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Autologous Serum in Dry Eye Disease

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ABSTRACT

Background: The tear film overlays the ocular surface and provides the interface between the eye and the external environment. The tear film is essential for the nutrition and protection of the ocular surface and for clear vision as the tear film is the first refractive surface of the eye.

Aim of the Work: the purpose of this study was to review the efficacy, complications and safety of using autologous serum in dry eye.

Patients and Methods: thirty patients of moderate to severe dry eye selected from Ophthalmology Out-Patient Clinics, Al-Hussein University Hospitals. *All patients were subjected to* Schirmer 1 test, Tear break – up time (TBUT), and Fluorescein clearance test

Results: The mean value of Schirmer 1 test before the use of autologous serum was 2.83 mm ± 0.83 SD while after use of autologous serum was 5.33 mm ± 9.99 SD. The mean value of TBUT test before the use of autologous serum was 9.50 sec ± 1.20 SD while after use of autologous serum was 9.433 sec ± 1.52 SD. The mean value of FCT before the use of autologous serum was 100 % positive while after use of autologous serum was 76.7 % positive. The difference between before and after use of autologous is statistically significant as P-value < 0.001.

Conclusion: this study revealed that autologous serum eye drops were found effective and safe in treatment of severe dry eye disease, as evidenced by improvement in subjective assessment of symptoms, Schirmer's 1teast, tear film break-up time (TBUT) and fluorescein clearance test (FCT).

Keywords: Autologous Serum, Dry Eye Disease

INTRODUCTION

The positive effects of the application of autologous serum in the treatment of dry eye patients are known since 1984 according to the research of Fox et al. However, the lack of knowledge about its action mechanism at the eye surface level kept its utilization in clinical practice from growing until the end of the decade when Tsubota in 1999 described its successful use in eyes with persistent epithelial defects [1,2].

Dry eye disease (DED) is also called keratoconjunctivitis sicca or, more recently, dysfunctional tear syndrome. In 2007, the International Dry Eye Workshop defined it as a multifactorial disorder of the tear film and ocular surface that results in eye discomfort, visual disturbance, and often ocular surface damage[3].

Autologous serum contains various factors that are also present in tears including Vitamin A, Epidermal growth factor, transforming growth factor-β (TGF-β), basic fibroblast growth factor, Insulin like growth factor, Substance P as well as proteins such as lactoferrin and lysozyme [4].

The lack of these epitheliotrophic factors e.g., in dry eye, can result in severe ocular surface disorders such as persistent epithelial defects. In such cases surgical attempts as punctual occlusion, frequently fail [5,6].

Also, with increasing severity of aqueous deficiency, the application frequency of tear substitutes increases, their turnover is reduced, and the ocular surface becomes more susceptible to toxicity from preservatives resulting in corneal blindness. Autologous serum is an unpreserved artificial tear substitute, with slightly hypotonic or physiologic electrolyte composition and biologic buffers, which improves corneal epithelial barrier function, patient comfort and may address parts of the underlying multifactorial pathogenesis of dry eye [7,8].

Since autologous serum preparation is a body fluid, it is able to transmit infections; another drawback of autologous serum treatment lies in the frequent blood extractions, mainly in the groups requiring prolonged treatment [9].

The purpose of this study was to review the efficacy, complications and safety of using autologous serum in dry eye.

PATIENTS AND METHODS

This study included a total of thirty patients of moderate to severe dry eye attending at Ophthalmology Out-Patient Clinics, Al-

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Hussein University Hospitals. Approval of the ethical committee and a written informed consent from all the subjects were obtained. This study was conducted between December and September 2017. **The study was** 6201 **approved by the Ethics Board of Al-Azhar University.**

Exclusion criteria: Patients were excluded if they had the following criteria:

1. Lacrimal gland disease.
2. Lacrimal gland obstruction.

All patients were subjected to the following:

1. History taking.
2. Ophthalmological examination including:
   - Visual acuity assessment.
   - Anterior segment evaluation with the slit lamp bio-microscopy including lid margin for meibomian gland dysfunction, cornea for punctate epithelial erosions, conjunctiva and tear film for debris.
   - Intraocular pressure measurement.
   - Fundus examination using indirect ophthalmoscopy.
3. Investigations of dry eye:
   - Schirmer 1 test
   - Tear break – up time (TBUT)
   - Fluorescein clearance test

Preparation and use of autologous serum eye drops:

Blood was obtained by venipuncture and centrifuged for separation of serum. The serum is carefully separated in a sterile manner and diluted by saline to 20%. The final preparation is divided into 5ml bottles with ultraviolet light protection since vitamin A is easily degraded by light. The bottles are stored in a freezer (ideally at −20°C) until required.

