Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833, VOL 15, ISSUE 6, 2024

Comparative Analysis of Eye Moisture Retention: Carboxy Methyl Cellulose Formulations with and without Additional Excipient Ingredients

Veeralakshmanan S[1], Rinita R [2],Biju Gopal[3], Arsha Ressal S A [4]

[1,2,3,5]Junior Resident,[3] Professor Department of Opthalmology,Sree mookambika institute of medical sciences, Kannyakumari,TamilNadu,India.

Corresponding Author: Rinita R,Junior Resident, Department of ophthalmology, Sree Mookambika Institute of Medical Sciences College Kanyakumari, Tamil Nadu, India,email id;Veeralakshmanan80@gmail.com

ABSTRACT:

Background

Dry eye syndrome (DES) is a common condition characterized by insufficient tear production or excessive tear evaporation, leading to discomfort, visual disturbances, and potential damage to the ocular surface. Carboxy methyl cellulose (CMC) is frequently used in artificial tears for its viscosity and lubricating properties. The addition of glycerin and balanced electrolytes to CMC formulations may enhance moisture retention and support ocular surface health, potentially offering superior relief from DES symptoms.

Materials and Methods

This study is a randomized, double-blind, controlled trial comparing the efficacy of CMC with glycerin and balanced electrolytes (Group A) versus plain CMC (Group B) in maintaining ocular moisture and alleviating DES symptoms. A total of 100 participants, aged 18-65, were randomized into two groups. The primary outcome was the improvement in Ocular Surface Disease Index (OSDI) scores over eight weeks. Secondary outcomes included changes in tear break-up time (TBUT), Schirmer test results, and patient-reported comfort and satisfaction. Adverse events were also monitored.

Results

Group A showed significant improvement in TBUT, with mean times increasing from 6±2 seconds at baseline to 11±3 seconds at Week 12, compared to 8±2 seconds in Group B. Schirmer test results indicated greater tear production in Group A, with mean values rising from 7±3 mm at baseline to 12±4 mm at Week 12, versus 9±3 mm in Group B. OSDI scores

improved significantly more in Group A, with a mean reduction of 20 points, compared to 12 points in Group B. Participant comfort and satisfaction were higher in Group A throughout the study. Adverse events were similar in both groups, with slightly fewer reported in Group A.

Conclusion

CMC with glycerin and balanced electrolytes is more effective than plain CMC in improving tear stability, tear production, and patient comfort in DES management, with a comparable safety profile. These findings support the use of additional excipients in enhancing the therapeutic efficacy of artificial tears.

KEYWORDS: *Dry eye syndrome, carboxy methyl cellulose, glycerin, balanced electrolytes, tear film stability, ocular surface disease index*

INTRODUCTION:

Dry eye syndrome (DES) is a prevalent condition that affects millions worldwide, characterized by insufficient tear production or excessive tear evaporation, leading to symptoms such as irritation, redness, and visual disturbances[1]. The pathophysiology of DES involves a complex interplay between tear film instability, hyperosmolarity, inflammation, and damage to the ocular surface. This multifactorial nature of DES necessitates a comprehensive approach to its management, often involving the use of artificial tears to restore and maintain ocular surface hydration and integrity[2,3].

Artificial tears are commonly formulated using various excipients that serve to enhance the retention time and moisture-holding capacity of the tears. Among these, carboxy methyl cellulose (CMC) is a widely used polymer due to its high viscosity and lubricating properties, which help in alleviating the symptoms of DES by forming a protective barrier on the ocular surface. CMC's efficacy as a moisture-retaining agent has been well-documented, making it a staple in the formulation of artificial tears[4,5].

Despite the effectiveness of CMC, there has been ongoing research to improve the performance of artificial tears by combining it with other excipients. One such approach involves the addition of glycerin and balanced electrolytes. Glycerin, a humectant, attracts and retains water, thus potentially enhancing the hydrating effect of CMC. Balanced

electrolytes, on the other hand, help maintain the osmotic balance and support the health of the ocular surface cells, which could further contribute to the efficacy of the formulation[6,7].

Several studies have explored the individual components of this proposed formulation. For instance, research has demonstrated that CMC is effective in increasing tear film break-up time and reducing symptoms of dryness and irritation in patients with DES . Glycerin, meanwhile, has been shown to improve hydration and reduce discomfort associated with dry eye[8] . The role of electrolytes in ocular health is also well-documented, with studies indicating that balanced electrolyte solutions can support epithelial integrity and function[9].

However, there is limited research directly comparing the efficacy of a combined formulation of CMC with glycerin and balanced electrolytes against plain CMC. This gap in the literature underscores the need for a comprehensive study that evaluates not only the symptomatic relief provided by these formulations but also their impact on tear film stability, ocular surface health, and patient quality of life.

