

# Efficacy of Topical Diluted Autologous Serum in Patients of Dry Eye in Bundelkhand Region.

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## ABSTRACT

**Background:** The dry eye is a symptom complex occurring as sequelae to deficiency or abnormalities of the tear film which can lead to the persistent and progressive damage of the ocular surface. Conventional artificial tear therapies are limited in supplying the neurotrophic factors, vitamins, and immunoglobulins necessary for the health of the ocular surface. Serum has been shown to contain essential tears components in comparable concentrations to natural tears. Present study has been done to evaluate the effectiveness of diluted autologous serum eyedrops in relieving patients' symptoms and improvement in corneal phenotype in patients of dry eye. **Methods:** The study included 36 eyes of 25 patients with dry eye disorder from Bundelkhand region only, who were prescribed 20% diluted autologous serum eye drops along with artificial tears. Patients were asked to apply this serum 8-10 times per day in affected eye and they were examined on end of 1st, 2nd, 4th, 6th and 8th week to determine the efficacy of the treatment. Evaluation of efficacy of autologous serum treatment for dry eye, was determined by comparing subjective and objective score calculated by a scoring system suggested by "National Eye Institute: Industry workshop on clinical trials" from day 1 to every subsequent visit for follow up. **Results:** We noticed that after 8 weeks' treatment of topical diluted autologous serum, 35 cases of dry eyes showed decrease in subjective as well as objective score and only 1 case of eye did not show improvement after 8-week treatment. **Conclusion:** We concluded that the use of 20% diluted autologous serum tears appears to be a safe and good therapy in cases of dry eye disorder as it was effective in improvement of symptoms and objective signs even in severe dry eye disorder.

**Keywords:** Autologous serum, dry eye, serum eyedrop

## INTRODUCTION

The dry eye per se is not a disease entity, but a symptom complex occurring as sequelae to deficiency or abnormalities of the tear film. Moist ocular surface is maintained by a collective interplay of factors like sufficient quantity of tears, normal composition of tear film, normal lid closure and regular blinking of lids. Incompetency in any of above factor might lead to dry eye.<sup>[1]</sup> Tear film/precorneal film consist of three layers from posterior to anterior, which are mucus layer, aqueous layer and lipid or oily layer. Thinnest Mucus layer consists of mucin secreted by conjunctival goblet cells and glands of Manz. Thickest Aqueous layer consists of tears secreted by the main and accessory lacrimal glands. Outermost Lipid or oily layer formed at air-tear interface from the secretion of Meibomian, Zeis, and Moll glands. Important etiology of dry eye include aqueous tear deficiency (congenital

alacrimia, paralytic hyposecretion, primary and secondary Sjogren's syndrome and idiopathic hyposecretion etc), Mucin deficiency dry eye (hypovitaminosis A/ xerophthalmia, Stevens-Johnson syndrome, trachoma etc), Lipid deficiency and abnormalities (chronic blepharitis and chronic meibomitis), Impaired eyelid function (Bell's palsy, exposure keratitis, ectropion) and Epitheliopathies.<sup>[1]</sup> This condition usually effects individuals with age  $\geq$  40 years, but lifestyle modification like excessive use of televisions, gaming consoles, computers, tablets or smartphones,<sup>[2]</sup> sitting in air conditioned room or using blowers/heaters in winters etc. has also contributed in number of sufferer from younger age groups too. Long standing dry eyes patient might show corneal changes in the form of punctate epithelial erosions and filaments. Conventional treatment of dry eye includes artificial tears, protective glasses and punctal occlusion. But oftendry eye patients with corneal epithelial erosion continue to have sign and symptoms despite prolonged use of these conventional methods. Essential tears component, such as epidermal growth factor (EGF), vitamin A, transforming growth factor  $\beta$  (TGF $\beta$ ), are, however, lacking in artificial tears, as the key constituents of these are water and

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electrolytes.<sup>[3]</sup> Serum has been shown to contain essential tears components in comparable concentrations to natural tears Therefore,<sup>[4]</sup> the present study has been done to evaluate the effectiveness of diluted autologous serum eyedrops in relieving patients' symptoms and improvement in corneal phenotype in patients of dry eye.

