Research Article

A comparative analysis of cost-effectiveness of topical medications for the treatment of dry eye syndrome in a tertiary care teaching hospital at Dehradun, Uttarakhand

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Abstract

Background: Dry eye is a common ophthalmological disorder causing ocular discomfort and affecting individual's daily activities. Artificial tears had been the mainstay of treatment since long. Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the newer treatment modalities.

Objective: This study compares cost-effectiveness of topical medications used for the treatment of dry eye syndrome in a tertiary care teaching hospital.

Materials & 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), aged 18–70 years, and all diagnosed cases of dry eye in ophthalmology outpatient department were selected. Patients were divided into two groups: group I ($n = 30$) topical carboxymethyl cellulose (CMC) and group II ($n = 30$) CMC + NSAID. Diagnostic tests included were Schirmer's test and tear breakup time (TBUT). Comparison and analysis of cost, efficacy, and safety between the two groups was carried out at the end of the study period (12 weeks) using GraphPad InStat software. *p*-Value of <0.05 was considered statistically 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. The Schirmer's and TBUT test values were significantly improved in group I and II ($p < 0.001$) on intra-group comparison. Burning, stinging, blurring of vision, photophobia, and hyperemia were among the common adverse effects seen. Intergroup comparison showed significant difference in total cost per prescription per day, total cost per prescription, and total cost of treatment between group I and group II ($p < 0.001$).

Conclusion: This study showed high total cost per prescription per day, total cost per prescription, and total cost of treatment in the patient group receiving NSAID along with CMC as compared to CMC alone. As dry eye is a prevalent condition with the potential for a high economic burden, additional studies are needed to further characterize the economic impact.

KEY WORDS: Dry eye, artificial tear, nonsteroidal anti-inflammatory drugs, cost-effectiveness.

Introduction

Dry eye has been defined 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" by the National Eye Institute/Industry Workshop on Clinical Trials in Dry Eyes.[1] A dry eye produces discomfort and reduced vision when the tear film becomes chronically unstable and repeatedly breaks up between blinks, exposing the corneal and conjunctival epithelium to evaporation.[2] The treatment of dry eyes has traditionally involved hydrating and lubricating the ocular surface, which includes usage of artificial tear drops [carboxymethyl cellulose (CMC)].[3,4] As inflammation is a key component in the pathogenesis of dry eye, nonsteroidal anti-inflammatory drugs (NSAIDs) have recently been evaluated in dry eye clinical trials and animal models.[5,6] Although artificial tears continue to be the first line of treatment, NSAIDs may be considered for patients who

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continue to have symptoms despite aqueous enhancement therapies. Recent studies have suggested that dry eye syndrome may pose a considerable economic burden on the patient and the society.[7,8] Patients with dry eye syndrome not only have ocular discomfort but also visual disturbances; therefore, the impact is significant and affects individual's daily activities, such as driving and reading as well as social functioning and productivity.[8] As dry eye is the most common disorder in ophthalmology practice, this study was conducted to compare the cost-effectiveness of topical medications for the treatment of dry eye syndrome in a tertiary care teaching hospital at Dehradun, Uttarakhand.

Materials and 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 1 year (January 2013 to December 2013). A total of 60 patients with dry eye were included in the study. Before commencement of the study, approval was taken from institutional ethics committee and written informed consent was obtained from the participants.

Study Design

This was an open-label study carried out in 60 patients with dry eye attending the ophthalmology OPD from January 2013 to December 2013. Patient selection criteria included patients of either sex (male/female), aged 18–70 years, and all diagnosed cases of dry eye in ophthalmology OPD. Patients with any previous ophthalmology surgery or any uncontrolled systemic disease affecting eye were excluded for the study. 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 carried out in each case. Specific emphasis was given on the treatment and any lifestyle modifications followed by the patient as instructed by the doctor. 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) carboxymethyl cellulose (0.5%) eye drop (one drop in each eye) three times a day (TDS) . Group II (n = 30) carboxymethyl cellulose (0.5%) eye drop TDS + ketorolac (0.5%) eye drop TDS, or bromfenac (0.09%) eye drop TDS (one drop in each eye). Once the patients were included in the study groups and stabilized for a period of 2 weeks, they were followed up at 6 and 12 weeks. The Schirmer's and tear breakup time (TBUT) tests were carried out at 0, 2, 6, and 12 weeks. The Schirmer's test was conducted by measuring the amount of wetting of Whatman 41 filter paper, 5-mm wide and 35-mm long. The result was expressed as millimeters 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. The patients were examined thoroughly at each follow-up visit and presence of any adverse event due to the drugs administered was evaluated.

