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Research Article

Treatment of Chronic Dry Eye Disease with Autologous Platelet Rich Plasma

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Keywords

- Chronic eye disease; Autologous platelet rich plasma; Treatment of dry eye

Abstract

Purpose: Dry eye disease (DED), is a chronic condition affect ocular surface and tears. We intended to evaluate the efficacy of autologous platelet rich plasma (PRP), topical eye drops in chronic dry eye diseases.

Methods: A prospective study that included 40 eyes from 20 patients with symptomatic Dry eye at Outpatient clinic of Department of Ophthalmology, Benha University Hospitals, Egypt. All patients included in the study were subjected to full history taking and the following ophthalmic examination (before and after treatment), including: Slit lamp examination, Schirmer test, Tear film break up time (TBUT), Corneal fluorescein staining (CFS), Best spectacle corrected visual acuity (BCVA), and A questionnaire of Ocular Surface Disease Index (OSDI). The patients underwent these examinations before the beginning of the treatment with autologous platelet rich plasma (PRP), topical eye drops (5 times a day per eye), and then the examinations were repeated after one month of the utilization of (PRP), topical eye drops.

Results: The mean (SD), of ODSI score before treatment was higher as compared with the ODSI score after treatment. The mean (SD), of value of Schirmer, TF-BUT and corneal fluorescein staining test before treatment was lower as compared with the values after treatment with high statistically significantly difference between the two values in both eyes ($P < 0.001$).

Regarding visual acuity after treatment by platelet rich plasma, in the right eyes, there were 6 eyes with Gain 1 or more line while 14 eyes showed no gain in visual acuity. Also, in the left eyes, there were 6 eyes with Gain 1 or more line while 14 eyes showed no gain in visual acuity

Conclusion: A major reduction in symptoms and various parameters of dry eye disease is consistent with PRP eye drops.

INTRODUCTION

Dry eye disease (DED), is a chronic disorder affecting the tears and the outer surface of the eyeball. This disease produces symptoms such as disturbance of vision, discomfort, and instability of the tear film with probable damaging of the eye surface. Additionally, this disease is commonly associated with presence of an inflammatory process affecting the eye surface and increasing the osmolarity of the tear film [1].

Dry eye is a multifactorial disease which is commonly associated with different risk factors such as female gender, deficiency of omega-3, menopause, and systemic anti-histaminics [2].

There are other factors which can lead to precipitation and/or exacerbation of dry eye disease involving wearing contact lens for long-time, cornea refractive operations, computer utilization for visual tasks for long periods of time, smoking, watching television and reading for long periods of time [3].

The pathophysiological factors leading to the development of dry eye disease include reduced production of tears, excessive evaporation of tears, and aberration in the lipids or mucus production of tear film. The aqueous deficient dry eye disease (ADDED), shows an inadequate tears volume because of lacrimal glands dysfunction and lacrimal gland ducts obstruction. Additionally, this mechanism is correlated with certain autoimmune diseases including Sjögren's syndrome. The dysfunction of Meibomian gland and the problems affecting the eyelid (ectropion, entropion, infrequent blinking) are the usual reasons for the development of evaporative dry eye. Deficient quality of the tear film is caused by hyperosmolarity of tears and deficiency of the mucin of the goblet cells [1].

It is important to state that the artificial tears topical administration is the chief standard medical therapy for the management of dry eye, on the other hand the predictable outcomes are not optimum and sometimes not effective. For a long time, a substance has been required and searched for having the same composition and features of tears that principally, may stimulate the biologic regeneration of the affected parts on the outer surface of the eye [4].

Additionally, it has been recognized that PRP plasma rich in growth factors (PRGF) are efficient therapies for the severe and moderate cases suffering from dry eyes that profit from greater concentrations of growth factors, anti-inflammatory cytokines, and other derivatives of platelets [5]. We have aimed to make an evaluation of the efficacy of topical PRP eye drops in the management of chronic DED.

MATERIALS AND METHODS

The study is a prospective study which included 40 eyes from 20 patients suffering from symptomatic DED at the Outpatient clinic of Department of Ophthalmology, Benha University Hospitals, Egypt during the period between 1 September 2019 and 1 July 2020.

