Original Article

Carboxymethyl Cellulose versus Hydroxypropyl Methylcellulose Tear Substitutes for Dry Eye Due to Computer Vision Syndrome: Comparison of Efficacy and Safety

Rahul M. Rajendraprasad, Gagandeep Kwatra[1], Nitin Batra[2]

Medical Advisor, Novo Nordisk India, Bengaluru, Karnataka, Departments of [1]Pharmacology and [2]Ophthalmology, Christian Medical College and Hospital, Ludhiana, Punjab, India

Abstract

Background: Prolonged use of visual display terminal images on electronic devices such as computers frequently leads to symptoms of dry eye. Tear substitutes form the mainstay of treatment for mild-to-moderate dry eye. **Aim:** The study aimed to evaluate the efficacy and safety of carboxymethyl cellulose (CMC) versus hydroxypropyl methylcellulose (HPMC) tear substitutes for dry eye due to computer vision syndrome (CVS). **Materials and Methods:** This was a prospective, randomized, comparative, and open-labeled study. The efficacy of CMC 0.5% and HPMC 0.3% tear substitutes was compared in 180 participants (90 in each group) with dry eye. Change in Ocular Surface Disease Index (OSDI) score, Schirmer I test score, and tear film break up time (TF-BUT) were used as efficacy parameters. Safety was monitored on all visits. **Results:** The baseline OSDI score 23.48 and 23.32 in Group A and B, respectively, decreased with treatment in both groups on all follow-up visits as compared to the baseline (day 90: 13.9 ± 3 vs. 14.81 ± 3.17, *P*: 0.01). 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. An initial stinging was reported by one participant, each in both groups. **Conclusion:** CMC and HPMC tear substitutes were equally efficacious and safe in reducing symptoms of dry eye due to CVS.

Keywords: *Carboxymethyl cellulose, computer vision syndrome, dry eye syndrome, hydroxypropyl methylcellulose, tear substitutes*

Introduction

As per the 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."[1] The prevalence of dry eye syndrome increases with age and ranges from 5.5% to 37.7%.[2] In the Indian population, hospital-based prevalence of dry eye has been reported to vary from 18% to 27%.[3]

The etiology of dry eye still remains unclear though some known risk factors are older age, female gender, arthritis, smoking, hormone-replacement therapy, and environmental factors such as low relative humidity.[4] Prolonged exposure to visual display terminals images on electronic devices such as computers and video games leads to reduced blink rate, which generate ocular discomfort and subsequently dry eye.[5]

The Occupational Safety and Health Administration department of US Government has defined computer vision syndrome (CVS) as a "complex of eye and vision problems that are experienced during and related to computer use; it is a repetitive strain disorder that appears to be growing rapidly in workers using computers for more than 3 h/day."[6]

A key principle for the management of dry eye disease is an augmentation of tear film through the topical administration of artificial tear substitutes. These tear substitutes are the mainstay of treatment for mild-moderate dry eye symptoms. These products enhance tear stability and help to retain moisture in eye, thus relieving the symptoms of CVS.[7]

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Address for correspondence:
Dr. Gagandeep Kwatra, Department of Pharmacology, Health Sciences Block, Christian Medical College and Hospital, Ludhiana, Punjab, India.
E-mail: kwatragagandeep@gmail.com

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Carboxymethyl cellulose (CMC) is a cellulose polymer with a carboxylic group and has a high viscosity. It has bioadhesive properties, and its anionic nature may be the reason for high retention time on the cornea. Hydroxypropyl methylcellulose (HPMC), also known as hypromellose, is a semisynthetic polymer. It is less viscous than CMC due to its molecular size but is known to have emollient properties.[8]

In this study, we compared the efficacy and safety of two commonly used tear substitutes containing CMC 0.5% and HPMC 0.3% in participants diagnosed with dry eye due to CVS. This was the first time two commonly used tear substitutes were compared in CVS using both qualitative and quantitative tests of dry eye disease.

Materials and Methods

Study design

This was a prospective, randomized, comparative, and open labeled study, conducted by enrolling the patients, visiting the outpatient clinic of department of ophthalmology. The sample size was calculated as 180 (90 in each group) based on previous studies with an $\alpha = 0.05$ and $\beta = 0.2$.[9,10] Patients diagnosed to have dry eye due to CVS and to satisfy the inclusion were enrolled in the study after getting the informed consent. The study procedures followed the Helsinki Declaration of 1975, as revised in 2000. The study was approved by the institutional ethics committee and research board.

Inclusion criteria

Participants of both genders aged 18 years and above with an average computer use of ≥3 h at a stretch per day or ≥15 h a week for at least 3 months presenting with ocular symptoms (blurring of vision, headache, dry eyes, redness of eyes, or eye strain) were considered to have CVS.[11]

Exclusion criteria

Participants with known hypersensitivity to the study medications and those who had used any other topical ophthalmic medications within 14 days (other than tear substitutes) were excluded from the study. Other criteria for exclusion were a history of active ocular infection or ocular allergy, ocular surgery within 12 months, recurrent herpetic keratitis, use of contact lenses, systemic medications (such as diuretics, antidepressants, anxiolytics, and antihypertensives), and any systemic diseases/syndromes associated with dry eye (Sjogren's syndrome and other autoimmune diseases).

