Comparative evaluation of efficacy and safety of carboxymethylcellulose either alone or in combination with non-steroidal anti-inflammatory drug in the treatment of dry eye in a tertiary care teaching hospital

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INTRODUCTION

Dry eye is a multifactorial disease of the ocular surface and tear film which results in ocular discomfort, visual disturbances, and tear instability with potential damage to the cornea and conjunctiva. It has been defined by The National Eye Institute/Industry Workshop on Clinical Trials in dry eyes as “a disorder of the tear film due to tear deficiency or excessive tear evaporation, which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort.”1 The overall prevalence of dry eye syndrome is estimated to be 5-35% in various population and the symptoms increase with age.2 The treatment of dry eyes has traditionally involved hydrating and lubricating artificial tears. The newer medications include non-steroidal anti-inflammatory drugs (NSAIDs) for the treatment of dry eye disorders. This study was designed to compare the effect of topical carboxymethylcellulose (CMC) alone or in combination with topical NSAID for the treatment of dry eye in a tertiary care teaching hospital.

METHODS: A total of 60 patients diagnosed with dry eye were enrolled for a study period of 1 year. Patient of either sex (male/female), age between 18 and 70 years, and all diagnosed cases of dry eye in ophthalmology outpatient department were selected. Patients (n=60) were stabilized on CMC for 2 weeks and thereafter divided into two groups. Group I (n=30) received only topical CMC; Group II (n=30) received CMC+NSAID. The patients were followed up to 12 weeks. Diagnostic tests included Schirmer’s test and tear break up time (TBUT). Ocular Surface Disease Index (OSDI) was used for assessing the Quality of Life. Analysis was done using GraphPad InStat software. p<0.05 was considered significant.

RESULTS: This was an open-label study revealing a mean age of 46.0±1.79 years. Females (56.67%) showed a significantly higher prevalence of dry eye symptoms compared to males (43.33%). The mean duration of illness was 1.95±0.16 years. Schirmer’s test, TBUT test values and OSDI score in Group I and Group II at 0 and 12 weeks revealed significant intragroup difference (p<0.0001). At 12 weeks intergroup comparison in Schirmer’s test value (p>0.05) and TBUT test value (p>0.05) showed no significant difference while OSDI score revealed significant difference (p<0.05). Burning, stinging, blurring of vision, photophobia, and hyperemia were among the common adverse effects seen.

CONCLUSION: Both groups showed significant improvement in Schirmer’s test and TBUT test value and OSDI score at the end of the study. Intergroup comparison showed a significant difference with reference to OSDI score. Patients receiving NSAID reported more adverse effects.

Keywords: Dry eye, Carboxymethylcellulose, Non-steroidal anti-inflammatory drugs
difficulty with daily tasks than those without dry eye. The Ocular Surface Disease Index (OSDI) is a validated tool for measuring the subjective severity of dry eye. The treatment was designed to compare the effect of topical CMC alone or in combination with topical NSAID for the treatment of dry eye in a tertiary care teaching hospital at Dehradun, Uttarakhand.

METHODS

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

Study design

This was an open-label study done in dry eye patients attending the ophthalmology OPD from January 2013 to December 2013. A total of 60 consecutive patients suffering from dry eye were included in the study. Patient selection criteria included patients of either sex (male/female), age between 18 and 70 years and diagnosed cases of dry eye. Exclusion criteria were 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 3 times a day), Group II (n=30) CMC (0.5%) eye drop TDS+Ketorolac (0.5%) eye drop TDS or Bromfenac (0.09%) eye drop TDS (one drop in each eye 3 times a day). After stabilization, patients were followed up at 6 and 12 weeks. The parameters assessed in the present study included Schirmer’s test, tear break up time (TBUT) test and OSDI. The treatment groups were compared and results were analyzed using unpaired and paired t-test in GraphPad InStat software. p≤0.05 was considered to be significant.

RESULTS

A total of 60 patients were included in the study who had a mean age of 46.0±1.79 years. Male:female ratio was 1:1.31. Mean duration of illness was 1.95±0.16 years (Table 1). Baseline characteristics of all the patients enrolled for the study in reference to Schirmer’s test, TBUT test and OSDI score were similar in the two groups as shown in the Table 1. Safety profile was assessed by noting the adverse events reported during the study. All results were expressed as mean±standard error of the mean.

The mean value of Schirmer’s test at the start of the study was 7.7±0.70 mm. The mean value of TBUT was 4.88±0.43 sec. The mean value of OSDI score at the start of the study was 89.68±0.70. At the end of 2 weeks, baseline Schirmer’s test value in Group I was 8.17±0.78 mm (p<0.005). In

Table 1: Baseline characteristics of the patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I (n=30)</th>
<th>Group II (n=30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>46±1.79</td>
<td>46±1.79</td>
<td></td>
</tr>
<tr>
<td>Male:female</td>
<td>1:1.31 (43.33%, 56.67%)</td>
<td>1:1.31 (43.33%, 56.67%)</td>
<td></td>
</tr>
<tr>
<td>Mean duration of illness (years)</td>
<td>1.95±0.16</td>
<td>1.95±0.16</td>
<td></td>
</tr>
<tr>
<td>Schirmer’s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>7.8±0.81</td>
<td>7.6±0.6</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>7.8±0.81</td>
<td>7.6±0.6</td>
<td></td>
</tr>
<tr>
<td>TBUT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>4.93±0.44</td>
<td>4.83±0.43</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>4.93±0.44</td>
<td>4.83±0.43</td>
<td></td>
</tr>
<tr>
<td>OSDI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>87.64±1.41</td>
<td>90.22±1.05</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>87.64±1.41</td>
<td>90.22±1.05</td>
<td></td>
</tr>
</tbody>
</table>