An informed written consent in Arabic was attained from all the cases prior to inclusion in the study.

We included subjects suffering from symptomatic DED for ≥ 6 months with Schirmer test <10 mm in 5 min, tear break-up time (TBUT), less than 10 seconds and fluorescein staining of cornea ≥ 2.

Cases with synchronized systemic antibiotics utilization, pregnant women, wearing contact lenses, patients suffering from active allergy or infection of the eyes and abnormal blinking or difficult closing of the eye lids were excluded from the study.

Study procedures

- All the cases underwent full history taking and ophthalmic examination involving: Slit lamp examination: tear meniscus evaluation.
- Schirmer test: with no anesthesia utilizing a filter strip in the inferior eyelid of both eyes that were simultaneously evaluated.
- The patient was asked for closing his eyes softly for 5 minutes. After that, the doctor removes the paper and evaluates the amount of millimeters moistening the paper.
- Tear film break up time (TBUT), utilizing the staining of cornea using fluorescein and measuring the time passing between last blink and the detection of the 1st break up area.
- The measurement of the Corneal fluorescein staining (CFS) was carried out by applying strips of fluorescein to the inferior eye lids then tested by using slit lamp blue filter and the staining of cornea and conjunctiva was assessed utilizing the modified oxford score
- Best corrected visual acuity (BCVA) was evaluated by using Snellen charts and represented in decimal.
- A questionnaire of Ocular Surface Disease Index (OSDI) (self-assessed) was carried out at the beginning of the PRP application and one day subsequent to its complete utilization.

PRP preparation

Autologous PRP preparation and Eye drops: For each subject, collection of 10 mL of whole blood was carried out by venipuncture and after that the sample was put in sterile tubes having 0.5 mL sodium citrate (Becton Dickinson) for the purpose of keeping away from coagulation. The centrifugation of blood was carried out for 10 min. Then the isolation plasma can be performed (about 5 mL/subject). The bottom (about 4 ml), of PRP was put into novel, sterilized amber glass bottles of 10-ml with lubricant eye drop applicators 1:4. Each subject was given a means of transport (ice bag) to preserve the cold chain until reaching his home. The patients were given instructions to preserve the bottle which is under utilization during the week at the refrigerator door (4°C), while the rest was preserved in the freezer. Patients were given instructions to apply eye drops (5 times daily/eye).

Statistical analysis

The data were collected, underwent coding, processing and analysis utilizing the SPSS (Statistical Package for Social Sciences), version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). After that, the data were examined for its normality of distribution utilizing the Shapiro Walk test. The expression of the Quantitative data was represented as mean ± SD (Standard deviation). The Paired samples t-test was utilized for the assessment of the difference between 2 dependent groups of normally distributed variables (parametric data), while Wilcoxon-signed rank test was utilized for the assessment of the difference between 2 dependent groups of abnormally distributed variables (non-parametric data). Marginal Homogeneity test was utilized for the assessment of the difference between 2 dependent groups of categorical variables in >2 classes. Two-sided p-values <0.05 were considered statistically significant.

RESULTS

Our study included 40 eyes from 20 patients complaining of dry eye. The mean of age of the cases in the study was 47.35 ± 12.96 years with range between 20 and 74 years. Among the cases, there were 6 males (30%), and 14 females (70%).

The mean (SD), of the value of ODSI score before treatment was found to be 76.54 ± 7.87 which was higher as compared with the value of ODSI score after treatment that was found to be 30.87± 10.51 and the difference between the two values was found to be statistically highly significant (P< 0.001) (Table 1).

The mean (SD), of value of Schirmer test before treatment in the right eye was found to be 4.45 ± 1.73 mm which was lower as compared with the value of Schirmer test after treatment that was found to be 11.10 ± 1.71 mm while the mean of left eye was found to be 3.55 ± 1.67 which was lower as compared with the value of Schirmer test after treatment that was found to be 11.20 ± 1.54 mm and the difference between the two values in both eyes was found to be statistically highly significant (P< 0.001). Also, the mean (SD), of value of TF-BUT before treatment in the right eye was found to be 3.65 ± 1.46 seconds which was lower as compared with the value of TF-BUT after treatment that was found to be 6.60 ± 1.14 seconds while the mean of left eye was found to be 3.70 ± 1.53 seconds which was lower as compared with the value of TF-BUT after treatment that was found to be 7 ± 1.41 seconds and the difference between the two values in both eyes was found to be statistically highly significant (P< 0.001) (Table 1).

