Efficacy of Carboxymethylcellulose 1% vs Rebamipide 2% in Dry eye disease [DED]: a comparative study.

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Abstract: Dry eye disease [DED] is an ocular film disease impacting millions of people globally. It is characterized by an unstable tear film leading to symptoms such as eye irritation, redness, foreign body sensation, photophobia and blurring of vision. This comparative study aims to evaluate the efficacy of Carboxymethylcellulose (CMC) 1% versus Rebamipide 2% eye drops in the management of dry eye disease (DED). It was a single-blinded prospective comparative study. A total of 100 DED patients were enrolled in the study, and after randomization, they received either CMC 1% or Rebamipide 2% eye drops. The patients were instructed to instil one drop in each eye four times a day for 12 weeks. Follow-up visits were scheduled at four and twelve weeks, during which tear film function and tear secretion tests were performed. The results indicated that both CMC 1% and Rebamipide 2% were effective in improving symptoms of DED. The rebamipide group gave better results at the end of 12 weeks in the improvement of multiple evaluating criteria as compared to the CMC group. Both drugs decreased the severity of dry eye disease. Also, the efficacy of rebamipide has been found to be better than carboxymethyl cellulose. This study suggests that both CMC 1% and Rebamipide 2% may be useful in the management of DED *(Abstract)*

Keywords: Dry eye disease, CMC, rebamipide,

I. Introduction

Dry eye disease [DED] is a multifactorial ocular film disease affecting a significant proportion of the population worldwide. An unstable tear film is its defining factor. It is characterised by symptoms such as eye irritation, redness, foreign body sensation, photophobia and blurring of vision.[1] Patients with DED have a reduced quality of life in terms of vision-related activities and a reduced potential to use video monitors for employment, negatively impacting their living situation.[2,3] Furthermore, the disease burden of DED has socioeconomic ramifications.[2] Various factors, such as ageing, environmental factors, and medical conditions, can cause dry eye syndrome.[4]

DED has an impact on millions of people globally. The prevalence of DED in India is higher than the global prevalence and ranges from 18.4% to 54.3%. [5,6]

Rebamipide 2% and Carboxy Methylcellulose (CMC) 1% eye drops are two commonly used lubricating eye drops in the management of dry eye syndrome.

Carboxymethylcellulose (CMC), a high-molecular-weight polysaccharide, is a viscous polymer utilised in artificial tears to extend their ocular surface residence time.[7] CMC leads to the lengthened tear retention time due to its anionic nature, influencing the tear film stability and resulting in decreased tear film hyperosmolarity and potential inflammation relief. [8,9]

Rebamipide ophthalmic suspensions have been clinically shown to be an effective treatment for dry eyes, mucin-induced damage to the corneal epithelium, and tear instability. Rebamipide has the potential to be a beneficial first-line treatment for severe dry eye and other ocular surface problems due to its capacity to alter epithelial cell function, enhance tear stability, and lower inflammation without causing any known significant side effects.[10]

This article aims to compare the effectiveness of Rebamipide 2%, and CMC 1% eye drops in patients with dry eyes.

II. Materials And Methodology

A randomised prospective comparative interventional trial was conducted in the Ophthalmology department of Dr Vikhe Patil Hospital, Ahmednagar, Maharashtra. The study was conducted on a total of 100 dry eye patients visiting the OPD from the period of August 2022 to February 2023. Following receiving approval from the Ethics Committee, the study was conducted. All patients who visited the ophthalmology outpatient department throughout the trial period and who met the inclusion criteria were included in the study after providing written informed consent.

Inclusion criteria consist of the following:

1. Age >18years and of either sex
2. Patient diagnosed with dry eye according to diagnostic guidelines published in 2007 by the Dry Eye Workshop.[11]

The patient underwent an examination in the following order:

i. Patient history, perhaps using a symptom-oriented questionnaire.
ii. Tear film break-up time with fluorescein [TBUT]
iii. Schirmer test with/without anaesthesia
iv. Examination of the eyelid margins and meibomian gland orifices with the expression of meibomian secretion

3. Best corrected visual acuity (BCVA) more than 6/18.

Positive symptoms of dry eye, such as a foreign body sensation, dryness, photophobia, eye pain, and blurred vision, were also noted.