On the day of use the autologous serum is thawed, aspirated through the rubber cap of the sealed vial with a hypodermic needle and syringe, and transferred to a sterile dropper bottle to be used 5 times daily. Once a bottle is thawed for use it is kept stored in a fridge at 4°C between applications. A fresh bottle is thawed and used for treatment every 24 hours.

Statistical Analysis: [10]

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) [11] Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level.

RESULTS

This study included 30 subjects. All live in Cairo. They all were between 53-72 years old. The mean age was 63.01 years ± 5.09 SD. Sex of patients was 18 (60%) females and 12 (40%) males. Table 1 and figure 1 show the demographic data of the patients.

Table (1): Distribution of the studied cases according to demographic data (n=30)

	No.	%
Sex		
Male	12	40.0
Female	18	60.0
Age (years)		
Min. – Max.	53.0 – 72.0	
Mean ± SD.	63.10 ± 5.09	
Median	64.0	

All patients were subjected to history taking, slit lamp examination, fundus examination, the diagnostic tests (Tear break – up time, Fluorescein clearance test and Schirmer 1test) before and after using of autologous serum therapy. Table 2 and figure 2 show the descriptive analysis of the studied cases according to Schirmer's 1 test.

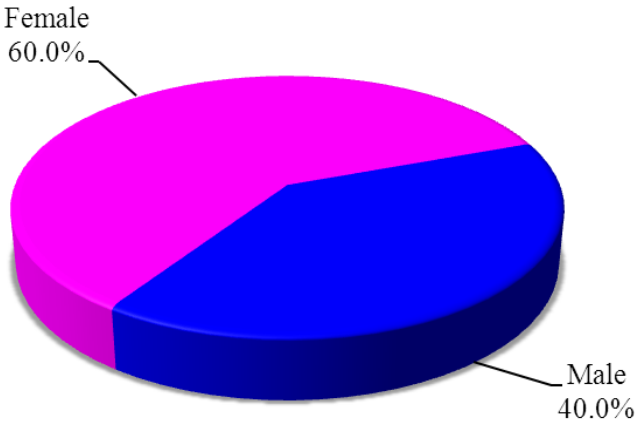

Fig. 1: Distribution of the studied cases according to Sex (n=30).

Table (2): Descriptive analysis of the studied cases according to Schirmer's 1 test (n=30)

	Before autologous serum	2 week after autologous serum	t	P
Schirmer's 1 test				
Min. – Max.	2.0 – 5.0	3.0 – 7.0		
Mean ± SD.	2.83 ± 0.83	5.33 ± 0.99	13.138*	<0.001*
Median	3.0	5.0		

t, p: t and p values for Paired t-test for comparing between before autologous serum and 2 week after autologous serum
*: Statistically significant at $p \leq 0.05$

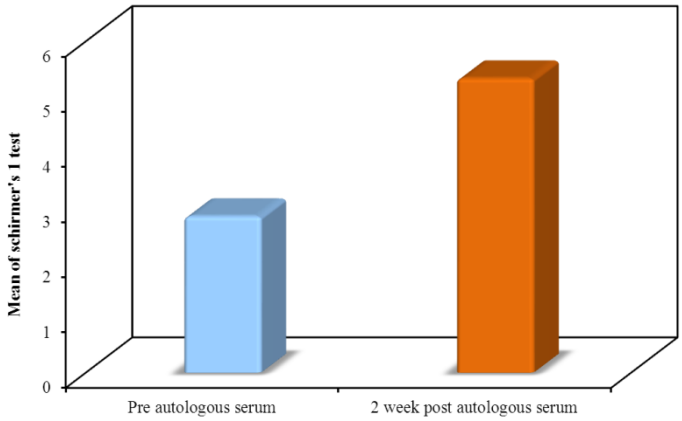

Fig. 2: Descriptive analysis of the studied cases according to schirmer's 1 test (n=30)

Table 3 shows the Schirmer 1test before and after use of autologous serum. There is statistically significant improvement after autologous serum with P value <0.001. Mean Schirmer before the use of autologous serum was 2.83 mm ± 0.83 SD while after use of autologous serum was 5.33 mm ± 9.99 SD.

