Original Research Article

Autologous serum eye drops V/S Lubricating Eye Drops in Treatment of Dry Eye Disease

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Abstract

Purpose – To compare efficacy of Autologous serum eye drops vs that of Lubricating eye drops in patients of Dry eye disease.Methods – A single blind randomised control trial was conducted over a period of 6 months (from June 2022 to December 2022 after due approval from departmental ethics committee.378 patients who visited our OPD with typical complaints of Dry eye disease (due to any cause) were given the option of centrifuging a small quantity (10 ml) autologous blood and use eye drops prepared from its serum or go with conventional eye drops.90 patients chose autologous serum eye drops (Group A) where as rest were alternatively given CMC(0.5%w/v) and sodium hyaluronate (0.1 to 0.3%w/v) and patients were asked to follow-up after 15days,30 days and 90 days. Schirmer I test score, and tear film break up time (TF-BUT) were used as efficacy parameters. Safety was monitored on all visits.Subjective Improvement in symptoms were duly noted. The scores of Schirmer I test improved in both Gorup A as well as Group B, but a greater improvement was seen in Group A (at day 90: 22.75 ± 3.04 mm vs. 21.78 ± 3.36 mm, *P*: 0.04). The values of TF-BUT improved in both groups, the difference being statistically insignificant.
Conclusion- Autologous plasma was almost equally effacious with slightly more improvement seen in TBUT while CMC and Sodium hyaluronate tear substitutes were equally efficacious and all three were safe in reducing symptoms of dry eye.

Introduction

DEWS II global dry eye definition, “Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film and accompanied by ocular symptoms, in which tear film instability, hyperosmolarity, ocular surface inflammation, and damage along with neurosensory abnormalities play etiological roles.” The prevalence of dry eye syndrome increases with age and ranges from 5.5% to 37.7%. In the Indian population, reports of hospital-based prevalence of dry eye varies from 18% to 27%.(1)

Dry eye can cause a variety of symptoms which includes but is not limited to

- A scratchy feeling, like there’s something in eye
- Stinging or burning feelings in eye
- Red eyes
- Sensitivity to light
- Blurry vision

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The tear film is made of three layers.(2)

- An oily layer
- A watery layer
- A mucus layer

Each layer of the tear film serves a specific purpose.
Oily layer is the outer layer of the tear film making the tear surface smooth and keeping tears from drying up quickly. It is secreted by meibomian glands.(2-3)
The **watery layer** is the middle layer. It makes up the most volume of tears. It keeps the eye clean.This layer is secreted from the lacrimal glands in the eyelids. (2-3)
The **mucus layer** is the inner layer of the tear film. This helps spread the watery layer over the eye’s surface, keeping it moist. (2-3)
Increase in age is the main cause of dry eye,other important causes which can lead to dry eye include n diseases, such as rheumatoid arthritis, Sjögren’s syndrome, thyroid disease, and lupus, Blepharitis,Entropion or ectropion , wind, smoke, or dry climate, reading and other activities that reduce blinking such as computer vision syndrome, using contact lenses for a long time, refractive eye surgery,

- Medications, such as:(4)
  - Diuretics
  - Beta-blockers,
  - Allergy and cold medications
  - Anxiety and antidepressant medicines
  - Cardiac medications

Study design - This was a prospective, randomized, comparative, and open labelled trial, conducted by enrolling the patients, visiting the outpatient clinic of the department of ophthalmology. Patients diagnosed to have dry eye due to any cause and to satisfy the inclusion criteria were enrolled in the study after getting the informed consent. The study procedures followed the Helsinki Declaration of 1975. The study was approved by the institutional ethics committee. This trial was conducted over a period of 6 months (from June 2022 to December 2022 after due approval from departmental ethics committee.378 patients who visited our OPD with typical complaints of Dry eye disease (due to any cause) were given the option of centrifuging a small quantity (10 ml) autologous blood and use eye drops prepared from its serum or go with conventional eye drops.87 patients chose autologous serum eye drops (Group A) where as rest were given CMC(0.5%w/v) or sodium hyaluronate (0.1 to 0.3%w/v) and patients were asked to follow-up after 90 days. Schirmer I test score, and tear film break up time (TF-BUT) were used as efficacy parameters. Safety was monitored on all visits. Subjective Improvement in symptoms were duly noted. The Chi-square test was used to find the association between categorical variables. P value ≤0.05 was considered statistically significant.