Exclusion criteria consist of individuals having a history of chronic contact lens use, systemic ocular disorders, and local ocular

Right eye	Test Group 1(CMC)			Test Group 2 (Rebamipide)			Comparison
	Pre-treatment `	Post-treatment after 12 weeks	Significance (p-value)	Pre-treatment	Post-treatment after 12 weeks	Significance (p-value)	Group 1 versus Group 2
Tear film Break Up Time (sec)	7.68±1.72	12.62±1.6	P<0.001	7.60±1.60	14.36±1.74	P<0.001	P<0.001
Mean Schirmer's Test 1 Value(mm)	4.42±2.47	10.75±3.22	P<0.001	4.68±2.60	14.08±3.02	P<0.001	P<0.001
Mean Schirmer Test 2 Value(mm)	5.54±2.93	13.47±2.4	P<0.001	5.78±2.81	16.64±2.28	P<0.001	P<0.001

conditions known to induce dry eyes or ocular surface abnormalities. Patients with ocular surface conditions or local or systemic drugs known to produce dry eyes were also prohibited from participating in the trial.

Following single blinding, the patients were randomly split into two equal groups: Group A received CMC at 1%, while Group B received rebamipide at 2%. Every patient was instructed to inject one drop into each eye four times per day for 12 weeks. A follow-up visit was scheduled for the patient at 4 and 12 weeks. Each follow-up visit included a slit lamp examination of the patient along with measurements of their tear film function (by TBUT, tear film break-up time) and tear secretion test (Schirmer's I, Schirmer's II), with the results being documented.

III. Statistical Analysis

A randomised controlled study was carried out. Each outcome is shown as a number, percentage, and mean with a standard deviation (SD). A t-test was used at the conclusion of the study for quantitative measurements, and the Chi-square test was used for qualitative measures. The Z test was used to compare continuous variables between the groups. A p-value of 0.05 or less is regarded as significant.

IV. Result

The study involved 200 eyeballs from 100 dry-eye patients. Around 57% of men and 43% of women participated in the study. The participants' average age ranged from 18 to 56 years, or 42 ±9.4. During the day of the initial visit, at four weeks and twelve weeks, the response to 2% rebamipide eye drops and 1% CMC was recorded.

The scores for foreign body sensation, dryness, photophobia, eye pain, and blurred vision in the 2% rebamipide and 1% CMC groups, respectively, were the same in both treatment groups at the first visit. After 4 and 12 weeks, the 2% rebamipide group significantly outperformed the 1% CMC group in all five dry eye-related ocular symptom scores. From the baseline, a significant change was seen.

In the CMC and rebamipide groups, the mean TBUT values in the right eye at baseline were 7.68 and 7.60, respectively. The mean scores at 4 weeks were 8.4 and 9.9, respectively; after 12 weeks, they were 12.62 and 14.36, respectively. This difference was statistically significant (p 0.05). The left eye showed a similar pattern.

The baseline Mean Schirmer test 1 value in the right eye for the CMC and Rebamipide groups were 4.42 and 4.68, respectively. The mean scores at 4 weeks (6.1 and 7.9, respectively) and 12 weeks (10.75 and 14.08, respectively) differed significantly (p0.05). At baseline, the CMC and Rebamipide groups' respective mean values for the right eye's Mean Schirmer test 2 were 5.54 and 5.78. The mean scores at 4 weeks were 9.40 and 11.80, respectively. At 12 weeks, they were 13.47 and 16.64. There was a significant difference (p0.05) between the mean scores. For both tests, the left eye showed similar results.