## MATERIALS AND METHODS

The present prospective study was conducted in Department of Ophthalmology, Rajkiya Medical College, Jalaun, Uttar Pradesh, India from 16.03.16 to 16.03.18 (2 years). The study included 36 eyes of 25 patients with dry eye disorder from Bundelkhand region only, who were prescribed 20% diluted autologous serum eye drops along with artificial tears. In this study we included only those patients with symptoms of dry eyes who gave consent for this treatment, followup and the study, whose Break up time (BUT) was  $\leq 5$  seconds & Schirmer's test without anesthesia  $< 5$  mm at 5 minutes and they showed staining of ocular surface on Rose Bengal and Fluorescein staining.

### Criteria for patient exclusion

Patients who discontinued the treatment or who failed to visit for regular follow up were not considered for the study.

Patients with presence of any of the following factor were not prescribed autologous serum eye drops

1. Patient with active infection (acute herpes simplex/herpes zoster keratitis).
2. Vitamin A deficiency, diabetes,
3. Progressive corneal melting due to any immunological process.
4. Recurrent corneal erosion syndrome.
5. Pregnant/ Lactating women.
6. Patients with known complex medical history (immune-mediated disease, blood cancers)
7. patients who were known to use ayurvedic, homeopathic or other remedies for above symptoms.

Autologous serum teardrops were prepared by taking 20 ml of peripheral blood from the patient under aseptic technique. The blood was then centrifuged for 5 min at 4000 revolutions/min. The serum was separated and was diluted to 20% with sterile saline. The solution was then put into a bottle with black paper coating on surface for protection from light to prevent degradation of vitamin A. The patients were instructed to store the eye drops in the freezer compartment of domestic refrigerator for no more than 1 month.<sup>[3]</sup>

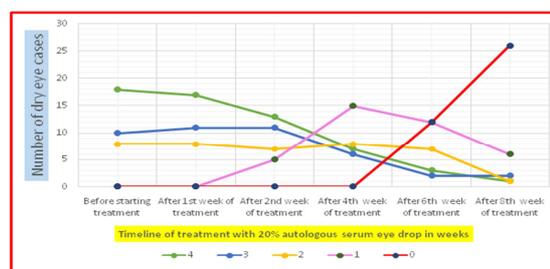
Patients were asked to apply this serum 8-10 times per day in effected eye and they were examined on end of 1st, 2nd, 4th, 6th and 8th week to determine the efficacy of the treatment. Weaning of serum drops was done in patients who have beneficial effect and continued if there was any worsening of symptoms after withdrawal of serum drops.

Evaluation of efficacy of autologous serum treatment for dry eye, was determined by comparing subjective and objective score calculated by a scoring system suggested by "National Eye Institute: Industry workshop on clinical trials" from day 1 to every subsequent visit for follow up.<sup>[5]</sup>

Subjective scoring was done by the following grading method: - where 4 grades represent severity of patient symptoms viz. grade 0—no symptoms, grade 1- mild symptoms (i.e. irritation, itching, burning in eye) with no discomfort, grade 2- moderate symptoms with occasional discomfort but no interference with daily activities, grade 3- severe symptoms with frequent discomfort but no interference with daily activities, grade 4- very severe symptoms with constant discomfort and interference with daily activities.

