Research Article

Comparative evaluation of topical carboxymethyl cellulose either alone or in combination with topical corticosteroid in the treatment of dry eye in a tertiary-care teaching hospital

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Abstract

Background: The treatment of dry eyes has traditionally involved hydrating and lubricating the ocular surface, which include usage of artificial tear drops [carboxymethyl cellulose (CMC)]. Corticosteroids possess potential anti-inflammatory properties, thereby used in controlling inflammation in many organs. FDA has approved the prescription of topical corticosteroids for corticosteroid-responsive inflammatory conditions such as dry eye diseases. **Aims and Objective:** To compare the effect of topical CMC alone or in combination with topical corticosteroid for the treatment of dry eye in a tertiary-care teaching hospital. **Materials and Methods:** A total of 60 patients diagnosed with dry eye were enrolled for a study period of 1 year. Patients (n = 60) were stabilized on CMC for 2 weeks and there then divided into two groups: group I (n = 30), CMC; group II (n = 30), CMC + corticosteroid. The patients were followed up for 12 weeks. Diagnostic tests included Schirmer's test and tear breakup time (TBUT) test. Quality of life was assessed by Ocular Surface Disease Index (OSDI). Analysis was done by t test; $p < 0.05$ was considered significant. **Results:** Schirmer's values in groups I and II at 0 and 12 weeks were 7.8 ± 0.81 and 15.4 ± 0.62 ($p < 0.0001$) and 7.43 ± 0.42 and 17.53 ± 0.25 ($p < 0.0001$), respectively. TBUT values in groups I and II at 0 and 12 weeks were 4.93 ± 0.44 and 9.36 ± 0.35 ($p < 0.0001$) and 4.5 ± 0.38 and 10.43 ± 0.22 ($p < 0.0001$), respectively. OSDI score in groups I and II at 0 and 12 weeks were 87.64 ± 1.41 and 54.25 ± 1.09 ($p < 0.0001$) and 91.17 ± 1.13 and 53.55 ± 1.14 ($p < 0.0001$), respectively. At 12 weeks, intergroup comparison in Schirmer's test ($p < 0.05$), TBUT test ($p < 0.05$), and OSDI score ($p < 0.05$) was done. Burning and stinging, photophobia, discharge, ocular infection, and increased intraocular pressure were among the common adverse effects seen. **Conclusion:** Both groups showed significant improvement in Schirmer's test, TBUT test, and OSDI score at the end of study. Intergroup comparison showed significant improvement in the group where corticosteroid was added. Adding corticosteroid ameliorated the symptoms rapidly but short-term use recommended because of adverse effects.

KEY WORDS: Dry Eye; Carboxymethyl Cellulose; Corticosteroid; Schirmer's Test; Tear Breakup Time Test; Ocular Surface Disease Index

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Introduction

Dry eye syndrome comprises a variety of conditions characterized by ocular discomfort symptoms and associated with less tear production or abnormally rapid tear film evaporation. The National Eye Institute/Industry Workshop on Clinical Trials in Dry Eye has defined dry eye as "a disorder of the tear film due to tear deficiency or excessive tear evaporation, which causes damage to the inter-palpebral ocular surface and is

associated with symptoms of ocular discomfort."[1] The increase in the knowledge of dry eye pathology has modified the definition of dry eye syndrome from being a trivial ocular disorder involving secretion deficiency or excess tear evaporation to detailing a multifactorial disease, involving chronic inflammation or tear film instability.[2] Dry eye syndrome becomes increasingly prevalent with age with overall prevalence estimated to be 5%–35% in various populations.[3] The treatment of dry eyes has traditionally involved hydrating and lubricating the ocular surface, which include usage of artificial tear drops [carboxymethyl cellulose (CMC)].[4] Corticosteroids possess potential anti-inflammatory properties, thereby used in controlling inflammation in many organs. The FDA has approved the prescription of topical corticosteroids for corticosteroid-responsive inflammatory conditions such as dry eye diseases.[5] In a study, it was found that patients with dry eye significantly reported difficulty with daily tasks than those without dry eye.[6] The Ocular Surface Disease Index (OSDI), a validated tool, is used for assessing the subjective severity of dry eye.[7] As dry eye is a common disorder in ophthalmology practice, this study was designed to compare the effect of topical CMC alone or in combination with topical corticosteroid for the treatment of dry eye in a tertiary-care teaching hospital at Dehradun, Uttarakhand, India.