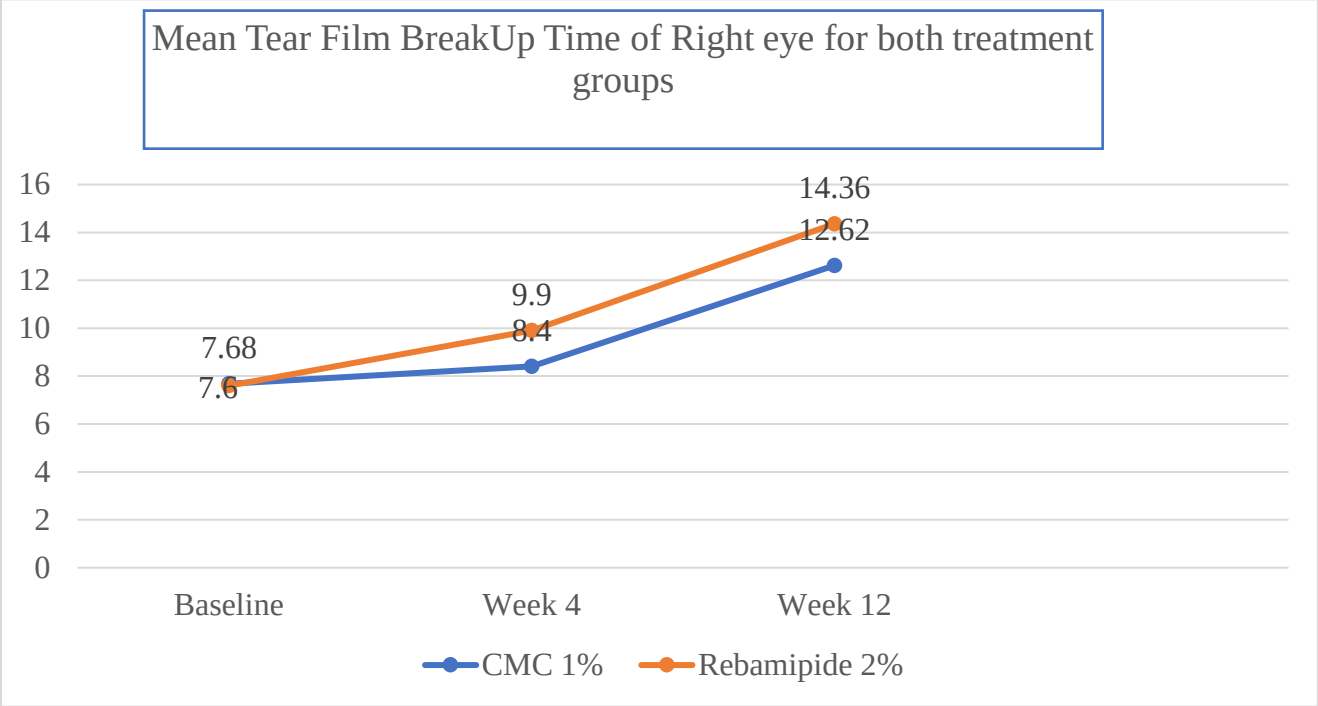
Tear function tests in two groups were compared both within and between groups. All tear function tests showed statistically significant differences between the two groups from pre-treatment scores to follow-up after 12 weeks (p0.001).

When the findings of groups 1 and 2 were examined, it was shown that patients in group 2[rebamipide] had statistically significantly more improvement than patients in group 1 (p 0.001) in all tear function tests.