Inclusion criteria - Participants of bith genders aged 18 years and above presenting with symptoms of dry eye disease.

Exclusion criteria – Any known hypersensitivity to the study medications and those who had used any other topical ophthalmic medications within 14 days (other than tear substitutes) or will be prescribed any other topical ophthalmic solution other than tear substitutes were excluded from the study.

Study procedure - The participants underwent a clinical workup including a detailed history and an ophthalmic examination. Those who fulfilled the inclusion criteria were enrolled in the study after obtaining a written informed consent. Participants were divided into two groups : group A who had opted for Autologous serum eye drops made by centrifugation of autologous blood and Group B received CMC (0.5%w/v)or Sodium hyaluronate tear substitute for 90 days.

Centrifugation is a mechanical process which involves the use of the centrifugal force to separate particles from a solution according to their size, shape, density, medium viscosity and rotor speed.(5)

Serum Preparation - Collect whole blood in a microcentrifuge tube. After collection of the whole blood, allow the blood to clot by leaving it undisturbed at room temperature. This usually takes 15-30 minutes. Remove the clot by centrifuging at 1,000-2,000 x g for 10 minutes in a refrigerated centrifuge. The resulting supernatant is designated serum. Following centrifugation, it is important to immediately transfer the liquid component (serum) into a clean microcentrifuge tube using a pipette. The samples should be maintained at 2-8°C while handling. If the serum is not analyzed immediately, the serum should be stored and transported at –20°C or lower. It is important to avoid multiple freeze-thaw cycles because this is detrimental to many serum components.

Serum were then stored in sterile empty bottled containers and given to patients.

Efficacy parameters were assessed on days 15 (±2 days), 30 (±2 days), and 90 (±2 days).In addition to the tear substitute use, we advised participants to blink voluntarily more often.

A questionnare Ocular Surface Disease Index (OSDI) was administered to participants on all visits.

a. Tear film break up time (TF-BUT) – The tear film stained with sodium fluorescein 1% was observed with a slit-lamp biomicroscope, and the time noted after instructing the patient to blink. The time taken for the first appearance of a dry spot was recorded as the "tear film break up time" or TF-BUT. A TF-BUT of <10 s was taken as dry eye.(6)This was evaluated at baseline, days 30, and 90.
b. Schirmer Test-I – This was performed by folding 5 mm at the top end of Whatman filter paper strip. It was placed in lower conjunctival sac at the junction of lateral one-third and medial two-thirds of the lower eyelid. It was left in place for 5 min or until 30 mm of the strip becomes wet. The strip was removed and the wet portion measured. This was performed on day 0 and day 90.(6)
c. Adverse drug reaction (ADR) monitoring was done on all visits. In addition, the participants were advised to report an ADR if experienced as soon as possible.(6)
d. Statistical tests were applied as follows:

    1. Quantitative variables were compared using Mann–Whitney test (as the data sets were not normally distributed) between the two groups.
    2. Qualitative variables were correlated using Chi-square test/Fisher's exact test.

A *P* value of < 0.05 was considered statistically significant.The data was entered in MS EXCEL, and their analysis was done using SPSS (Statistical Package for the Social Sciences) software version 20.0 IBM, Chicago,USA.

Demographic features

Age and gender distribution :In this study, out of a total of 378 participants, 50.6% of participants were in the age group of 21–30 years, while 30% of the participants were in the age group of 18–20 years [Table 1]. Overall, there was a slight female preponderance with 51.67% of the participants being female [Table 2].

Table 1:Age distribution of study participants

Age distribution (years)	Study group (%)		Total (%)	*P*
	A	B		
18–20	26 (28.89)	89 (31.11)	115 (30.02)	0.172
21–30	50 (55.56)	131 (45.56)	181 (47.88)	
31–40	8 (8.89)	45 (15.56)	53 (14.02)	
41–50	4 (4.44)	3 (1.11)	7(1.85)	
>50	2 (2.22)	20 (6.67)	22 (5.82)	
Total	90	288	378	

Table 2:Gender distribution of study participants

Gender	**Study group (%)**		**Total (%)**	***P***
	A	**B**		
Female	52 (57.78)	131 (45.49)	183 (48.41)	0.102
Male	38 (42.22)	157(54.51)	195 (51.59)	
Total	90	288	378	

Comparison of efficacy and safety between the groups

Ocular surface disease index score :OSDI score was considered as the primary efficacy parameter, was comparable in Group A and B at baseline: 23.29 and 23.21, respectively, with a *P* = 0.726. Improvement was seen in OSDI scores on all follow-up visits in both groups, and the difference was statistically significant. A statistically significant difference between Groups A and B on all follow-up visits, as shown in Figure 1.

