ophthalmology. 2017 Nov;124(11S):S27-S33.
12. Drew VJ, Tseng CL, Seghatchian J, Burnouf T. Reflections on Dry Eye Syndrome Treatment: Therapeutic Role of Blood Products. Front Med (Lausanne). 2018 Feb 23;5:33.
13. Alio JL, Colecha JR, Pastor S, Rodriguez A, Artola A. Symptomatic dry eye treatment with autologous platelet-rich plasma. Ophthalmic Res. 2007;39(3):124-9. Epub 2007 Mar 19.
14. Rezende RMVM, Timbó BF, Feliciano RLE, Costa LCM, Gusmão LJMA, Lima GV, et al . Platelet-rich plasma in diabetic dry eye disease. Rev. bras.oftalmol. 2016 Aug; 75(4): 308-313.