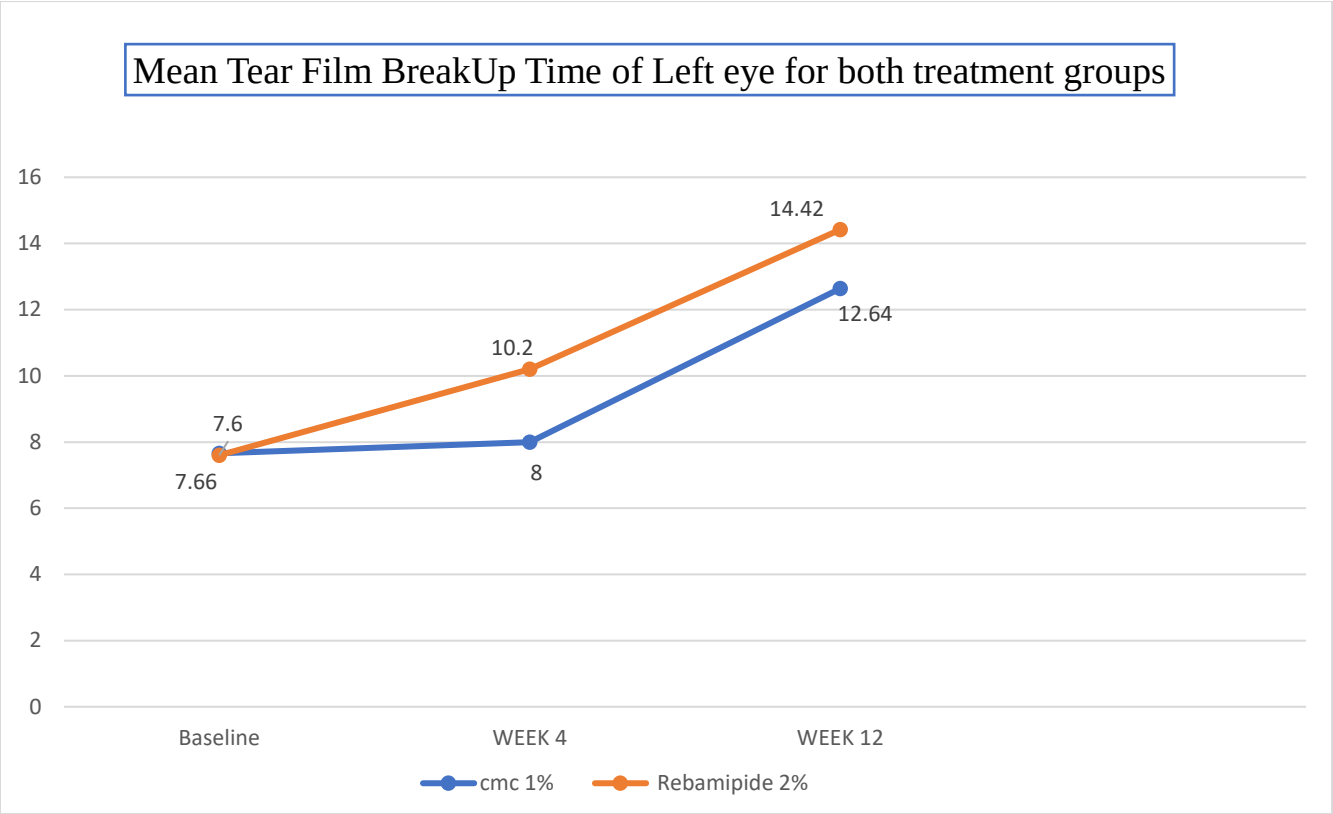
Side effects like dysgeusia were observed in 14 patients (28%) using Rebamipide, whereas only 8 patients (16%) using CMC reported side effects like irritation and stickiness.

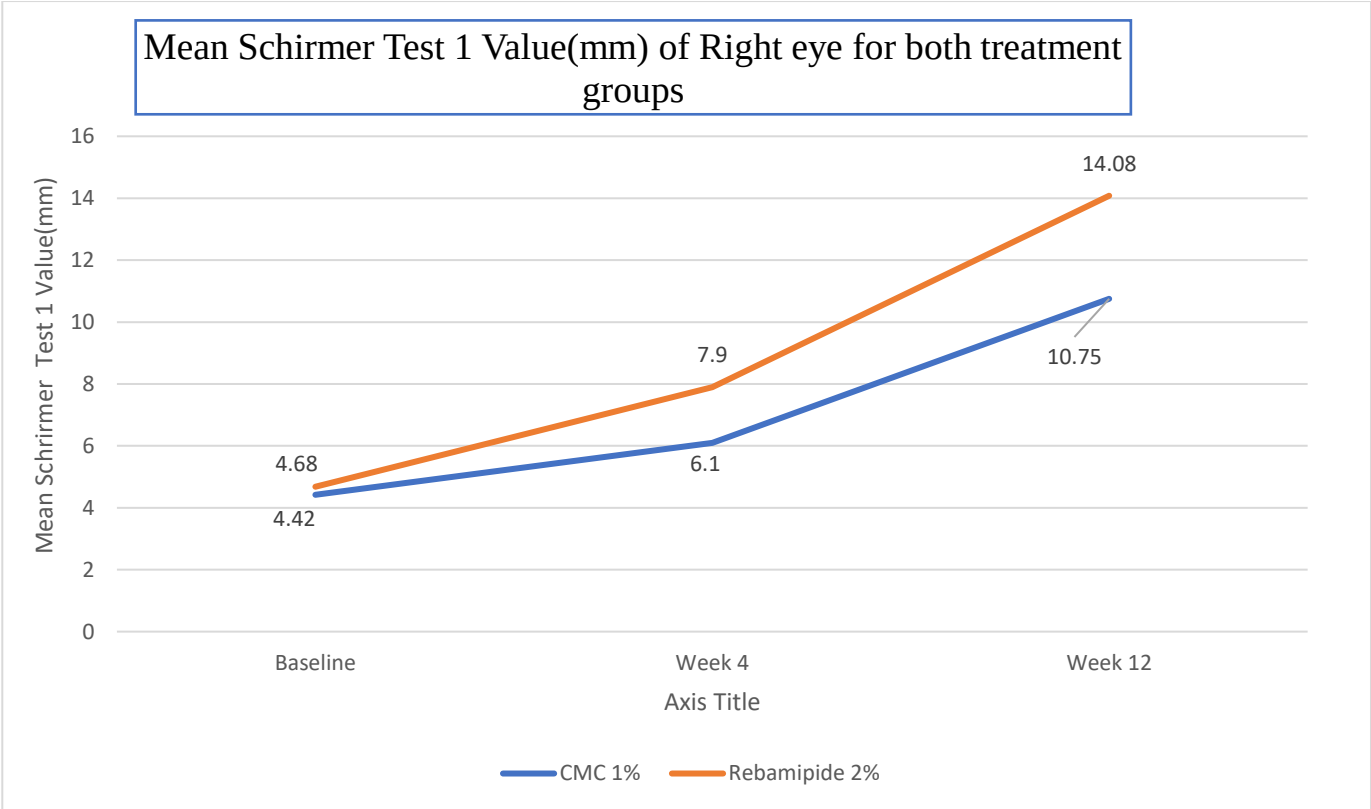
Result of right eye.