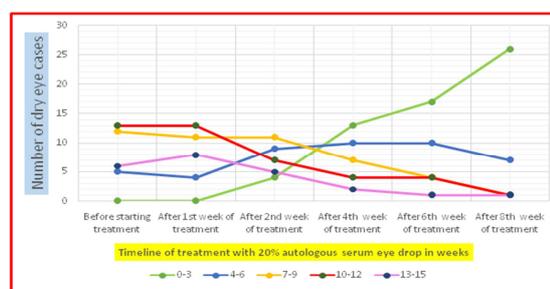
Objective scoring for ocular surface evaluation was done scoring system suggested by "National Eye Institute: Industry workshop on clinical trials"<sup>5</sup> Briefly, the NEI grading scale consists of a grid that divides the corneal area into five sections, each of which is assigned a score between zero and 3 depending of the amount and distribution of corneal Fluorescein staining; the total corneal Fluorescein staining score ranges from 0/15 (absence of corneal epitheliopathy) to 15/15 (severe epitheliopathy). While in nasal and conjunctival region, each region of each eye is divided into 3 parts, hence score of conjunctival damage noted by rose Bengal staining ranges from 0/18 to 18/18.

## RESULTS



**Figure 1: Frequency distribution of dry eye cases before and after autologous serum treatment on the basis of subjective score**

\*\*Coloured lines represent subjective scores



**Figure 2: Frequency distribution of dry eye cases before and after autologous serum treatment on the basis of objective score (Fluorescein staining score)**

\*\* Coloured lines represent objective scores (Fluorescein staining score)

**Table 1: Frequency distribution of dry eyes before and after autologous serum treatment on the basis of subjective score**

Subjective score (grade)	Observed number of dry eye condition					
	Before starting treatment	After 1st week of treatment	After 2nd week of treatment	After 4th week of treatment	After 6th week of treatment	After 8th week of treatment
4	18	17	13	7	3	1
3	10	11	11	6	2	2
2	8	8	7	8	7	1
1	0	0	5	15	12	6
0	0	0	0	0	12	26

(Total number of patients= 25, Total number of dry eye cases=36)  
(Chi square test: X<sup>2</sup>= 166.8 df=20 p<0.00001)

**Table 2: Frequency distribution of dry eye cases before and after autologous serum treatment on the basis of objective score (Fluorescein staining score)**

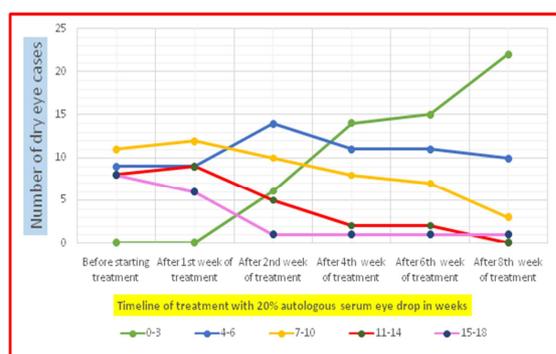
Fluorescein staining score	Observed number of dry eye condition						
	Before starting treatment	After 1st week of treatment	After 2nd week of treatment	After 4th week of treatment	After 6th week of treatment	After 8th week of treatment	
0-3	0	0	4	13	17	26	
4-6	5	4	9	10	10	7	
7-9	12	11	11	7	4	1	
10-12	13	13	7	4	4	1	
13-15	6	8	5	2	1	1	

(Total number of patients= 25, Total number of dry eye cases=36)  
(Chi square test: X<sup>2</sup>= 101.6 df=20 p<0.0001)

**Table 3: Frequency distribution of dry eye cases before and after autologous serum treatment on the basis of objective score (Rose Bengal staining score)**

Rose Bengal staining score	Observed number of dry eye condition					
	Before starting treatment	After 1st week of treatment	After 2nd week of treatment	After 4th week of treatment	After 6th week of treatment	After 8th week of treatment
0-3	0	0	6	14	15	22
4-6	9	9	14	11	11	10
7-10	11	12	10	8	7	3
11-14	8	9	5	2	2	0
15-18	8	6	1	1	1	1

(Total number of patients= 25, Total number of dry eye cases=36)  
(Chi square test: X<sup>2</sup>= 81.9 df=20 p<0.0001)

**Figure 3: Frequency distribution of dry eye cases before and after autologous serum treatment on the basis of objective score (Rose Bengal staining score)**

\*\*Coloured lines represent objective scores (Rose Bengal staining score)

## DISCUSSION

In our study over 36 dry cases from 25 patients, there were 23 male and 2 female patients with age ranging from 38 to 55 years. Most common age group that suffered from dry eye was 50-60 years' age group. Mean age of the patient was 49.2 years. 11 patients had condition of dry eye on both side, 8 patients in the left eye and 6 patients in the right eye.