Study procedure

The participants first 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 using computer-generated random numbers: group A received CMC 0.5% and Group B received HPMC 0.3% tear substitute for 90 days.

Efficacy parameters were assessed on days 15 (±2 days), 30 (±2 days), and 90 (±2 days).

In addition to the tear substitute use, participants were advised to blink voluntarily more often during computer usage. Participants were advised to follow the "20-20-20 rule." As per this rule, participants were advised to look away from the computer at least every 20 min and gaze for at least 20 s at an object at least 20 feet away: this causes relaxation of the ocular muscles of accommodation.

Primary efficacy parameter

Change in ocular surface disease index score

This is the most frequently used survey instrument and is validated for the assessment of ocular surface disease severity in dry eye research. It consists of 12 questions that assess symptoms, functional limitations, and environmental factors related to dry eye. The maximum score is 100, which indicates complete disability and a score of zero indicates no disability.[12] Ocular Surface Disease Index (OSDI) questionnaire was administered to participants on all visits.

Secondary efficacy parameters

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.[13] 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 a special Whatman filter paper strip. It was placed in the lower conjunctival sac at the junction of the outer 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 from the eye and the wet portion measured. Schirmer test I (Schirmer test without anesthesia) measures basic plus reflex tear secretion. Although no absolute cutoff has been established for this test, <10 mm of strip wetting in 5 min is suggestive of an unhealthy tear film.[13] This was performed on day 0 and day 90.
c. Adverse drug reaction (ADR) monitoring was done on all visits. In addition, the participants were advised to report an ADR at any time.

Statistical analysis

The normality of data was tested by Kolmogorov–Smirnov test. If the normality was rejected, then nonparametric test was used.

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 and Wilcoxon ranked sum test within the group across follow-up

2. Qualitative variables were correlated using Chi-square test/Fisher's exact test.

A $P < 0.05$ was considered statistically significant.

The data was entered in MS EXCEL spreadsheet, and analysis was done using SPSS (Statistical Package for the Social Sciences) software version 21.0 IBM, Chicago,USA.

Results

Demographic features

Age and gender distribution

In this study, out of a total of 180 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].

Comparison of efficacy and safety parameters between the groups

Efficacy ocular surface disease index score

OSDI score, used as the primary efficacy parameter, was comparable in Group A and B at baseline: 23.38 and 23.32, respectively, with a $P = 0.728$. As compared to the baseline, there was an improvement in OSDI scores on all follow-up visits in both groups, and this difference was statistically significant. There was also a statistically significant difference between Groups A and B on all follow-up visits, as shown in Figure 1.

Schirmer *I* test values

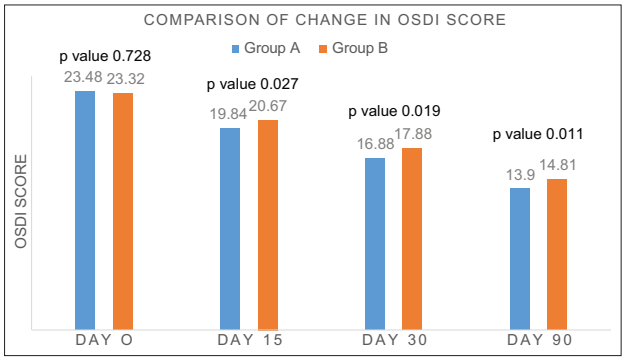

Figure 1: Comparison of ocular surface disease index score between the two groups at follow-up visits

Table 1: Age distribution of study participants

Age distribution (years)	Study group (%)		Total (%)	*P*
	A	B		
18–20	26 (28.89)	28 (31.11)	54 (30.00)	0.171
21–30	50 (55.56)	41 (45.56)	91 (50.56)	
31–40	8 (8.89)	14 (15.56)	22 (12.22)	
41–50	4 (4.44)	1 (1.11)	5 (2.78)	
>50	2 (2.22)	6 (6.67)	8 (4.44)	
Total	90	90	180	

The Schirmer *I*-test values were comparable between the two groups on day 0 (12.86 mm for Group A and 13.12 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 an improvement in symptoms. Group A showed a statistically significant increase in values as compared to Group B [Table 3].

Tear film break up time

The mean TF-BUT value for Group A and B was comparable at baseline: (10.56 s and 10.96 s, respectively; $P = 0.393$). TF-BUT values increased for both the groups on subsequent follow-up visits, which is indicative of an improvement in dry eye symptoms [Table 4]. There was no statistically significant difference between the groups on comparing the values on day 90 ($P = 0.4$).

Safety

Only one study participant, each from Group A and Group B had initial burning sensation when they used the respective tear substitutes for the first time. On subsequent usage, there was no discomfort reported, and therefore the participants continued with the prescribed medications. No other ADRs were reported.