Statistical Analysis

The treatment groups were compared and results were analyzed using paired *t*-test in GraphPad InStat software. *P*-value of ≤0.05 was considered to be statistically 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 and TBUT test were similar in the two groups as shown in Table 2. 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 7.7 ± 0.70 mm. The mean value of TBUT was 4.88 ± 0.43 s. 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 the Schirmer's test value was 8.4 ± 0.58 mm ($p < 0.0001$). At the end of 2 weeks, baseline TBUT value in group I was 5.4 ± 0.42 s ($p < 0.0008$) and in group II the TBUT value was 5.4 ± 0.36 s ($p < 0.0003$) [Table 3]. Hence the values were 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 carried out using the test values of Schirmer's test and TBUT. At 12 weeks, Schirmer's test value in group I was 15.4 ± 0.62 mm ($p < 0.0001$) and in group II the value was 16.5 ± 0.48 mm ($p < 0.0001$) [Figure 1]. At 12 weeks, TBUT

Table 1: Demographic profile of 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

All the values are expressed in mean ± SEM.

Table 2: Baseline characteristics of the patients

Parameters	Group I	Group II
Schirmer's	7.8 ± 0.81	7.6 ± 0.6
TBUT	4.93 ± 0.44	4.83 ± 0.43

All the values are expressed in mean ± SEM.

Table 3: Changes in Schirmer's and TBUT test values during the stabilization period (2 weeks) in the study drug groups

Groups (n = 30)	Schirmer's test (mm)		p-Value	TBUT test (s)		p-Value
	0 Weeks	2 Weeks		0 Weeks	2 Weeks	
I	7.8 ± 0.81	8.17 ± 0.78	<0.005	4.93 ± 0.44	5.4 ± 0.42	<0.0008
II	7.6 ± 0.6	8.4 ± 0.58	<0.0001	4.93 ± 0.43	5.4 ± 0.36	<0.0003

All the values are expressed in mean ± SEM.

test value in group I was 9.36 ± 0.35 s ($p < 0.0001$) and in group II, the value was 10.2 ± 0.23 s ($p < 0.0001$) [Figure 2]. At the end of study period (12 weeks), intergroup comparison between the study groups was done for the Schirmer's and TBUT test values [Figure 3]. Schirmer's test and TBUT test values in the intergroup comparison showed no significant difference between the study groups ($p > 0.05$). Overall, adverse events were reported in 22 patients out of 60 patients [Figure 4] with 13 patients in group I and 9 patients 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. Comparison of total cost per prescription per day, total cost per prescription, and total cost of treatment in different study drug groups were carried out at the end of the study period (12 weeks) [Figure 5]. In group I, the total cost per prescription per day, total cost per prescription, and total cost of treatment were 9.78, 136.95, and 821.70 INR,

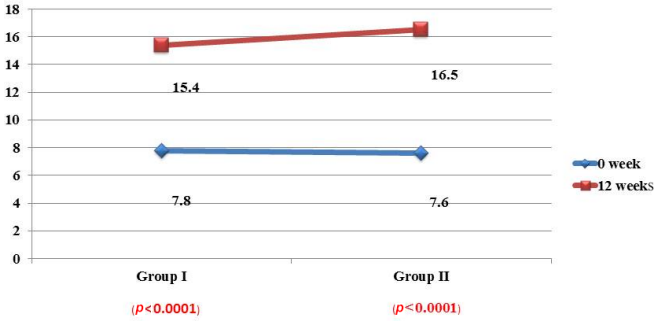

Figure 1: Comparison of Schirmer's test value at 0 weeks and 12 weeks.

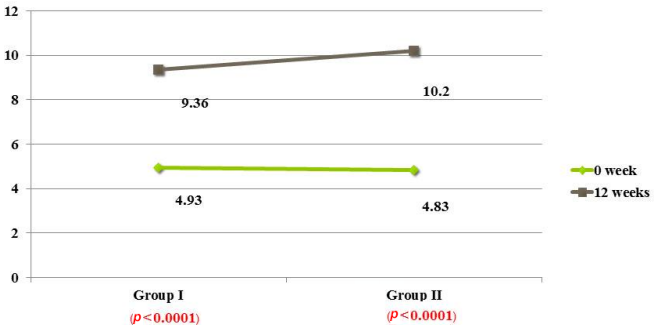

Figure 2: Comparison of Schirmer's test value at 0 weeks and 12 weeks.