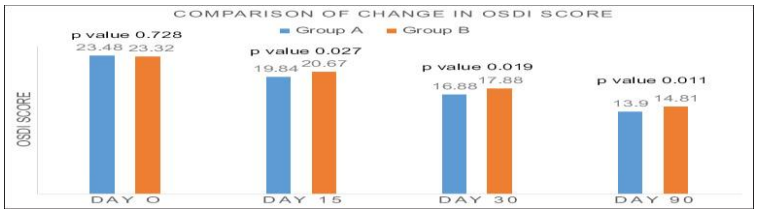

Figure 1 Comparison of ocular surface disease index score between the two groups at follow-up visits

Schirmer *I* test values:The Schirmer *I*-test values were comparable between the two groups on day 0 (12.79 mm for Group A and 13.03 mm for Group B; *P* = 0.341). On day 90, the values on day 90 in both Groups A and B showed an increase compared to the baseline [Table 3]. The increase in value indicates symptomatic improvement. Group A showed a statistically significant increase in values as compared to Group B [Table 3].

Table 3:Comparison of Schirmer-I score between the two groups

	Group A*	**Group B***	***P***
Day 0	12.86±3.18	13.12±3.42	0.341
Day 90	22.75±3.04	21.78±3.36	0.04

*Values represent mean±SD. SD: Standard deviation

The scores of Schirmer I test increased in both groups, with a greater improvement in Group A (at day 90: 22.75 ± 3.04 mm vs. 21.78 ± 3.36 mm, *P*: 0.04). The values of TF-BUT improved in both groups, the difference being statistically insignificant.

Conclusion

Autologous plasma was almost equally effacious with slightly more improvement seen in TBUT while CMC and Sodium hyaluronate tear substitutes were equally efficacious and all three were safe in reducing symptoms of dry eye.

Discussion

We evaluated the efficacy and safety of Autologous serum eye drops and CMC/Sodium hyaluronate tear substitute in participants in the age group of 18–60 years.(7) The results of the study show that the tear substitutes are efficacious in reducing dryness of eyes as evident from the reduction of OSDI score and improvement in secondary parameters, namely, Schirmer test and TF-BUT. The safety of these drugs is also reflected in the study results.(8)The OSDI score reduced with treatment in both groups all follow-up visits. This showed that both the tear substitutes were efficacious in reducing the symptoms of dry eye. (9-10)These results are similar to other studies where an improvement in OSDI scores has been shown with the use of serum and CMC/Sodium hyaluronate tear drops.(11-12) Both tear substitutes are efficacious in reducing symptoms as they moisturize the ocular surface and due to their high viscosity increases their retention time and hence beneficial effect to the patient.(13) The improvement in OSDI score was greater for Group A (Autologous Serum Eye Drops) as compared to Group B (CMC or Sodium Hyaluronate) tear substitutes; the results were statistically significant. Only slightly greater improvement shown by Group A.Schirmer *I*-test values, assessed on day 0 and day 90, showed an improvement in both groups. Group A participants, who received Autologous serum tear substitutes, showed a higher improvement in comparison with Group B who received CMC/Sodium Hyaluronate eye drops.Tear TF-BUT values increased for Groups A and B on subsequent follow-ups, but there was no statistically significant difference between the two groups. Being a part of ones own body the autologous serum eye drops may have some additional properties which could be responsible for their higher efficacy when compared with CMC/Sodium hyaluronate eye drops.(14)The study included most clinically relevant tests and questionnaire to assess the condition. The major limitations of the study are the inability to assess patient adherence to the therapy, use of an open-label study design, and the inability to include osmolarity testing.Although a statistically significant difference in the mean OSDI score and Schirmer test was seen, the present study fails to establish any clinically significant difference between Autologous serum eye drops vs CMC/Sodium hyaluronate eye drops.(15) Large-scale double-blind studies may be required to validate the findings of this study in future.

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