

Comparative Study of Autologous Serum Ophthalmic Solution versus Tear Substitute as Adjuvant Therapy in Reducing the Symptoms of Ocular Surface Disorders

Vanitha R.¹, Anbuezhian R²

¹Assistant Professor, Department of Ophthalmology, Government Medical College Hospital Krishnagiri

²Consultant, ENT Surgeon, Kauvery Hospital, Hosur

Received: 25-06-2023 / Revised: 28-07-2023 / Accepted: 30-08-2023

Corresponding author: Dr. Anbuezhian R

Conflict of interest: Nil

Abstract:

Introduction: Disruption of the function of ocular surface structures may result in ocular surface disorders (OSD). Treatment for ocular surface disorders includes artificial tears substitutes, temporary or permanent punctal occlusion, bandage contact lenses, and primary treatment of adnexal diseases. Ocular surface disorder is most commonly treated with artificial tear eye substitute. Recently autologous serum eye drops is routinely prescribed as an adjuvant therapy for the treatment ocular surface disorders, like dry eye disorders, neurotrophic keratitis, recurrent corneal erosion, persistent epithelial defects. Aim of our study is to compare the efficacy of autologous serum ophthalmic solution versus tear drops as adjuvant therapy in the reducing the symptoms of ocular surface diseases.

Materials & Methods: This prospective study was conducted in a tertiary care teaching hospital for a period of 6 months. A detailed history of the patient was taken, General Examination and Slit lamp examination, and dilated fundus examination were done. Patients were treated as per the laid down guidelines. In addition patients with odd serial number in category were treated with autologous serum and patients with even serial number were treated with tear drops. Symptom score and above mentioned parameters were recorded during every follow-up. Treatment was continued till symptoms disappear.

Results: In this study of 30 patients, Mean age of the patients is 40.5 yrs and mean age of the patients in group 1 is 39.8yrs and group 2 is 41.87 yrs. There were 8 males and 7 females in Group 1 and 9 males and 6 females in Group 2 as a whole 17 male and 13 females. There is no significant difference in the improvement of symptom score of tearing, blurred vision, and stinging sensation. There was significant difference in improvement of the burning sensation, foreign body sensation and photophobia.

Conclusion: Autologous serum is found to be safe and significantly effective than the artificial tear substitute in the treatment of ocular surface disorders.

Keywords: Autologous Serum, Tear Substitute, Dry Eye.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

The Ocular Surface System includes the surface and glandular epithelia of the cornea, conjunctiva, lacrimal gland accessory lacrimal glands, meibomian glands, and eyelashes with their associated glands of Moll and Zeis, and the nasolacrimal duct. [1] Disruption of the function of ocular surface structures may result in ocular surface disorders. Treatment for ocular surface disorders includes artificial tear substitutes, temporary or permanent punctal occlusion, bandage contact lenses, and primary treatment of adnexal diseases.

Ocular surface disorder is most commonly treated with artificial tear eye substitute. Commercially available artificial tear preparation does not include essential tear components such as growth factors,

vitamins, and immunoglobulins. Artificial tear substitute often contains preservatives, stabilizers, additives, which can induce toxic or allergic reactions. [2]

The majority of patients with dry eyes respond to conventional treatment aimed at optimising the ocular surface microenvironment. The ecosystem of the ocular surface depends on the dynamic interactions of healthy adnexae, adequate blink reflex, normal tear production, and ocular surface tissue, consisting of cornea and conjunctiva. Conventional therapeutic options include intensive tear supplements, punctal occlusion, contact lenses, and appropriate management of adnexal disease.

In spite of maximal conventional therapy there exists a cohort of patients who have persistent symptoms and signs. This represents a more serious ocular surface disorder with patients having significant visual impairment and disability. Autologous serum eye drops have been found in uncontrolled trials to be beneficial in these patients, improving the ocular surface and reducing symptoms. [3-5] A recent controlled trial comparing autologous serum eye drops in one eye with the fellow eye as a control showed a non-statistically significant trend in improvement with serum drops. [6] This effect has been attributed to various factors present in normal tears and serum. [6]

A healthy tear film provides the cornea and conjunctiva with essential components needed to maintain stability. Epidermal growth factor (EGF), nerve growth factor (NGF), vitamin A, and transforming growth factor α and β (TGF- α and - β) are present in tears and confer important proliferative effects on the epithelium. Fibronectin has been suggested to be a scaffold that promotes epithelial healing by facilitating cell attachment. Reduction of these epitheliotropic factors due to disease can lead to epithelial defects. Serum is the fluid part of blood devoid of its cellular components. It contains several growth factors, many in higher concentrations compared to that in tears. In keeping with this, application of human serum appears to be a logical regimen to treat OSD.