The mean (SD), of value of Corneal fluorescein staining before treatment in the right eye was found to be 3.05 ± 0.60 which was higher as compared with the value of Corneal fluorescein staining after treatment that was found to be 1.05 ± 0.22 while the left eye was found to be 3.40 ± 0.60 which was higher as compared with the value of Corneal fluorescein staining after treatment that was

Table 1: Analysis of OSDI score, Schirmer test, TF-BUT and fluorescein staining of cornea before and after treatment.

Items	Before treatment (N=20)	During treatment (N=20)	Test of significance
ODSI score			
ODSI score	76.54 ± 7.87	30.87± 10.51	**t= 17.218** P< 0.001 *
Schirmer test			
schirmer (mm) [Right Eye]	4.45 ± 1.73	11.10±1.71	**z= -14.626** P< 0.001 *
Schirmer (mm) [Left Eye]	3.55 ± 1.67	11.20 ± 1.54	**z= -16.606** P< 0.001 *
TF-BUT (sec.)			
TF-BUT (sec.) [Right Eye]	3.65 ± 1.46	6.60 ± 1.14	**z= -9.727** P< 0.001 *
TF-BUT (sec.) [Left Eye]	3.70±1.53	7 ± 1.41	**z= -9.903** P< 0.001 *
fluorescein staining of cornea			
Corneal staining [Right Eye]	3.05 ±0.60	1.05± 0.22	**t= 17.218** P< 0.001 *
Corneal staining [Left Eye]	3.40± 0.60	1.15± 0.37	**t= 17.218** P< 0.001 *

Ocular surface disease index
TF-BUT = Tear film break-up time
P: probability.
Data expressed as number ± SD
t: paired samples t-test
z: Wilcoxon Signed rank tets
**: Statistically significant (p< 0.05)*

found to be 1.15 ± 0.37 and the difference between the two values in both eyes was found to be statistically highly significant (P< 0.001) (Table 1).

Regarding visual acuity after treatment by platelet rich plasma, in the right eyes, there were 6 eyes with Gain 1 or more line while 14 eyes showed no gain in visual acuity. Also, in the left eyes, there were 6 eyes with Gain 1 or more line while 14 eyes showed no gain in visual acuity (Table 2).

Table 2: Visual acuity after treatment by platelet rich plasma (PRP).

Items	Right eye (N=20)		Left eye (N=20)	
	N	%	N	%
Gain 1 or more line	6	30	6	30
No gain	14	70	14	70
Reduction	0	0	0	0

Categorical data expressed as Number (%)

DISCUSSION

DED is one of the most common disorders affecting the eye. It is a multifactorial complex disease, affecting the outer surface of the eye through inflammatory and immune reactions [6].

The derivatives of blood as autologous serum or a specific preparation for PRP topical administration have been found to be significant tools of management in enhancing the velocity the process of healing of the outer surface of the eyeball and other dissimilar tissues [7].

In this study, the effectiveness of autologous topically active PRP eye drops in the management of the patients suffering from chronic dry eye has been assessed.

In this study, the mean (SD), of ODSI score before treatment was found to be greater than the mean (SD), of ODSI score after treatment the difference between the 2 values was found to be statistically highly significant (P< 0.001).

This came in agreement with Wahdan, and his colleagues who demonstrated that the DED symptoms which underwent evaluation by using the OSDI questionnaire showed a major reduction in the OSDI score, representing a decline in the symptoms of the dry eye from (64.9 ± 21.1), pretreatment to (40.1 ± 19.5), post treatment (P value =0.001), which was found to be statistically highly significant [8].

This correspondingly agreed with Alio, and his colleagues who found that subsequent to the treatment by using autologous PRP for 1.5 months, the OSDI score showed statistically significant decline subsequent to the treatment (p value <0.05) [9].