Justification

The comparison of a formulation of CMC with glycerin and balanced electrolytes against plain CMC is based on the potential for superior therapeutic effects. This is because DES, a condition that significantly impacts the quality of life, can have substantial benefits for patients. The combination of glycerin with CMC may enhance the moisture retention capability of artificial tears, providing prolonged relief from DES symptoms. Balanced electrolytes, such as potassium, magnesium, and calcium, play a crucial role in maintaining the health of the ocular surface, mimicking the natural tear film more closely, supporting regeneration and repair. CMC with glycerin and balanced electrolytes could provide better tear film stability, reducing the frequency of artificial tear application required by patients. Additionally, glycerin may possess mild anti-inflammatory properties, which when combined with balanced electrolytes could help reduce inflammation and promote healing of the ocular surface, resulting in symptom relief and addressing one of the underlying causes of DES[10,11].

Given these potential benefits, a comparative study evaluating the efficacy of CMC with glycerin and balanced electrolytes against plain CMC is not only justified but necessary. This study aims to provide evidence-based insights into whether the addition of glycerin and electrolytes can significantly enhance the therapeutic outcomes for DES patients.

AIMS AND OBJECTIVES:

To evaluate and compare the efficacy of carboxy methyl cellulose (CMC) with glycerin and balanced electrolytes as excipients versus plain carboxy methyl cellulose in maintaining ocular moisture and alleviating symptoms of dry eye syndrome.

Objectives

1. To assess and compare the tear film break-up time (TBUT) and tear osmolarity in patients using CMC with glycerin and balanced electrolytes versus plain CMC over a period of four weeks.
2. To evaluate and compare patient-reported outcomes on symptom relief and quality of life using standardized dry eye questionnaires (such as the Ocular Surface Disease Index) between the two formulations over a period of four weeks.

MATERIALS AND METHODS:

1. Study Groups:
    - Group 1: Subjects using eye drops containing CMC with Glycerin and Balanced Electrolytes.
    - Group 2: Subjects using eye drops containing Plain CMC.
2. Eye Drop Formulations:
    - CMC with Glycerin and Balanced Electrolytes:
        - Carboxy Methyl Cellulose (0.5% - 1%)
        - Glycerin (0.2% - 0.5%)
        - Balanced Electrolytes (including Na+, K+, Ca2+, and Mg2+ in appropriate concentrations)
        - Preservatives (if required)
        - Purified water (to make up the volume)
    - Plain CMC:
        - Carboxy Methyl Cellulose (0.5% - 1%)
        - Preservatives (if required)

- Purified water (to make up the volume)

3. Subjects:
    - Inclusion Criteria:
        - Adults aged 18-65 with dry eye symptoms.
        - Willing to comply with study protocol and follow-up visits.
    - Exclusion Criteria:
        - History of ocular surgery or trauma within the last 6 months.
        - Current use of any other ocular medication.
        - Known allergy to any component of the eye drops.
4. Equipment:
    - Standardized questionnaires for symptom assessment (e.g., Ocular Surface Disease Index - OSDI).
    - Schirmer's test strips for measuring tear production.
    - Fluorescein strips and slit lamp biomicroscope for ocular surface staining.
    - Non-invasive tear breakup time (NIBUT) measuring device.

Methods

1. Study Design:
    - Randomized, double-blind, controlled trial.
    - Duration: 8 weeks.
    - Sample Size: At least 50 subjects per group to ensure statistical power.
2. Randomization:
    - Subjects will be randomly assigned to either Group 1 or Group 2 using computer-generated random numbers.
3. Blinding:

- Both the subjects and the investigators assessing the outcomes will be blinded to the group assignments.

4. Baseline Assessment:
    - Collect demographic data and medical history.
    - Perform baseline OSDI questionnaire.
    - Conduct Schirmer's test, NIBUT measurement, and fluorescein staining.
5. Intervention:
    - Group 1 will receive eye drops with CMC, Glycerin, and Balanced Electrolytes, to be used as per the prescribed dosage (e.g., one drop in each eye, four times a day).
    - Group 2 will receive Plain CMC eye drops, to be used as per the same prescribed dosage.
6. Follow-Up Visits:
    - Scheduled at Week 2, Week 4, and Week 8.
    - At each visit, repeat OSDI questionnaire, Schirmer's test, NIBUT measurement, and fluorescein staining.
    - Monitor for any adverse effects.
7. Outcome Measures:
    - Primary Outcome: Improvement in OSDI score from baseline to Week 8.
    - Secondary Outcomes:
        - Increase in Schirmer's test values from baseline to Week 8.
        - Improvement in NIBUT from baseline to Week 8.
        - Reduction in corneal and conjunctival staining scores from baseline to Week 8.
8. Data Analysis:

- Compare mean changes in OSDI scores, Schirmer's test values, NIBUT, and staining scores between the two groups using t-tests or appropriate non-parametric tests.
- Use repeated measures ANOVA to assess changes over time within and between groups.
- Statistical significance will be set at $p < 0.05$.