Discussion

We evaluated the efficacy and safety of two commonly used tear substitutes, CMC and HPMC in participants in the age group of 18–60 years. The results of the study show that the tear substitutes are efficacious in reducing dryness

Table 2: Gender distribution of study participants

Gender	Study group (%)		Total (%)	*P*
	A	B		
Female	52 (57.78)	41 (45.56)	93 (51.67)	0.101
Male	38 (42.22)	49 (54.44)	87 (48.33)	
Total	90	90	180	

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

Table 4: Comparison of tear film break up time between Group A and Group B

	Group A*	Group B*	*P*
Day 0	10.56±3.27	10.96±2.82	0.393
Day 30	15.12±3.21	15.32±2.73	0.679
Day 90	16.22±3.19	16.64±2.72	0.400

*Values represent mean±SD. Values are measured in seconds. SD: Standard deviation

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.

In today's world, computers and laptops are used for different aspects of office work: accessing the Internet as well as for recreational purposes. Computer users mostly belong to the younger age group. In India, around 38% of internet users are in the age group of 25–34 years.[14] About 51% of participants who were diagnosed with CVS in our study are in the age group of 21–30 years. When combining the age groups 18–20 and 21–30 years, it comprised about 80% of study participants. Computer professionals are mainly from the younger generation, and they are more likely to be affected by computer-related problems such as CVS considering the need to spend long hours in front of visual display terminals.

The OSDI score reduced with treatment in both groups of study participants on all follow-up visits, starting from 15th day onward. This showed that both the tear substitutes were able to reduce the symptoms of dry eye due to CVS. These results are similar to other studies where an improvement in OSDI scores has been shown with the use of CMC and HPMC tear drops.[15,16] Both tear substitutes are efficacious in reducing symptoms as they moisturize the ocular surface and their high viscosity increases their retention time and persistence of beneficial effect to the patient. The improvement in OSDI score was greater for Group A (CMC) as compared to Group B (HPMC) tear substitutes; the results were statistically significant. The slightly greater improvement shown by the CMC group may be due to the higher mucoadhesive properties of CMC.[17,18]

Schirmer *I*-test values, assessed on day 0 and day 90, showed an improvement in both groups. Group A participants, who received CMC 0.5% tear substitutes, showed a higher improvement in comparison with Group B who received HPMC 0.3%. In a study comparing CMC with hyaluronate, a similar improvement in Schirmer test values was demonstrated by CMC and sodium hyaluronate study groups.[19] A study which compared CMC and HPMC drops in postoperative laser *in situ* keratomileusis patients reported that a fewer number of participants in the CMC group had dry eye symptoms at 2 weeks and 1-month follow-up, but there was no difference between the two groups at 3- and 6-month follow-up visits.[16]

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. Similar results were reported in a study by Comez *et al*., in which the use of HPMC 0.3% and CMC 0.5% eye drops demonstrated significant improvement in TF-BUT as compared to the baseline, but there was no difference between the two groups.[9]

Only one study participant each from Group A and Group B had an initial burning sensation when they used the respective tear substitutes for the first time. On subsequent usage, there was no discomfort reported, and therefore they continued to use the prescribed medications. Three participants in one study had keratitis, hypersensitivity reactions, and conjunctival hyperemia,[17] while other studies have not reported any adverse effects with the use of CMC.[10,20]

Besides being highly viscous and mucoadhesive, CMC may have some additional properties which could be responsible for the observed higher efficacy of CMC when compared with HPMC. CMC has been demonstrated to have a prolonged ocular residence time and good shear thinning properties in a small-angle neutron scattering and rheology study by Lopez *et al*.[18] An experimental study demonstrated that CMC may have a modulatory effect on corneal epithelial wound healing.[21] An earlier study shows that it may have a cytoprotective effect on the ocular surface when used before insertion of contact lens into the eye.[22] However, in the present study, although, we found a statistical difference between the two groups in the OSDI score and Schirmer test values, this difference may not be clinically significant.

The main strength of the study is the relevance of the study in the current scenario where online classes, webinars, along with video calls have increased exponentially due to the current pandemic. People are spending more time in front of the screen, and hence higher number of cases of CVS are likely to be seen in clinical practice. The study has a robust design and included the most clinically relevant tests and questionnaire to assess the condition. The main 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.

Both CMC and HPMC tear substitutes were efficacious in reducing subjective symptoms as indicated by improved OSDI score, supported by objective measures Schirmer I test values and TF-BUT. The study clearly gives evidence to support the use of tear substitutes in dry eye due to CVS.

Conclusion

Although there was a statistically significant difference in the mean OSDI score and Schirmer test, the present study fails to detect any clinically meaningful difference between CMC and HPMC. Hence, it could be concluded that CMC and HPMC provide a similar efficacy in CVS. Future large-scale double-blind studies may be planned to validate the findings of the present study.

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Ethical clearance

Study was conducted after approval from the Institutional Ethics Committee.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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