Materials and Methods

This study was conducted by the Department of Pharmacology in Ophthalmology OPD at SGRRIM&HS (Shri Guru Ram Rai Institute of Medical and Health Sciences), Dehradun, Uttarkhand, India, for a period of 1 year (January 2013 to December 2013). A total of 60 dry eye patients were included in the study. Before the commencement of study, approval was taken from Institutional Ethics Committee, and written informed consent was obtained from all the participants.

Study Design

This open-label study was done in 60 dry eye patients. Patients of either sex (male/female), aged between 18 and 70 years, and all diagnosed cases of dry eye were included in the study. Exclusion criteria were aged younger than 18 years or older than 70 years, any previous ophthalmology surgery, or any uncontrolled systemic disease affecting eye. The patients were given drugs on the basis of physician's discretion, depending upon the condition of the patient at the time of presentation. A detailed history was taken for each patient, and a thorough clinical examination was done in each case. Patients were stabilized initially for a period of 2 weeks with topical CMC and then subsequently divided into two groups on the basis of response to CMC: group I (n = 30) CMC (0.5%) eye drop TDS (one drop in each eye three times a day); group II (n = 30) CMC (0.5%) eye drop TDS + flurometholone (0.1%) e/d TDS or loteprednol (0.5%) e/d TDS (one drop in each eye three times a day). After stabilization, patients were followed up for 6 and 12 weeks. The parameters assessed in this study included Schirmer's test, tear breakup time (TBUT) test, and Ocular Surface Disease Index (OSDI). The Schirmer's test and tear breakup time (TBUT) test were done at 0, 2, 6, and 12 weeks. The OSDI score was evaluated at 0, 2, and 12 weeks. The Schirmer's test was done by measuring the amount of wetting of Whatman 41 filter paper, 5 mm wide and 35 mm long. The result was expressed as millimetres of wetting from the fold at 5 min. Wetting less than 5 mm was suggestive of severe dry eye; 5–10 mm being moderate; and 10–15 mm mild dry eye. For measuring TBUT, an impregnated fluorescein strip moistened with nonpreserved saline was instilled in the lower fornix of the eye of the patient. The patient was asked to blink several times. The unit of measurement was in seconds. A TBUT of less than 5 s was suggestive of severe dry eye; 5–10 s being moderate; and 10–15 s mild dry eye. OSDI is a 12-question survey tied to common symptoms that have an impact on quality of life.[2] Answers are scored on a 5-point scale from "none of the time" {0} to "all of the time" {4}. OSDI includes gauging how often a respondent's eyes have been sensitive to light or felt gritty in the previous week; whether or not the respondent has had difficulty reading or driving as a result of issues with his or her eyes; and whether or not the respondent felt any eye discomfort in windy or very dry environments.[8] The patients were examined thoroughly at each follow-up visit, and presence of any adverse event because of the drugs given was evaluated.

Statistical Analysis

The treatment groups were compared and the results analyzed by using paired "t" test in GraphPad Instat software; p value $\leqslant 0.05$ was considered to be significant.

Results

A total of 60 patients were included in the study, with a mean age of 46.0 ± 1.79 years. Male to female ratio was 1:1.31. Mean

Table 1: Baseline characteristics of the patients

Parameters	Number (%)
Total number of patients (n)	60
Mean age (years)	46 ± 1.79
Male:female	1:1.31 (43.33%, 56.67%)
Mean duration of illness (years)	1.95 ± 0.16
Schirmer's test	
Group I	7.8 ± 0.81
Group II	7.43 ± 0.42
TBUT test	
Group I	4.93 ± 0.44
Group II	4.5 ± 0.38
OSDI	
Group I	87.64 ± 1.41
Group II	91.17 ± 1.13

Table 2: Progressive changes in Schirmer's test, TBUT test, and OSDI score values during the study period

Groups	Schirmer's test		TBUT test		OSDI	
	Group I	Group II	Group I	Group II	Group I	Group II
0 week	7.8 ± 0.81	7.43 ± 0.42	4.93 ± 0.44	4.5 ± 0.38	87.64 ±1.41	91.17 ± 1.13
2 weeks	8.17 ± 0.78*	8.87 ± 0.38**	5.4 ± 0.42***	5.37 ± 0.36***	82.97 ± 1.67**	84.48 ± 1.36**
6 weeks	10.87 ± 0.74**	11.63 ± 0.37**	7.2 ± 0.38**	7.03 ± 0.31**	-	-
12 weeks	15.4 ± 0.62**	17.53 ± 0.25**	9.36 ± 0.35**	10.43 ± 0.22**	54.25 ± 1.09**	53.55 ± 1.14**