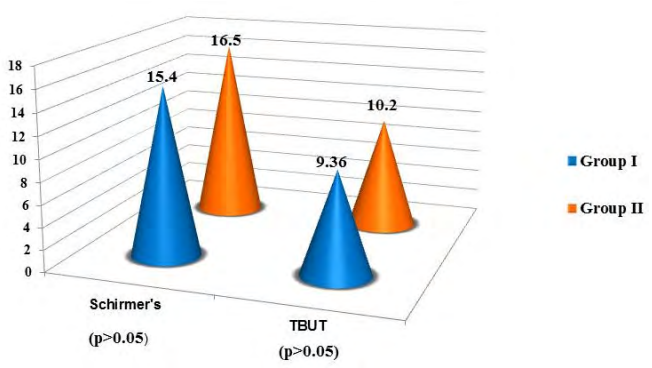

Figure 3: Intergroup comparison between the study drug groups at 12 weeks.

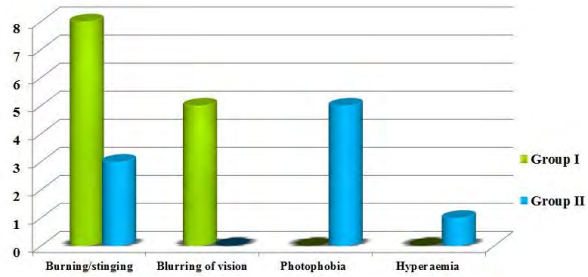

Figure 4: Adverse drug reactions in the study drug groups during the study period.

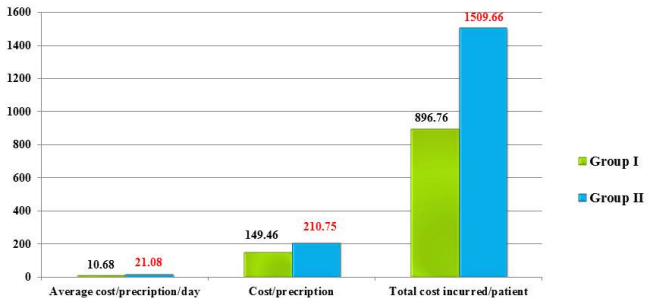

Figure 5: Intergroup cross analysis comparison between the study drug groups at 12 weeks.

respectively. In group II, the total cost per prescription per day, total cost per prescription, and total cost of treatment were 16.93, 196.95, and 1421.70 INR, respectively.

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 was 46.0 ± 1.79 years, reflecting the usual age of disease manifestation. This was comparable to the previous studies where the age groups 41–50 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, was exceptionally prone.[12] In our study, women (56.67%) had significantly higher prevalence of dry eye symptoms compared to men (43.33%). The men/women ratio in this study was 1:1.31, which is comparable to that of 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 finding was also substantiated in this study with significant improvement in the Schirmer's test and TBUT test in both the study drug groups. The Schirmer's test and TBUT values in each group continued to improve till the end of study period. This improvement in Schirmer's and TBUT tests was compared with that of previous studies.[14,16,18,19] At 12 weeks, comparison was conducted between group I and group II. No intergroup difference was found between the groups [Figure 3].

Recent studies have suggested that dry eye syndrome may pose a considerable economic burden on the patient and the society.[7,8] Patients with dry eye syndrome not only have ocular discomfort but also have visual disturbances; therefore, the impact is significant and affects individual's daily activities, such as driving and reading as well as social functioning and productivity.[8] Comparison of total cost per prescription per day, total cost per prescription, and total cost of treatment in the two study drug groups was carried out at the end of the study period (12 weeks). Our study showed high total cost per prescription per day, total cost per prescription, and total cost of treatment in the patient group receiving NSAID along with CMC compared to that of the group of patients receiving CMC alone. A new treatment must consider the relationship between cost and effect in dry eye.[20] Clegg et al.[21] estimated the annual cost associated with the management of dry eye patients and concluded that the economic impact of medication must be seriously considered in relation to its effect on dry eye so that it not only substitutes for but also complements the existing treatments of dry eye. 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 mild and were comparable to those reported in other clinical studies.[14–18]

Study Limitations

This study was an open-label study. The patients and the doctors were aware of the prescribed drugs. Hence, there are more chances of errors. Second, the sample size was small. Only 60 patients were included in the study, which may not be sufficient enough to demonstrate intergroup differences in efficacy of study drugs. Third, the duration of the 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 and TBUT test values than the patients who received only CMC. But no intergroup difference was found on comparing the study groups at the end of study period. NSAID cost much more than CMC; therefore economic impact must be seriously considered in relation to its effect on dry eye.

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