Table (3): Descriptive analysis of the studied cases according to tear break – up time (TBUT) (n=30)

	Before autologous serum	2 week after autologous serum	t	P
Tear break – up time (TBUT)				
Min. – Max.	4.0 – 9.0	6.0 – 12.0		
Mean ± SD.	6.50 ± 1.20	9.43 ± 1.52	20.469*	<0.001*
Median	6.0	9.0		

t, p: t and p values for Paired t-test for comparing between before autologous serum and 2 week after autologous serum
*: Statistically significant at $p \leq 0.05$

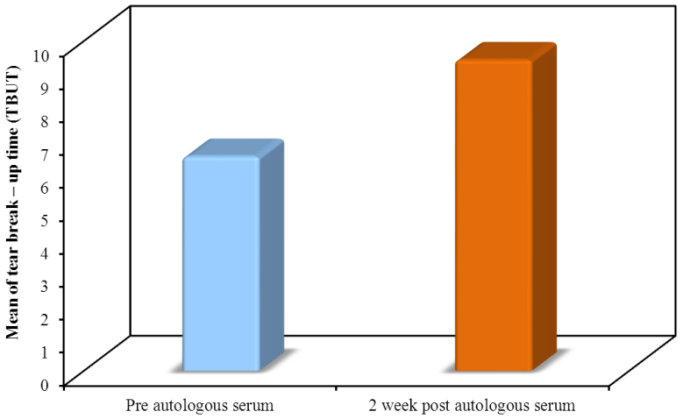

Fig. 3: Descriptive analysis of the studied cases according to tear break – up time (TBUT) (n=30).

Table 4 shows the tear break – up time test (TBUT) before and after use of autologous serum. There is statistically significant improvement after autologous serum with P value <0.001. Mean TBUT before the use of autologous serum was 6.50 sec ± 1.20 SD while after use of autologous serum was 9.433 sec ± 1.52 SD.

Table (4): Distribution of the studied cases according to fluorescein clearance test (n=30)

	Before autologous serum		2 week after autologous serum		McN p
	No.	%	No.	%	
Fluorescein clearance test					
Negative	0	0.0	7	23.3	0.016*
Positive	30	100.0	23	76.7	

McN p: p value for Chi square for McNemar test *: Statistically significant at p ≤ 0.05

Table 5 shows the fluorescein clearance test (FCT) before and after use of autologous serum. There is statistically significant improvement after autologous serum with P value <0.016. FCT before the use of autologous serum was 100 % positive while after use of autologous serum was 76.7 % positive.

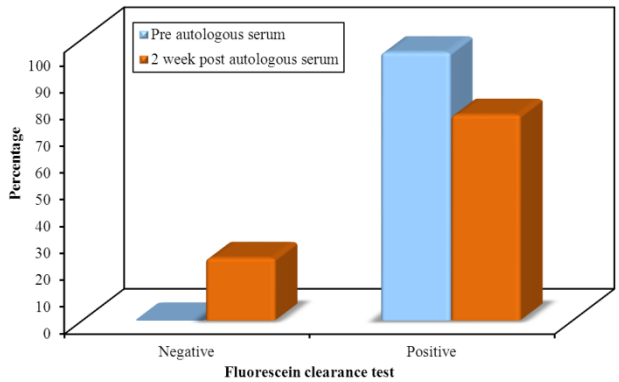

Fig. 4: Distribution of the studied cases according to fluorescein clearance test (n=30)

Complications encountered with autologous serum eye drops were minimal in the form of allergic conjunctivitis and eczema. These encountered in 7 patients only.

DISCUSSION

Dry eye is a common disorder, with an estimated 25% of patients in general ophthalmology. It is known that the incidence of dry eye increases with age and has a higher prevalence in women compared to men [12].

Symptoms of dry eye have been standardized by use of questionnaires. The most common complaints described by patients include dryness or irritation, light sensitivity, foreign body sensation, red eyes and symptom fluctuation in different

environmental conditions. However, it has also been noted that there is no strong correlation between signs and symptoms, particularly in mild dry eye. Therefore, the clinical diagnosis of dry eye needs to incorporate objective tests such as Schirmer's testing, fluorescein clearance and fluorescein breakup time (BUT) [12].