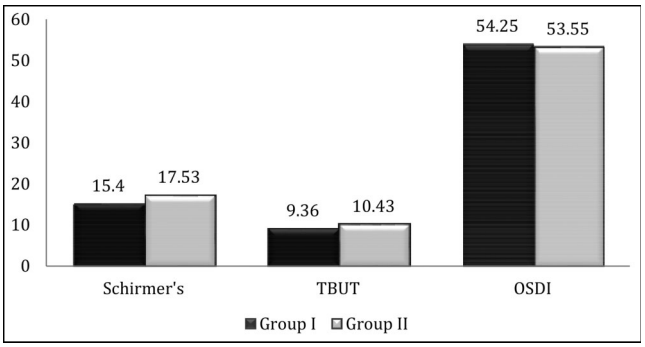
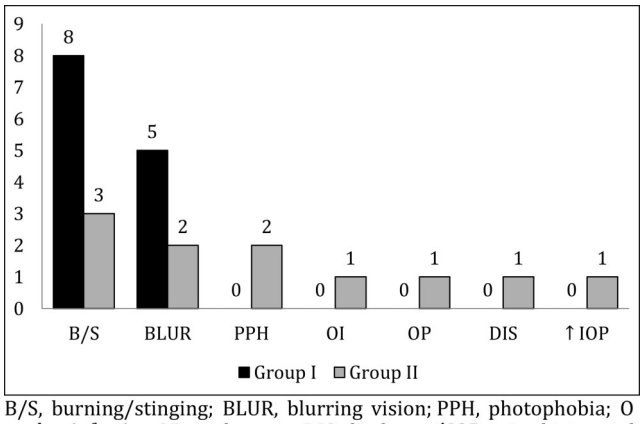


Figure 1: Intergroup comparison of Schirmer's test, TBUT test, and OSDI score values at 12 weeks.



B/S, burning/stinging; BLUR, blurring vision; PPH, photophobia; O ocular infection;OP, ocular pain, DIS, discharge,↑IOP, raised intraocul pressure

Figure 2: Safety assessment.

duration of illness was 1.95 ± 0.16 years. Baseline characteristics of all the patients enrolled for the study with reference to Schirmer's test, TBUT test, and OSDI score were similar in the two groups as shown in Table 1. Safety profile was assessed by noting the adverse events reported during the study. All results were expressed as mean ± SEM.

The mean value of Schirmer's test at the start of the study was 7.62 ± 0.61 mm. The mean value of TBUT was 4.71 ± 0.41 s. The mean value of OSDI score at the start of the study was 89.41 ± 1.27. At the end of 2 weeks, baseline Schirmer's test value in group I was 8.17 ± 0.78 mm ($p < 0.005$) and in group II was 8.87 ± 0.38 mm ($p < 0.0001$); baseline TBUT values in group I was 5.4 ± 0.42 s ($p < 0.0008$) and in group II was 5.37 ± 0.36 s ($p < 0.0003$); and baseline OSDI score in group I was 82.97 ± 1.67 ($p < 0.0001$) and in group II was 84.48 ± 1.36 ($p < 0.0001$) (Table 2). Hence, the values had significantly improved at 2 weeks when compared with day 0, and the difference was highly significant. The Schirmer's test and TBUT test values were also compared at 2 and 6 weeks in each group. At 6 weeks, the Schirmer's test value in group I was 10.87 ± 0.74 mm ($p < 0.0001$) and in group II was 11.63 ± 0.37 mm ($p < 0.0001$) At 6 weeks, the TBUT test value in group I was 7.2 ± 0.38 s ($p < 0.0001$) and in group II was 7.03 ± 0.31 s ($p < 0.0001$) (Table 2). Intragroup comparison of Schirmer's test values, TBUT test values, and OSDI score at 2 and 12 weeks was done. At 12 weeks, Schirmer's test value in group I was 15.4 ± 0.62 mm ($p < 0.0001$) and in group II was 17.53 ± 0.25 mm ($p < 0.0001$); TBUT test value in group I was 9.36 ± 0.35 s ($p < 0.0001$) and in group II was 10.43 ± 0.22 s ($p < 0.0001$); and the OSDI score in group I was 54.25 ± 1.09 ($p < 0.0001$) and in group II was 53.55 ± 1.14 ($p < 0.0001$) (Table 2).

At the end of study period (12 weeks), intergroup comparison between the study groups was done for the Schirmer's test values, TBUT test values, and OSDI score (Figure 1), which showed significant difference ($p < 0.01$). Overall, adverse events were reported in 24 of 60 patients (Figure 2): 13 in group I and 11 in group II. The predominant side effects were burning and stinging sensation followed by photophobia, ocular infection, blurring of vision, discharge from eye, ocular pain, and elevated intraocular pressure (IOP). The side effects in both the groups were mild and transient and did not necessitate stoppage of treatment.