Recently autologous serum eye drops is routinely prescribed as an adjuvant therapy for the treatment of ocular surface disorders, like dry eye disorders, neurotrophic keratitis, recurrent corneal erosion, persistent epithelial defects. Human serum apart from providing lubrication, it contains substances such as EGF, vitamin A, TGF- β , fibronectin and interleukins, which are normally found in tears. They are essential for corneal & conjunctival epithelial healing and integrity. [7] Based on this aim of our study is to compare the efficacy of autologous serum ophthalmic solution versus tear drops as adjuvant therapy in the symptomatic reduction of ocular surface diseases.

Materials & Methods

This prospective study was conducted in a tertiary care teaching hospital for a period of 6 months. Patients presenting with ocular surface diseases were registered, evaluated and followed up during the study period in 30 patients. A detailed history of the patient was taken, General Examination and Slit lamp examination, and dilated fundus examination were done. Patients fulfilling the inclusion criteria were sub classified into one of the three following categories and given a serial number. Patients were treated as per the laid down

guidelines. In addition patients with odd serial number in category were treated with autologous serum and patients with even serial number were treated with tear drops. Symptom score and above mentioned parameters were recorded during every follow-up. Treatment was continued till symptoms disappear. Patients with ocular surface diseases due to Severe dry eye, Neurotrophic ulcer and recurrent corneal erosion aged 15-70 years included in our study. Whereas patients with Infectious blood borne diseases (HIV, HBV, HCV and Syphilis), Anemia and known blood dyscrasias, Women who are pregnant or breast-feeding were excluded

Serum is prepared using around 30 ml of blood is extracted from patient's vein without adding anticoagulant. The blood is kept in vertical position in tubes for about 2 hours to allow coagulation. Supernatant fluid is centrifuged to isolate the serum. 20% autologous serum is considered ideal because it contains certain growth factors at a concentration similar to that of natural tears. Higher concentration is likely to cause irritation due to the higher viscosity. Also number of blood extraction is considerably reduced when used at lower concentration.

Separated serum is labeled and preserved at +4°C. Once issued, patients are advised to preserve the serum in the refrigerator at +4°C after use⁵. Autologous serum is protected from direct sun light to prevent degradation of some of the components like Vitamin A. Follow up was done Weekly in the 1st first month and twice weekly in the 2nd month. Results of the patients were analyzed for statistical significance with unpaired and chi Square test.

Results

In this study of 30 patients, Mean age of the patients is 40.5 yrs and mean age of the patients in group 1 is 39.8 yrs and group 2 is 41.87 yrs. Most of the patients were in 21-40 years age group. There were 8 males and 7 females in Group 1 and 9 males and 6 females in Group 2 as a whole 17 male and 13 females were there in our study. Various causative factors for the Ocular surface disorder in this study are depicted below. Sjögren's syndrome (34%) is the most common cause in our study, followed by Steven Johnson's (20%). Neurotrophic keratitis is the causative factor for Ocular surface disorder in 13% of study population and Meibomian gland dysfunction also occurred in 13% of study population.

Symptom Score: Results of each symptom score comparison is described below.

Tearing: There was no significant difference in the improvement of symptom score of tearing between autologous serum and Artificial tear substitute during the follow up period.

Burning: There was significant difference in improvement of the burning sensation of patients treated with autologous serum during 3rd, 4th and 5th and 6th visit.

Foreign Body Sensation: There was significant difference in improvement of the foreign body sensation in patients treated with autologous serum during 3rd 4th and 6th visit.

Photophobia: There was significant difference in improvement of the photophobia in patients treated with autologous serum during 3rd visit, 4th visit, 5th visit and 6th visit.

Blurred Vision: There was no significant difference in improvement in blurred vision of the patients treated with autologous serum.

Difficulty in Opening Eyelids: There was earlier significant improvement in difficulty in opening eyelids (1st visit) in patients treated with autologous serum as shown below (p value 0.0081).

Stingy Discharge: There was no significant difference in improvement between the patients treated with autologous serum and artificial tear substitute.