There is no clinical test available that provides a direct measurement of lacrimal gland secretion. Schirmer's 1 test is the most practical and most straightforward indirect test of lacrimal gland function. It measures basal and reflex tear secretion of the main and accessory lacrimal glands and the volume of the marginal tear film and tear lake. Fluorescein dye clearance is other indirect tests of lacrimal secretion, but they are not easily performed as part of a routine clinical examination. Tear BUT measurements assess the stability of the tear film. These tests lack sensitivity and specificity. Therefore, they should be used in combination with other tests to improve diagnostic accuracy [13].

Autologous serum contains various factors that are also present in tears including Vitamin A, Epidermal growth factor, transforming growth factor beta, basic fibroblast growth factor, Insulin like growth factor, Substance P as well as proteins such as lactoferrin and lysozyme. All these factors are essential for healthy functioning of ocular surface [4].

In our study, 30 subjects were enrolled. The age of the subjects ranged between 53 and 72 years of both sexes. Clinical data of all patients which included age, sex as well as a history of other diseases were obtained.

Subjects were excluded if they had lacrimal gland disease. All subjects were subjected to history taking, ophthalmological examination including visual acuity, slit lamp examination, intraocular pressure measurement, fundus examination, Schirmer 1 test, TBUT and fluorescein clearance test.

In our study, the mean value of Schirmer 1 test before the use of autologous serum was 2.83 mm ± 0.83 SD while after use of autologous serum was 5.33 mm ± 9.99 SD. The mean value of TBUT test before the use of autologous serum was 9.50 sec ± 1.20 SD while after use of autologous serum was 9.433 sec ± 1.52 SD. The mean value of FCT before the use of autologous serum was 100 % positive while after use of autologous serum was 76.7 % positive. The difference between before and after use of autologous is statistically significant as P-value < 0.001.

In agreement with that, Pan Q and Angelina A in their study at 2017, showed that 20% AS might provide some benefit in improving patient-reported symptoms over the short term (two weeks), but longer periods of follow-up provide no evidence of improvement over longer periods [14].

Also, Francesco Semeraro and Eliana Forbice in their study at 2014, they found that patients with dry eye disease of different etiologies showed improvement in both clinical signs and symptoms after therapy with AS eye drops [15].

Also, Takashi Kojima in his study at 2008 found significant improvements in tear stability, ocular surface vital staining scores, and pain symptom scores in patients treated with AS eye drops with no side effect [16].

Also, in other study, G Geerling, S MacLennan and D Hartwig show that serum supports viability, proliferation and migration of ocular surface epithelial cells better than unpreserved pharmaceutical tear substitutes [17].

Noda et al evaluated the efficacy of 20% autologous serum eye drops for dry eye after LASIK, by comparing subjective scores, tear function evaluated by Schirmer test and BUT, and ocular surface conditions by vital staining they reported that Rose Bengal score was improved in patients using autologous serum eye drops at 1 month (0.3 ± 0.7) and 3 months (0.1 ± 0.3) after LASIK compared to preoperative values (1.0 ± 1.3), whereas no differences were noted between before and after LASIK in patients using artificial tears [18].

Kojima et al shows that mean tear film breakup time, fluorescein score, Rose Bengal score and subjective symptom scores showed a significant improvement in the patients assigned to AS eye drops compared with those who used preservative-free artificial tears after 2 weeks of treatment [19].

CONCLUSION

The tear film overlays the ocular surface and provides the interface between the eye and the external environment. The tear film is essential for the nutrition and protection

of the ocular surface and for clear vision as the tear film is the first refractive surface of the eye.

Dry eye is a disorder of the tear film which occurs due to tear deficiency or excessive tear evaporation. Dry eye is a common condition reported by patients who seek ophthalmologic care. Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance and tears film instability, with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.

Autologous Serum contains various factors that are also beforesent in tears including Vitamin A, Epidermal growth factor, transforming growth factor beta, basic fibroblast growth factor, Insulin like growth factor, Substance P as well as proteins such as lactoferrin and lysozyme.

30 Egyptian subjects living in Cairo who attended Al-Hussein university hospital were enrolled in the study. All subjects were between 53 – 72 years old. Subjects were excluded if they had 3lacrimal gland disease. Full ophthalmological examination was performed together with Schirmer 1test, TBUT test and FCT to all the cases.

This study revealed that autologous serum eye drops were found effective and safe in treatment of severe dry eye disease, as evidenced by improvement in subjective assessment of symptoms, Schirmer's 1teast, tear film break-up time (TBUT) and fluorescein clearance test (FCT).

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