At the time of first visit, 50% cases of dry eye were of subjective score of 4, which was prevalent on left side. After 4 week of treatment with topical 20% autologous serum, percentage of cases with subjective score of 4 reduced to 19.44% and up to 2.8% after 8-week treatment.[Table 1]. At the time of first visit, 27.8% of dry eye cases had subjective score of 3 and 22.2% had subjective score of 2. After 8 week of treatment with topical 20% autologous serum, percentage of cases with subjective score of 4 and 3 reduced to 5.6% and 2.8% respectively [Table 1]. At the time of first visit, common symptoms in cases with subjective score of 4 were burning in the eye (70%) and foreign body sensation (63%).

On comparing subjective score of all the patients up to 8th week of treatment with topical diluted autologous serum, we noticed that in 2nd post treatment week, there was a notable increase in number of patients with low subjective score and decrease in number of patients with high subjective score, which means that use of topical diluted autologous serum significantly helped patients in getting relieved from their symptoms. [Figure 1] There was only 1 patient whose subjective score did not show any change despite 8-week treatment with

topical diluted autologous serum. Similar findings were also noted by other workers, who used autologous serum eye drops in these studies varied from 20% to 100%.<sup>[6-8]</sup>

In our study, we have used 20% diluted autologous serum in 36 dry eye cases instead of using undiluted serum, because the major drawbacks of using undiluted serum eye drops are the inconvenience of repeated blood draws, large volume of blood collection, and potential ocular irritation associated with extra viscosity of the eye drops, as high concentrations of serum proteins in 100% serum can alter the osmolarity and pH of the preparation.<sup>[9]</sup>

The rationale for diluting the serum to 20%, is also to decrease the concentration of TGF- $\beta$  in serum to a level equivalent to that in natural tears, as greater concentration of TGF- $\beta$  in serum than in tears, possibly retarding epithelial wound healing.<sup>[7]</sup> We also used high centrifugation force for serum preparation, as one study found much lower concentration of TGF- $\beta$  on using higher centrifugation force.<sup>[10]</sup>

On comparing objective scores calculated by scoring system suggested by "National Eye Institute: Industry workshop on clinical trials" based on rose Bengal and Fluorescein staining, we noticed that after 2 weeks' treatment of topical diluted autologous serum, number of patients with high objective score started to decrease and similar trend continued upto 8th week alike the finding of other workers. These change were statistically significant too, which means use of topical diluted autologous serum is efficacious in treating dry eye. [Table 2 & 3]. [Figure 2&3] Similar findings were also noted by other workers, who used 20% autologous serum eye drops in their studies.<sup>[3,4,11-13]</sup> Though some workers used undiluted (100%) autologous serum or 33-50% diluted autologous serum eye drops and found it efficacious in treating dry eye.<sup>[6,8,9,14,15]</sup>

Treatment of dry eye disorder/ocular surface disease with the use of serum eye drops has also been shown efficacious in our study. Although standard substitution therapy with artificial tears like hydroxypropyl methyl cellulose and carboxymethylcellulose are effective in providing lubrication to the ocular surface, but are unable to substitute the nutrients and factors present in natural tears.<sup>[16]</sup>

## CONCLUSION

We concluded that the use of 20% diluted autologous serum tears appears to be a safe and good therapy in cases of dry eye disorder as it was effective in improvement of symptoms and objective signs even in severe dry eye disorder. It can also be used for treating postoperative corneal epithelial defect following various ocular surgeries. Future research is needed to determine the

optimum concentration of serum for specific diseases.

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