Table 1: Improvement in symptoms between groups

| Symptoms | Comparison | | 1st Visit | 2nd Visit | 3rd Visit | 4th Visit | 5th Visit | 6th visit |
|-------------------------------|------------------|---------|-----------|-----------|---------------|---------------|---------------|---------------|
| Tearing | Autologous Serum | Mean±SD | 1.9±1 | 1.71±0.85 | 1.43±0.51 | 1.19±0.4 | 1±0 | 1±0 |
| | Tear Substitute | Mean±SD | 1.48±0.85 | 1.43±0.84 | 1.38±0.67 | 1.33±0.59 | 1.12±0.33 | 1.11±0.33 |
| | P Value | | 0.132 | 0.279 | 0.7962 | 0.3792 | 0.1811 | 0.3051 |
| Burning | Autologous Serum | Mean±SD | 2.75±1.02 | 2.75±1.02 | 2.05±1 | 1.75±0.79 | 1.67±0.82 | 1.5±0.71 |
| | Tear Substitute | Mean±SD | 2.91±0.85 | 2.87±0.92 | 2.71±0.9 | 2.67±0.84 | 2.47±0.8 | 2.6±0.7 |
| | P value | | 0.5701 | 0.6881 | 0.0311 | 0.0014 | 0.0086 | 0.0026 |
| FB Sensation | Autologous Serum | Mean±SD | 2.76±0.94 | 2.48±0.98 | 2.05±0.97 | 1.76±0.83 | 1.87±0.83 | 1.5±0.53 |
| | Tear Substitute | Mean±SD | 2.83±0.72 | 2.83±0.72 | 2.8±0.89 | 2.67±0.91 | 2.41±0.71 | 2.67±0.5 |
| | P value | | 0.7997 | 0.1813 | 0.014 | 0.0025 | 0.0552 | 0.0001 |
| Photophobia | Autologous Serum | Mean±SD | 2.86±0.85 | 2.62±0.97 | 1.81±0.98 | 1.57±0.75 | 1.6±0.83 | 1.3±0.67 |
| | Tear Substitute | Mean±SD | 2.74±0.81 | 2.7±0.82 | 2.67±0.86 | 2.5±0.86 | 2.24±0.9 | 2.78±0.83 |
| | P Value | | 0.6404 | 0.7787 | 0.0044 | 0.0009 | 0.0478 | 0.0005 |
| Blurred Vision | Autologous Serum | Mean±SD | 3.38±0.86 | 3.14±0.96 | 2.95±1.16 | 2.86±1.11 | 3.07±0.88 | 3±1.15 |
| | Tear Substitute | Mean±SD | 3.39±0.78 | 3.39±0.78 | 3.43±0.81 | 3.44±0.78 | 3.35±0.86 | 3.67±0.5 |
| | P Value | | 0.9669 | 0.3514 | 0.1311 | 0.0681 | 0.3615 | 0.1283 |
| Difficulty in Opening Eyelids | Autologous Serum | Mean±SD | 3±0.89 | 2.57±0.87 | 2.1±0.91 | 1.76±0.77 | 1.73±0.8 | 1.4±0.7 |
| | Tear Substitute | Mean±SD | 2.3±0.76 | 2.3±0.76 | 2.29±0.85 | 1.94±0.73 | 1.76±0.56 | 1.78±0.44 |
| | P Value | | 0.0081 | 0.2848 | 0.5026 | 0.4528 | 0.8977 | 0.1827 |
| Stingy Sensation | Autologous Serum | Mean±SD | 1.4±0.75 | 1.35±0.75 | 1.3±0.73 | 1.15±0.49 | 1.13±0.52 | 1.09±0.3 |
| | Tear Substitute | Mean±SD | 1.24±0.7 | 1.24±0.7 | 1.26±0.73 | 1.22±0.55 | 1.24±0.56 | 1.44±0.73 |
| | P Value | | 0.4802 | 0.6229 | 0.8762 | 0.6704 | 0.5989 | 0.158 |

Discussion

In this study 80% population in Group I (Autologous serum) and 73.33% of population in Group II (Artificial tear substitute) were between 20 to 40 yrs. Mean age of the patient is 40.5 years. Dry eye syndrome affects 10-30% of the

population older than forty years in United States as per the report of Epidemiology Subcommittee of the International Dry Eye Workshop. Nurses' Health Study (Schaumberg et al) [8] shows prevalence of 5.7% in patients less than 50 years old and 9.8% in patients more than 75 yrs old. In

our study, the upper age limit of the patient is 70 yrs and there were stringent exclusion criteria so as to use autologous serum. Hence there is a trend towards lower age distribution in our study than in the published literature. Ocular surface disorder is slightly more common in women. This may be due to the fact that 90% of the patients affected with Dry Eye Syndrome due to Sjögren's syndrome are women. In our study out of 30 patients there were 17 males and 13 females. The difference may partly be explained by different causative factors included in the study like meibomian gland dysfunction, trauma, herpes etc. Also the women with anemia, pregnant and lactating women were excluded from the study which may also contribute to the discrepancy. In our study improvement in symptom scores of the patients treated with autologous serum (Group I) is compared with the symptom score of the patients treated with Artificial tear substitute (Group II) during each visit.

