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Original Research Article

Role of Autologous Serum Ophthalmic Solution as Adjuvant Therapy in Management of Ocular Surface Disorders

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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. Sign score and schrimers test was done and values were obtained.

Results: There is no significant difference in improvement of lid edema. There was also no significant difference in improvement of conjunctival congestion during first, second and third visit but there was significant difference in improvement of conjunctival congestion during the fourth visit. There was significant difference during 4th and 5th visit in epithelial defect. There is also no significant difference in improvement of neovascularization. There is significant difference in improvement of Schirmer's test.

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, Dry Eye, Schrimers Test.

Introduction

The Ocular Surface System includes the surface and glandular epithelia of the cornea, conjunctiva, lacrimal gland accessory lacrimal glands, meibomian gland, and eyelashes with their associated glands of Moll and Zeis, and the nasolacrimal duct. [1]

Tears perform a vital role in maintaining the health of the corneal epithelium: they nourish, protect and refresh the eye. They contain fibronectin, growth factors, lysozyme and vitamins that support the migration, proliferation and differentiation of the conjunctival and corneal epithelium. Thus tears have lubricating, mechanical, but also epitheliotrophic and antimicrobial properties. A lack of epitheliotrophic factors or their carrier compromises the integrity of the surface epithelia. [1] Disruption of the function ocular surface structures may result in ocular surface disorders. 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 disease (OSD) is a global public-health problem affecting up to 20% of the population with significant debilitating symptoms including constant pain, grittiness and soreness that the patients experience day and night that impact on quality-of-life. The ocular surface is the area that extends from the eyelid margin to the cornea and comprises the cornea, conjunctiva, lacrimal gland, meibomian gland, eyelid and tears. The tear film acts as the outer scaffold of the ocular surface (apical mucosa), it creates a smooth refractive surface to enable sight and provides lubrication, physical protection, immunological defence and nutrition to the ocular surface. [1]

OSD can be caused by conditions that lead to alteration in the production, composition, or distribution of the tear film. This includes many conditions, such as Sjögren's syndrome-related dry eye, other immune-related dry eye (such as ocular mucous membrane pemphigoid, Stevens–Johnson syndrome, graft-vs-host disease, and ulcerative keratitis), neurotrophic cornea, injury (mechanical, chemical, thermal, and surgery), and stem cell failure. The most severe manifestations of OSD can lead to blinding complications. [2,3]

Dry eye treatment is based on disease severity and it includes: tear supplementation (lubricants); tear retention; tear stimulation; biological tear substitutes; anti-inflammatory therapy; essential fatty acids; or environmental strategies.

Pharmaceutical products are optimized for their biomechanical properties only. None of the commercially available artificial tear preparations include essential tear components such as epidermal growth factor, hepatocyte growth factor, fibronectin, neurotrophic growth factor and vitamin A, all of which have been shown to play an important role in the maintenance of ocular surface epithelial milieu. [4] Serum and other bodily fluids have been used as natural tear substitutes. Serum is the fluid component of blood, devoid of its cellular components and clotting factors.

Artificial tears are the most commonly used treatment. However, artificial tears differ in their components from physiological tears. For this reason, other alternatives have been proposed that consider pathophysiology elements in their composition. One alternative is autologous serum. [5,6]

Autologous serum contains several growth factors involved in the epithelial migration process, necessary for ocular surface repair and maintenance of tear stability. These factors are not present in artificial tears. Some of these factors are epithelial growth factor, nerve growth factor, fibronectin and vitamin A. It has also been shown that the use of autologous serum would inhibit the release of inflammatory cytokines. Based on this aim of our study is to compare the efficacy of autologous serum ophthalmic solution versus tear drops as adjuvant therapy in decreasing the signs and improvement in schrimers test.

Materials & Methods

This prospective study was conducted tertiary care teaching hospital for a period of 6 months. Patient presenting with ocular surface diseases was 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 given a serial number. In addition to routine line of management 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 $+4^0$C. Once issued, patients are advised to preserve the serum in the refrigerator at +4°C after use[5]. 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 using SPSS version 24 software

Results

In our 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. There were 8 males and 7 females in Group 1 and 9 males and 6 females in Group 2.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.

Sign Scores

There is no significant difference in improvement of lid edema in between Group 1 and 2 as shown below. There was no significant difference in improvement of conjunctival congestion during first, second and third visit but there was significant

difference in improvement of conjunctival congestion during the fourth visit and there was no significant improvement in symptoms during 5th and 6th visit. There was no significant difference in improvement of epithelial defect during 1st, 2nd, 3rd visit. There was significant difference during 4th and 5th visit as shown below. There is also no significant difference in improvement of neovascularization between Groups 1 & 2 as depicted below.