Ethical Considerations

- Obtain informed consent from all participants.
- Ensure confidentiality and the right to withdraw from the study at any time.
- Seek approval from an appropriate institutional review board (IRB) or ethics committee.

RESULTS:

Table 1: Participant Demographics

Demographic Parameter	**Group A (CMC with Glycerin and Electrolytes)**	**Group B (Plain CMC)**
Number of Participants	50	50
Age (mean ± SD)	45 ± 10 years	46 ± 9 years
Gender (M/F)	22/28	20/30
Duration of Dry Eye (mean ± SD)	5 ± 3 years	5 ± 4 years
Contact Lens Users	15	17

Table 1 presents the demographic data of the study participants. Both Group A (CMC with Glycerin and Electrolytes) and Group B (Plain CMC) comprised 50 participants each. The average age of participants in Group A was 45 years (±10), while Group B had a mean age of 46 years (±9), indicating a well-matched age distribution between the groups. Gender distribution was relatively balanced, with Group A having 22 males and 28 females, and Group B consisting of 20 males and 30 females. The mean duration of dry eye was similar across the groups, with Group A reporting 5 years (±3) and Group B reporting 5 years (±4).

Additionally, the number of contact lens users was comparable between the groups, with 15 in Group A and 17 in Group B, ensuring that the baseline characteristics were evenly distributed.

Table 2: Baseline Ocular Surface Disease Index (OSDI) Scores

Time Point	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
Baseline	45 ± 15	44 ± 16	0.78

Table 2 shows the baseline OSDI scores for both groups. The mean OSDI score for Group A was 45 (±15), while Group B had a mean score of 44 (±16). The p-value of 0.78 indicates no statistically significant difference between the two groups at baseline, suggesting that both groups started with similar levels of ocular surface disease.

Table 3: Tear Break-Up Time (TBUT) in Seconds

Time Point	**Group A (Mean ± SD)**	**Group B (Mean ± SD)**	**p-value**
Baseline	6 ± 2	6 ± 2	0.85
Week 4	9 ± 3	7 ± 2	0.02
Week 8	10 ± 3	8 ± 2	0.01
Week 12	11 ± 3	8 ± 2	<0.01

Table 3 highlights the changes in TBUT over the study period. At baseline, both groups had a similar TBUT of 6 seconds (±2), with a p-value of 0.85, indicating no significant difference initially. However, by Week 4, Group A showed a significant improvement in TBUT to 9 seconds (±3) compared to 7 seconds (±2) in Group B, with a p-value of 0.02. This trend continued, with Group A reaching 10 seconds (±3) at Week 8 and 11 seconds (±3) at Week 12, whereas Group B had 8 seconds (±2) at both time points. The p-values of 0.01 and <0.01 at Weeks 8 and 12, respectively, highlight the significant improvement in Group A compared to Group B.

Table 4: Schirmer Test Results (without anesthesia) in mm

Time Point	**Group A (Mean ± SD)**	**Group B (Mean ± SD)**	**p-value**
Baseline	7 ± 3	7 ± 3	0.92

Week 4	10 ± 4	8 ± 3	0.03
Week 8	11 ± 4	9 ± 3	0.02
Week 12	12 ± 4	9 ± 3	<0.01

Table 4 provides the Schirmer test results, which measure tear production. Both groups started with a mean value of 7 mm (±3) at baseline, with no significant difference (p-value of 0.92). Over time, Group A exhibited a greater increase in tear production, with 10 mm (±4) at Week 4, 11 mm (±4) at Week 8, and 12 mm (±4) at Week 12. In contrast, Group B showed a more modest increase to 8 mm (±3), 9 mm (±3), and 9 mm (±3) at the corresponding time points. The p-values of 0.03, 0.02, and <0.01 at Weeks 4, 8, and 12, respectively, indicate significant differences favoring Group A.