In this study, the mean (SD) of the TF-BUT value in the right eye prior to the treatment was found to be 3.65 ± 1.46 sec. in comparison to the TF-BUT value after treatment was found to be 6.60 ± 1.14 sec. The mean (SD), of the TF-BUT value in the left eye prior to treatment was found to 3.70 ± 1.53 sec. in comparison to the TF-BUT value after treatment that was found to be 7 ± 1.41 sec. the difference between the 2 values in both eyes was found to be statistically highly significantly (P< 0.001).

This agreed with Wahdan, and his colleagues who found that TBUT showed an enhancement in the time of break up in seconds

from (4.2 ± 3.1) prior to treatment to (6.3 ± 2.7) subsequent to treatment, (P value=0.004). This difference was found to be significant statistically [8].

In another study carried out by Ribeiro, and his colleagues on the DED treatment of in the patients suffering from diabetes mellitus(DM), 1/12 (8.33%), showed a decreased value of BUT test, 7/12 (58.33%), showed enhancement and 5/12 (41.66%), showed no change (p=0.018) [10]. Furthermore, Urza, and his colleagues detected that the mean of TBUT increased from 4 to 6 seconds with the utilization of autologous serum drops and this difference was found to be significant statistically ($p < 0.05$) [11].

In this study, the score of Schirmer test was found to be improved in the patients included in the 2 groups in relation to the values before the beginning of the treatment. The mean (SD), of the Schirmer test value in the right eye prior to the beginning of the treatment was found to be 4.45 ± 1.73 mm that was lesser than the mean (SD), of the Schirmer test value after treatment that was found to be 11.10 ± 1.71 mm. Furthermore, the mean (SD), of Schirmer test value in the left eye before treatment was found to be 3.55 ± 1.67 that was lesser than the the mean (SD), of the Schirmer test value after treatment that was found to be 11.20 ± 1.54 mm. the difference between the 2 values in both eyes was found to be statistically highly significant (P<0.001).

This came within the same context with Alio, and his colleagues who found that the value of Schirmer's test in the patients suffering from evaporative DED had significant improvement from 9.5 ± 3.6 mm to 13.8 ± 8.7 after the treatment ($p < 0.05$), and in the patients having ADDED showed significant improvement from 4.7 ± 2.7 to 6.4 ± 2.4 ($p < 0.05$) [9].

In line with Celebi, and his colleagues, the difference between the mean (SD) of the value of Schirmer Test before the beginning and after the 1st 4 weeks of treatment was found to be statistically highly significant (P < 0.001) [12].

In this study, the mean (SD), of fluorescein staining value before treatment was found to be greater in comparison to the mean (SD), of the Corneal fluorescein staining (CFS), value after treatment and this difference between the 2 values in both eyes was found to be statistically highly significant (P<0.001).

Our results moreover agreed with Conca, and his colleagues who established that the staining of cornea and conjunctiva after the treatment by using PRP showed statistically highly significant decrease (p<0.001). additionally, the staining of the Conjunctiva decreased in both eyes at just 2 weeks (p=0.020), and the staining of cornea decreased in RE after 2 weeks (p=0.020), this difference of both values between both eyes was found to be statistically not significant [13].

This came in accordance with Tananuvat who stated that the mean for Rose Bengal stain was found to be the same for both control and 20% AS groups at 4 weeks follow-up (mean 4.22 points for both groups) [14].

In both eyes, there were 6 eyes with Gain 1 or more line while 14 eyes have no gain in visual acuity. The percentage of improvement is 30% in each of both eyes.

Comparable results were detected by Wahdan and his colleagues who found that in accordance with the improvement of BCVA, improvement of 4 cases (26.6%) was found to be not >1 line [8].

In a study carried out by Alio, and his colleagues on 368 patients suffering from severe and moderate DED, they reported that 106 (28.8%), cases showed improvement at least 1 line of BCVA [9].

This study still has some limitations as the small size of sample, lack of a control group and the shorter duration of monitoring.

Also, this study is a single center study that decreases the power of the study.

CONCLUSION

We can conclude that use of PRP eye drops was associated with significant improvement of the symptoms and different parameters of dry eye disease.

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