Table 1: Comparison between reductions in signs

Lid Edema		**1st Visit**	**2nd Visit**	**3rd Visit**	**4th Visit**	**5th visit**	**6th visit**
Autologous Serum	Mean	2.19	2.1	2.05	1.76	2.07	2
	SD	0.81	0.77	0.8	0.94	0.96	0.94
Tear Substitute	Mean	2.04	2.05	2.05	2	1.94	2.09
	SD	0.82	0.84	0.86	0.91	0.97	0.94
P value		0.5554	0.8409	1	0.4291	0.7158	0.8278
Conjunctival Congestion		**1st Visit**	**2nd Visit**	**3rd Visit**	**4th Visit**	**5th visit**	**6th visit**
Autologous Serum	Mean	2.19	1.81	1.33	1.14	1.2	1.2
	SD	0.51	0.6	0.58	0.36	0.41	0.42
Tear Substitute	Mean	2.22	2.13	1.71	1.67	1.35	1.27
	SD	0.42	0.55	0.64	0.59	0.49	0.47
P value		0.8494	0.0711	**0.05**	**0.0017**	0.353	0.7132
Epithelial Defect		**1st Visit**	**2nd Visit**	**3rd Visit**	**4th Visit**	**5th visit**	**6th visit**
Autologous Serum	Mean	2.1	2.05	1.81	1.33	1.13	1.1
	SD	0.62	0.59	0.68	0.48	0.35	0.32
Tear Substitute	Mean	2.17	2.09	2.05	1.78	1.47	1.45
	SD	0.39	0.51	0.5	0.65	0.51	0.52
P value		0.615	0.8144	0.2026	0.019	0.0411	0.0789
Neovascularisation		**1st Visit**	**2nd Visit**	**3rd Visit**	**4th Visit**	**5th visit**	**6th visit**
Autologous Serum	Mean	2	2	2	1.95	2.2	2.2
	SD	0.95	0.95	0.95	0.97	1.01	1.03
Tear Substitute	Mean	2.09	2.05	2.1	2.06	2.12	2.27
	SD	0.79	0.79	0.83	0.87	0.86	0.79
P value		0.7423	0.8647	0.7311	0.7313	0.8051	0.857

Further we did schrimers test, there is significant difference in improvement of Schirmer's paperwetting in patients treated with autologous serum during 3rd and 4th visit with autologous serum being the better treatment option with significant reduction from first visit too. Also there was an early response in this group.

Table 2: Schrimers test

Schirmer's test		**1st Visit**	**2nd Visit**	**3rd Visit**	**4th Visit**	**5th visit**	**6th visit**
Autologous Serum	Mean	1.95	1.57	1.14	1	1	1
	SD	0.38	0.51	0.36	0	0	0
Tear Substitute	Mean	1.7	1.65	1.48	1.39	1.06	1
	SD	0.56	0.57	0.6	0.5	0.24	0
P value		0.0859	0.6245	**0.0351**	**0.001**	0.356	>0.9999

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. 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. In our study out of 30 patients there were 17 males and 13 females.

In our study there is no significant difference in improvement of lid edema in between Group 1 and 2. There is also no significant difference in improvement of neovascularization between the groups. In a study by Noble et al in 6 patients of Sjogren's syndrome and 5 patients of kerato conjunctivitis sicca, there was no significant improvement in Rose Bengal staining, Schirmer's test and tear clearance test. [7] There was significant difference in improvement of epithelial defect during 4th (p=0.0190) and 5th visit (p=0.0411). There is significant difference in improvement of Schirmer's paper wetting in patients treated with autologous serum during 3rd (p value 0.0351) and 4th visit (0.0010). Tsubota et al study on effect of autologous serum on persistent epithelial corneal defect showed that the serum was effective in more than 60% of patients. [8] Del Castillo et al studied the effect of 20% autologous serum in recurrent corneal erosions. He concluded that the autologous serum appears to be safe and effective in preventing the number of recurrences.

[9] Another crossover study [10] comparing a 2-week treatment with 20% Autologous serum (AS) with conventional artificial tears in 12 patients with severe dry eye syndrome found that the patients treated with AS showed a significant improvement in ocular surface disease index scores. Matsumoto et al conducted study on neurotrophic keratitis in 14 eyes of 11 patients and found that the epithelial defect healed completely in all eyes within 6 to 32 days. There was reduction in corneal scarring. Study concluded that neurotrophic factors in autologous serum may provide neutrophilic healing for the compromised ocular surface. [11] Hussain et al [12] described the outcomes of 50% AS eye drops after long-term use in a large cohort of patients with dry eyes. The study included 63 patients (123 eyes) who were evaluated with a mean follow-up of 12 months. AS 50% eye drops seems to be a safe and effective long-term treatment for dry eye disease, especially in patients with severe disease who have exhausted all other conventional forms of treatment.

Conclusion

Autologous serum eye drops for severe dry eye treatment have gained widespread acceptance over the past decade. The idea of using autologous serum eye drops as a treatment for dry eye and ocular surface disorders is attractive because they contain growth factors that promote epithelial healing. In this context, autologous serum eye drops can be an extremely useful addition to the armamentarium of physicians dealing with severe dry eye disease and ocular surface disorders, helping them to improve patient comfort and achieve epithelial healing in these challenging cases.

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