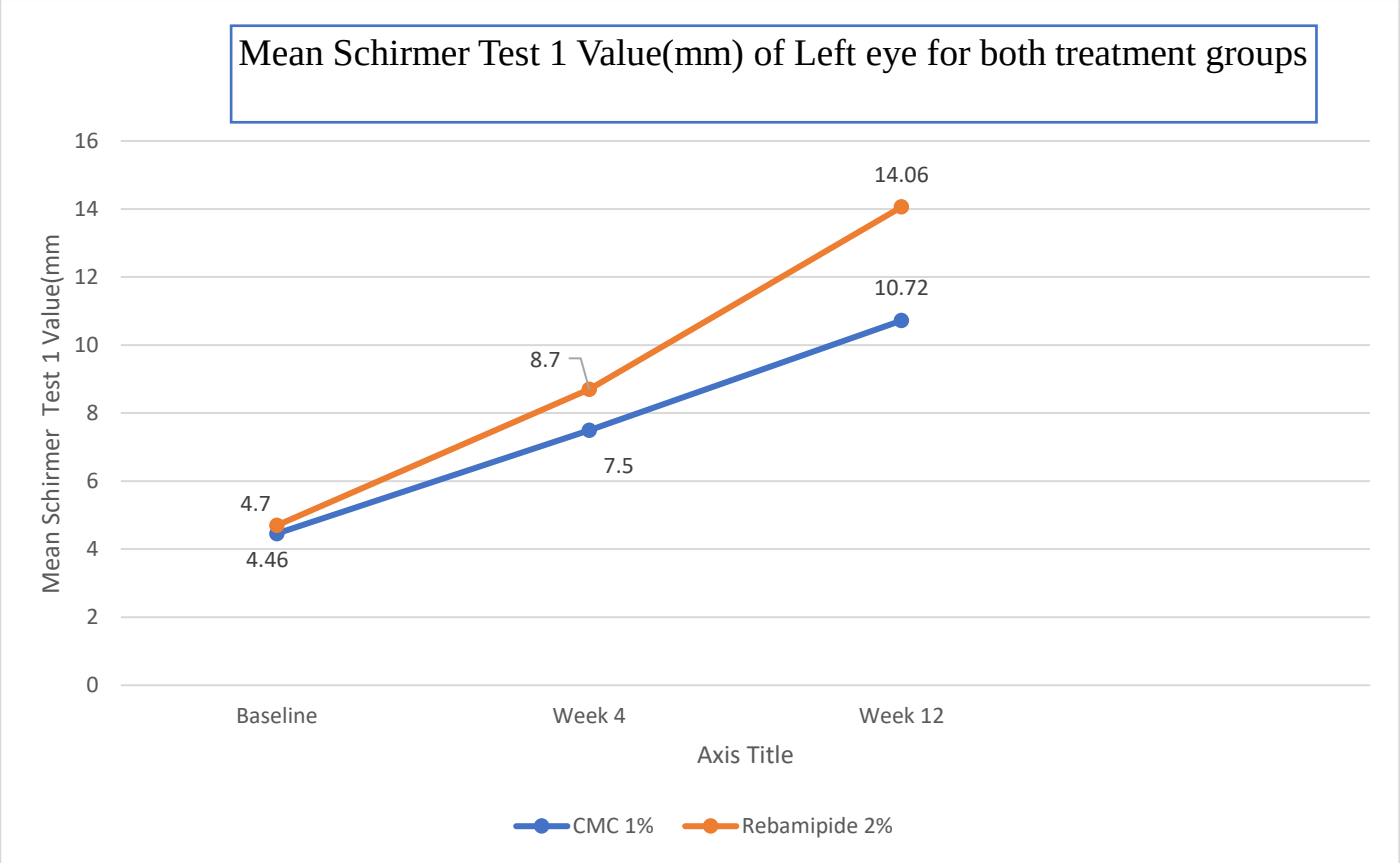
Result of left eye

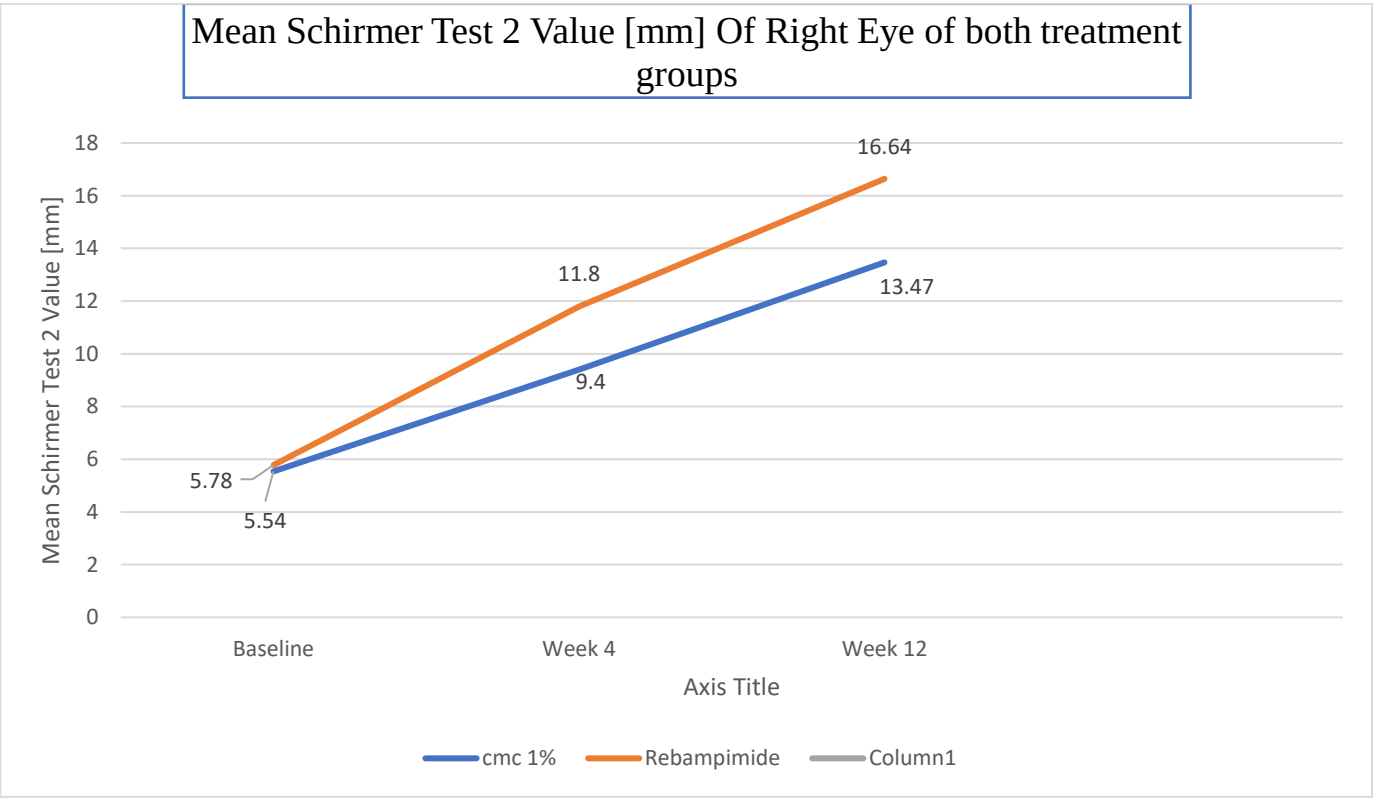


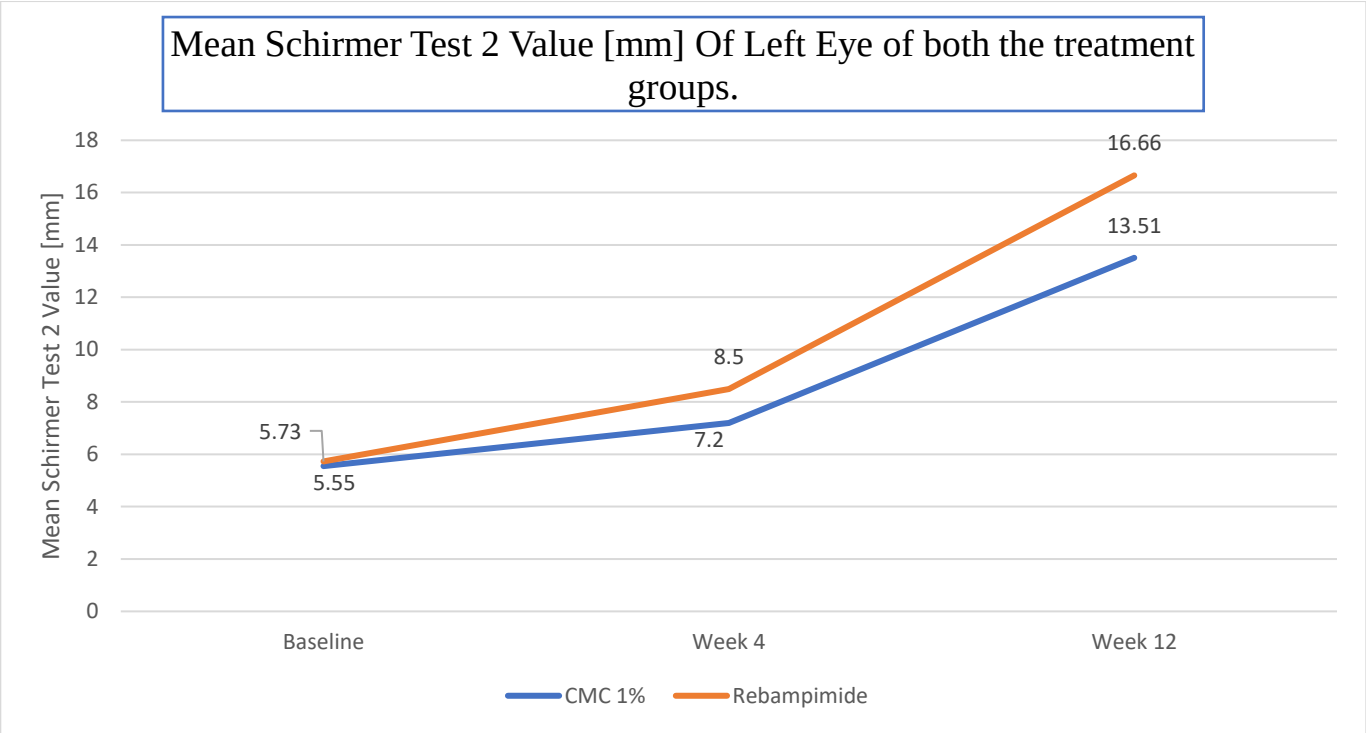
Left eye	Test Group 1(CMC)			Test Group 2 (Rebamipide)			Comparison
	Pre-treatment	Post-treatment after 12 weeks	Significance (p-value)	Pre-treatment	Post-treatment after 12 weeks	Significance (p-value)	Group 1 Versus Group 2
Tear film Break Up Time (sec)	7.66±1.70	12.64±1.4	P<0.001	7.60+1.60	14.42±1.70	P<0.001	P<0.001
Mean Schirmer's Test 1 Value(mm)	4.46±2.39	10.72±3.23	P<0.001	4.70±2.62	14.06±3.03	P<0.001	P<0.001
Mean Schirmer Test 2 Value(mm)	5.55±2.90	13.51±2.20	P<0.001	5.73±2.85	16.66±2.25	P<0.001	P<0.001