Discussion

Dry eye is a common complaint among middle-aged and older adults, and its prevalence increases progressively with age.[9–11] The average age of patients in this study were 46 ± 1.79 years, reflecting the usual age of disease

manifestation. This was comparable with the previous studies where the age group of 41–50 years and 40–49 years showed a relative peak in the prevalence of dry eye symptoms.[12,13] This peak reflects a dry eye state induced by environmental exposure, to which this age group, being the most active occupationally, is exceptionally prone.[12] In our study, women (56.67%) had significantly higher prevalence of dry eye symptoms compared with men (43.33%). The male:female ratio in this study was 1:1.31, which is comparable with previous studies.[11,12,14]

Eearlier studies have shown that CMC and corticosteroids are effective in the treatment of dry eye symptoms.[15–17] This finding was also substantiated in this study with significant improvement in the Schirmer's test, TBUT test, and OSDI values in both the study groups. Several randomized trials have demonstrated that short-term topical corticosteroid use, as long as 4 weeks, improves signs and symptoms of dry eye.[5] Previous study has shown that 0.5% loteprednol and 0.1% fluorometholone are effective in patients with dry eye.[18,19] Patients with dry eye syndrome not only have ocular discomfort but also visual disturbances; therefore, the impact is significant, affecting individual daily activities such as driving and reading, as well as social functioning and productivity, which affects quality of life of the patients.

The Schirmer's test values, TBUT values and OSDI score in each group continued to improve till the end of study period. This finding was also substantiated in this study with significant improvement in the Schirmer's test and TBUT test in both the study groups. The improvement started to show at the end of 6 weeks and this improvement was highly significant ($p < 0.0001$). This correlates well with earlier studies that have shown that CMC and corticosteroids start showing their effects within 6 weeks.[15–,20] Improvement in OSDI score during the study period is comparable with previous studies.[6,16,21]

Intergroup comparison was done at 12 weeks. In our study, corticosteroids rapidly ameliorated the subjective symptoms among the patients with moderate or severe dry eye. There was a significant decrease in the patient's complaints in the group receiving topical corticosteroid during the study period. Significant difference was found between the groups with respect to Schirmer's test values, TBUT test values, and OSDI score. The improvement in Schirmer's test and TBUT test values is concordant with the studies by Avunduk et al[22] and Bragheeth and El-Kasaby,[19] which showed that dry eye patients receiving 0.1% fluorometholone plus artificial tear substitutes experienced lower symptom severity scores compared with patients receiving artificial tear substitute alone (Figure 1). All of these suggested that rapid anti-inflammatory activity with high performance of corticosteroid is very effective for patients with moderate or severe dry eye, which also provide evidence that nonspecific immune inflammation is involved in the development of dry eye.

Corticosteroid can improve the symptoms and signs of dry eye rapidly; however, their prolonged use can lead to increased infection, elevation of IOP, and cataract formation.[23] In our study, increased IOP occurred in only one patient, and hormone-related complications did not occur during the study period, suggesting that the application of topical corticosteroid for short term is safe. The patient complaining of brow pain (due to increased IOP) did not require any intervention or change of drug and was assured that the brow pain occurring because of the drug intake would disappear as soon as the drug is stopped. Other adverse effects noted during the study period were mild and did not require any alteration or discontinuation of study drugs. These adverse effects were comparable with those reported in previous clinical studies.[14–16,19,23]

Study Limitations

This was an open-label study, as both the doctor and the patient were aware of the medications being prescribed. Hence, there are more chances of errors; small sample size of only 60 patients may not be sufficient enough to demonstrate intergroup differences in evaluating the efficacy of study drugs. The duration of patient follow-up was just up to 12 weeks. A longer follow-up period may have yielded different results. Hence, keeping these limitations in view, further studies with larger sample size and longer duration are required to evaluate the efficacy and safety of CMC and corticosteroids in the treatment of dry eye.

Conclusion

Our study showed that the patients receiving corticosteroid along with CMC showed significant improvement in the Schirmer's test, TBUT test values, and OSDI scores compared with the group receiving CMC alone. Significant intergroup difference was found when comparing the Schirmer's test values, TBUT test values, and OSDI score at the end of study period. Although topical corticosteroids are effective, they are generally recommended only for short-term use as prolonged use may result in adverse events including ocular infection and raised IOP.

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