All the values are expressed in mean±SEM. TBUT: Tear break up time, OSDI: Ocular Surface Disease Index, SEM: Standard error of the mean.
Group II, the schirmer’s test value was 8.4±0.58 mm (p<0.0001). At the end of 2 weeks, baseline TBUT values in Group I was 5.4±0.42 sec (p<0.0008). In Group II, the TBUT values were 5.4±0.36 sec (p<0.0003) (Table 2). At the end of 2 weeks, baseline OSDI score in Group I was 82.97±1.67 (p<0.0001). In Group II, the OSDI score was 83.34±1.36 (p<0.0001) (Table 3). Hence, the values had significantly improved at 2 weeks as compared to day 0 and the difference was highly significant. At the end of study period (12 weeks), intragroup comparison was done by using the values of Schirmer’s test, TBUT and OSDI score. At 12 weeks Schirmer’s test values in Group I were 15.4±0.62 mm (p<0.0001). In Group II, the value was 16.5±0.48 mm (p<0.0001) (Figure 1). At 12 weeks TBUT test, values in Group I was 9.36±0.35 sec (p<0.0001). In Group II, the value was 10.2±0.23 sec (p<0.0001) (Figure 2). At 12 weeks OSDI score in Group I was 60.89±1.99 (p<0.0001). In Group II, the OSDI score was 54.25±1.09 (p<0.0001) (Figure 3). At the end of study period (12 weeks) intergroup comparison between the study groups was done for the Schirmer’s, TBUT test values and OSDI score (Figure 4). Intergroup comparison of Schirmer’s test and TBUT test values showed no significant difference (p>0.05), but OSDI score showed significant difference at 12 weeks (p<0.0001). Overall adverse events were reported in 22 patients out of 60 patients (Figure 5). 13 in Group I and 9 in Group II, the predominant side effects were burning and stinging sensation, followed by photophobia, blurring of vision and hyperemia. The side effects in both the groups were mild, 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 the present study was 46±1.79 years reflecting the usual age of disease manifestation. This was comparable to 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, females (56.67%) had significantly higher prevalence of dry eye symptoms compared to males (43.33%). The male:female ratio in the present study was 1:1.31 which is comparable to previous studies.11,12,14 Earlier studies have shown that CMC and NSAIDs are effective in the treatment of dry eye symptoms.15-17 This

### Table 2: Changes in Schirmer’s and TBUT test values during the stabilization period (2 weeks).

<table>
<thead>
<tr>
<th>Groups (n=30)</th>
<th>Schirmer’s test (mm)</th>
<th>p-value</th>
<th>TBUT test (sec)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 weeks</td>
<td>2 weeks</td>
<td></td>
<td>0 weeks</td>
</tr>
<tr>
<td>I</td>
<td>7.8±0.81</td>
<td>8.17±0.78</td>
<td>&lt;0.005</td>
<td>4.93±0.44</td>
</tr>
<tr>
<td>II</td>
<td>7.6±0.6</td>
<td>8.4±0.58</td>
<td>&lt;0.0001</td>
<td>4.83±0.43</td>
</tr>
</tbody>
</table>

All the values are expressed in mean±SEM. TBUT: Tear break up time, SEM: Standard error of the mean

### Table 3: Progressive changes in OSDI score during the study period.

<table>
<thead>
<tr>
<th>Groups</th>
<th>0 week</th>
<th>2 weeks</th>
<th>p-value</th>
<th>0 week</th>
<th>12 weeks</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>87.6±1.41</td>
<td>82.97±1.67</td>
<td>&lt;0.0001</td>
<td>87.6±1.41</td>
<td>60.89±1.99</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>II</td>
<td>90.22±1.05</td>
<td>83.34±1.36</td>
<td>&lt;0.0001</td>
<td>90.22±1.05</td>
<td>54.25±1.09</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

All the values are expressed in mean±SEM. OSDI: Ocular Surface disease index, SEM: Standard error of the mean
finding was also substantiated in the present study with significant improvement in the Schirmer’s test, TBUT test and OSDI questionnaire in both the study drug groups. The Schirmer’s test values, TBUT values and OSDI score in each group continued to improve till the end of study period. This improvement in Schirmer’s test and TBUT test values is comparable to previous studies. Improvement in OSDI score during the study period is comparable to previous studies. At 12 weeks, comparison was done between Group I and Group II. No intergroup difference was found between the groups with respect to Schirmer’s and TBUT test, but significant difference was found in OSDI score between the two study groups, this is in accordance with previous study (Figure 4).

Few adverse effects were noted during the study period which were mild and did not require any alteration or discontinuation of study drugs. These adverse effects were comparable to those reported in previous clinical studies.

**Study limitations**

This was an open-label study since both the doctor and the patient were aware of the medications being prescribed. Hence, there are more chances of errors. Second, a small sample size of only 60 patients was included in the study which may not be sufficient enough to demonstrate intergroup differences in evaluating the efficacy of study drugs. Third, 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 NSAIDs in the treatment of dry eye.

**CONCLUSION**

The patients who received CMC+NSAID had a more significant improvement in Schirmer’s, TBUT test values and OSDI score than the patients who received only CMC. However, no intergroup difference was found on comparing the Schirmer’s and TBUT values at the end of study period. Significant intergroup difference was found in OSDI score on comparison at the end of study period.

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**Conflict of interest:** None declared  
**Ethical approval:** The study was approved by the Institutional Ethics Committee

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