Table 5: Participant Comfort and Satisfaction Scores (0-10 scale)

Time Point	**Group A (Mean ± SD)**	**Group B (Mean ± SD)**	**p-value**
Week 4	8 ± 2	6 ± 3	<0.01
Week 8	8 ± 2	6 ± 2	<0.01
Week 12	9 ± 2	6 ± 2	<0.01

Table 5 summarizes participant comfort and satisfaction scores over the course of the study. At Week 4, Group A reported significantly higher comfort and satisfaction scores (8 ± 2) compared to Group B (6 ± 3), with a p-value of <0.01. This difference remained consistent, with Group A scoring 8 (±2) at Week 8 and 9 (±2) at Week 12, while Group B maintained scores of 6 (±2) at both intervals. The p-values of <0.01 at all time points reflect a significantly greater improvement in comfort and satisfaction for participants using CMC with Glycerin and Electrolytes.

Table 6: Adverse Events

Adverse Event	**Group A (n=50)**	**Group B (n=50)**
Eye irritation	3	5
Blurred vision	2	4
Headache	1	2
Increased tear production	4	2

Total number of adverse events	10	13

Table 6 details the adverse events reported by participants in both groups. Group A experienced fewer adverse events overall, with a total of 10 events compared to 13 in Group B. Specific adverse events included eye irritation (3 in Group A vs. 5 in Group B), blurred vision (2 in Group A vs. 4 in Group B), headache (1 in Group A vs. 2 in Group B), and increased tear production (4 in Group A vs. 2 in Group B). These results suggest that while both treatments were generally well-tolerated, Group A had a slightly better safety profile.

DISCUSSION:

The comparative study evaluating the efficacy of Carboxy Methyl Cellulose (CMC) with Glycerin and Balanced Electrolytes versus Plain CMC for maintaining ocular moisture provides valuable insights into treatment options for dry eye syndrome.

The demographic characteristics of the participants in this study were well-matched between the two groups, ensuring that any observed differences in outcomes were likely due to the treatment itself rather than confounding variables. Previous studies have also emphasized the importance of balanced demographic characteristics to reduce bias and enhance the validity of the results. For instance, research by Semp et al[12]. (2018) demonstrated similar demographic matching and stressed its significance in interpreting efficacy data accurately .

Both groups started with comparable OSDI scores, indicating similar levels of ocular surface disease severity at baseline. This alignment is consistent with findings from other studies that have used OSDI as a baseline measure, such as the work by Schiffman et al[13]. (2000), which established OSDI as a reliable metric for assessing dry eye severity . The lack of significant difference at baseline supports the notion that any subsequent differences in outcomes are attributable to the treatment rather than initial disease severity.

The improvement in TBUT for Group A (CMC with Glycerin and Electrolytes) over the study period is noteworthy. By Week 12, Group A's TBUT increased significantly more than Group B's. This finding aligns with previous studies, such as those by Solana et al[14]. (2014), which reported enhanced TBUT with the use of lubricants containing electrolytes and humectants like Glycerin, suggesting that these components contribute to a more stable tear film. In contrast, studies focusing solely on CMC, like that by Tauber et al[15]. (2010), have

shown moderate improvements in TBUT, highlighting the added benefit of electrolytes and Glycerin.

The Schirmer test results in this study indicated a more significant increase in tear production for Group A compared to Group B. This aligns with research by Mariasilva et al[16]. (2016), which found that lubricants containing Glycerin and electrolytes can enhance tear secretion more effectively than basic lubricants . The presence of electrolytes may help maintain osmotic balance, stimulating tear production more effectively than plain CMC.

Participant comfort and satisfaction were significantly higher in Group A throughout the study. This outcome is corroborated by previous studies, such as those by Piotr et al[17]. (2013), which highlighted the enhanced patient-reported outcomes with lubricants containing a combination of moisturizers and electrolytes . The addition of Glycerin, known for its humectant properties, likely contributed to the increased comfort and satisfaction reported by participants in Group A.

The incidence of adverse events was slightly lower in Group A, suggesting a marginally better safety profile for CMC with Glycerin and Electrolytes. This finding is consistent with previous studies that have reported similar safety profiles for lubricants containing additional moisturizing agents. For example, a study by Kelly et al[18]. (2021) reported that such formulations were generally well-tolerated with a low incidence of adverse effects . The slightly higher incidence of eye irritation and blurred vision in Group B aligns with the known side effects of using plain CMC, which can sometimes cause transient visual disturbances and discomfort.

CONCLUSION:

In conclusion, this study's results demonstrate that Carboxy Methyl Cellulose with Glycerin and Balanced Electrolytes is more effective than Plain CMC in improving tear stability, tear production, and participant comfort, with a comparable safety profile. These findings are consistent with previous research, which has similarly highlighted the benefits of adding Glycerin and electrolytes to ocular lubricants. Future studies could explore long-term outcomes and the efficacy of these formulations in diverse populations to further validate these findings.

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