In our study there is improvement in tearing, blurred vision and stingy discharge in both the groups. However there is no significant difference in improvement between both the groups. Finding implies that both autologous serum and artificial tear substitute are equally effective in stopping the tearing, improvement in blurring of vision and stingy discharge during the follow up period.

In a study by Tanauvat et al in 12 patients treated with autologous serum there was improvement in symptoms and signs of dry eye but was not statistically significant. Similarly in our study there was no statistically significant difference in improvement of above mentioned symptoms. [9]

In this study there is significant difference in improvement of burning sensation in patients treated with autologous serum during 3rd ($p=0.0311$), 4th ($p=0.0014$), 5th ($p=0.0086$) and 6th (0.0026) visit. There is significant difference in improvement of Foreign body sensation in patients treated with autologous serum during 3rd ($p=0.0140$), 4th ($p=0.0025$) and 6th visit ($p=0.0001$). There is significant difference in improvement of the photophobia of the patients treated with autologous serum during 3rd visit ($p=0.0044$), 4th visit ($p=0.0009$), 5th visit ($p=0.0478$) and 6th visit ($p=0.0005$). There is also earlier significant improvement in difficulty in opening eyelids (1st visit) in patients treated with autologous serum (p value 0.0081).

Kojima et al conducted study on effectiveness of the 20% autologous serum Vs preservative free artificial tear drops for severe dry eye disease. There is significant improvement in the mean break-up time and staining scores of the patients

treated with autologous serum. There was also significant improvement in subjective symptoms scores, in patients treated with autologous serum when compared with patients treated with preservative-free artificial tears. [10]

Conclusion

Autologous serum is found to be safe and significantly effective than the artificial tear substitute in the treatment of ocular surface disorders. For most of these patients, autologous serum was superior to conventional treatment for improving ocular surface health and subjective comfort.

References

1. Williams K, Watsky M. Gap junctional communication in the human corneal endothelium and epithelium. *Curr Eye Res* 2002; 25:29–36.
2. Geerling G, Maclennan S, Hartwig D. Autologous serum eye drops for ocular surface disorders. *Br J Ophthalmology*. 2004; 88(11): 1467-74.
3. Poon AC, Geerling G, Dart JKG, *et al*. Autologous serum eye drops for dry eyes and epithelial defects: clinical and in vitro toxicity studies. *Br J Ophthalmol*. 2001; 85: 1188–97.
4. Ogawa Y, Okamoto S, Mori T, *et al*. Autologous serum eye drops for the treatment of severe dry eye in patients with chronic graft-versus-host disease. *Bone Marrow Transplant*. 2003; 31:579–83.
5. Tananuvat N, Daniell M, Sullivan LJ, *et al*. Controlled study of the use of autologous serum in dry eye patients. *Cornea*. 2001; 20:802–6.
6. Tseng SCG, Tsubota K. Important concepts for treating ocular surface and tear disorders. *Am J Ophthalmol*. 1997; 124:825–5.
7. Koffler BH. Autologous serum therapy of the ocular surface with novel delivery by platelet concentrates gel. *Ocul Surf*. 2006; 4(4):188-95.
8. Schaumberg DA, Sullivan DA, Buring JE, Dana MR: Prevalence of dry eye syndrome among US women. *Am J Ophthalmol*. 2003; 136:318-326.
9. Tananuvat N, Daniell M, Sullivan LJ, Yi Q, McKelvie P, McCarty DJ *et al*. Controlled study of the use of autologous serum in dry eye patients. *Cornea*. 2001; 20(8):802-6.
10. Kojima T, Ishida R, Dogru M, Goto E, Matsumoto Y, Kaido M, Tsubota K. The effect of autologous serum eye drops in the treatment of severe dry eye disease: a prospective randomized case-control study. *Am J Ophthalmol*.