Mean Tear Film BreakUp Time of Left eye for both treatment groups
16
14
12
10
8
6
4
2
0
14.42
12.64
10.2
7.6
7.66
8
Baseline
WEEK 4
WEEK 12
cmc 1%
Rebamipide 2%


Mean Schirmer Test 1 Value(mm) of Right eye for both treatment groups
Mean Schirmer Test 1 Value(mm)
16
14
12
10
8
6
4
2
0
14.08
10.75
7.9
4.68
4.42
6.1
Baseline
Week 4
Week 12
Axis Title
CMC 1%
Rebamipide 2%


Mean Schirmer Test 1 Value(mm) of Left eye for both treatment groups
Mean Schirmer Test 1 Value(mm
16
14
12
10
8
6
4
2
0
14.06
10.72
8.7
7.5
4.7
4.46
Baseline
Week 4
Week 12
Axis Title
CMC 1%
Rebamipide 2%


Mean Schirmer Test 2 Value [mm] Of Right Eye of both treatment groups
Mean Schirmer Test 2 Value [mm]
18
16
14
12
10
8
6
4
2
0
16.64
13.47
11.8
9.4
5.78
5.54
Baseline
Week 4
Week 12
Axis Title
cmc 1%
Rebampimide
Column1



V. Discussion

Dry is a widespread disease which shows an increase in prevalence along with age [6]. In line with data from other dry eye studies, the age range of 34 to 45 years showed a relative peak in the prevalence of dry eyes in our study [12,13]. In our study, the average age of patients was 42 ±9.4. This age group tends to be more affected due to the high prevalence of contact lens usage, systemic drug effects, autoimmune diseases and refractive surgeries.

According to most of the research, dry eyes are more common in women than in men. [12,13,14]. But in our study, the prevalence was higher in males [57%] than in females [43%]. Farmers and workers who spent long hours in hazardous environments comprised about 67% of the population in our survey. They are subjected to extreme heat, sunshine, dust, and wind. Khurana et al. also showed that farmers and labourers had a higher chance of developing dry eyes (32% and 28%, respectively, of the dry eye patients), most likely as a result of prolonged exposure to unfavourable environments.[15] This can be the reason for more male preponderance in our study compared to females.

Our study found that both groups of patients showed a significant improvement in dry eye signs and symptoms[p<0.001%]. Still, it was observed that as compared to those who use CMC, patients using rebamipide eye drops had a significant improvement in their dry eye problems. Similarly, a 2% Rebamipide ophthalmic solution was found to be more effective than the CMC group in this 8-week trial by Dipak B. Patel et al. [16] in reducing both subjective symptoms and objective indicators of dry eye. These results demonstrated that the more potent medication for dry eyes is 2% Rebamipide. These outcomes match our findings as well.

Shizuka Koh et al. evaluated the effect of rebamipide ophthalmic suspension on optical quality in individuals with dry eye with a short break-up time (BUT) of the tear film. They discovered substantial increases in the tear film BUT were noted 2- and 4 weeks following therapy (P 0.001 for both comparisons).[18] These results are consistent with our observations.

VI. Conclusion

All objective and subjective indicators for assessing DED, such as the TBUT, Schirmer's test score, and DED symptoms, generally improve as a result of treatment with Rebamipide and CMC. As a result, the study shows that both medications employed in the trial were secure and efficient; however, Rebamipide was more efficient than CMC. Such advancements in treatment modalities should contribute to an enhanced quality of life in dry eye patients.

VII. References

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