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A Comparative Assessment of the Efficacy of Carbomer Gel and Carboxymethyl Cellulose Containing Artificial Tears in Dry Eyes

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Summary：The present study aimed to compare the clinical efficacy of a 0.4% carbomer gel and 1% carboxymethyl cellulose (CMC) containing artificial tears in treatment of dry eye patients. Sixty subjects with mean age of 45.89 years who had symptoms and signs of dry eye were enrolled in this prospective, investigator-masked and stratified random sampling study. The subjects were divided into two parallel groups with 30 subjects (60 eyes) in each group. One group received carbomer gel, and the other group received 1% CMC containing artificial tears. Subjects received the drops 3 to 4 times or more per day for 3 months. At the first visit time, the precorneal residence time of these two drops was measured. The efficacy was assessed by comparing the subjective symptoms (ocular dryness, foreign body sensation, burning sensation and pain), and the objective test results of tears breakup time, Schirmer's test and corneal fluorescein staining prior to the study and after the treatment. As a result, the ocular residence time of carbomer gel was significantly longer than that of 1% CMC (P<0.001). Most of the primary subjective symptoms and objective test results were improved after treatment in both carbomer gel group and 1% CMC group. As to the improvement of each symptom and objective test result, carbomer gel was more effective than 1% CMC group (P<0.01). In conclusion, carbomer gel had longer precorneal residence time and was more effective than 1% CMC in the treatment of patients with dry eyes.
Key words：carbomer gel; carboxymethyl cellulose; tears; dry eye; efficacy

Dry eye syndrome, or keratoconjunctivitis sicca (KCS), is a chronic eye disease that occurs from either decreased tear production or increased tear film evaporation. It damages the ocular surface and can cause debilitating symptoms of dryness and irritation, and is associated with an enhanced risk of corneal infection, and, when severe, can cause permanent visual impairment[1, 2]. With the aging of the population and wide use of electronic products, such as computer, dry eye is one of the most common ocular problems, particularly among older women[3-5]. The therapy of dry eye syndrome generally consists of artificial tears[6, 7]. Artificial tears can compensate for tear inadequacy and then protect the ocular surface and provide symptomatic relief. However, most of artificial tear preparations provide only short-term relief and short retention time and have to be used frequently to be effective. Preservatives are usually added to ophthalmic solutions to prevent contamination. Long-time frequent applications may not only cause inconvenience, but also even disrupt the tear film, impair epithelial cell membranes and damage the ocular surface due to the preservatives contained in the products[8-11].

In the past recent years, treatments for dry eyes have been improved by the use of adsorptive polymers leading to increased contact time and more relief of discomfort. Carbomer (polyacrylic acid) is a water-soluble polymeric resin that has been reported to maintain the tear film in contact with the eye for an extended period[12, 13]. In our previous work, we prepared a carbomer based gel. The present study compared the clinical efficacy of this domestic 0.4% carbomer gel with 1% carboxymethyl cellulose (CMC) containing artificial tear in treatment of dry eye patients.

1 MATERIALS AND METHODS

1.1 Agents

The 0.4% carbomer based gel contains 4.0 g carbomer in 1000 mL saline solution preserved with 0.1 g hexadecyl trimethyl ammonium bromide. pH was adjusted to 7.5 to 8.5. It was a colorless viscous gel with a density of 1.015 to 1.017 (at 25°C) and mobile viscosity of 300 to 400 mm^2/s (at 25°C). 1% CMC artificial tear was a product of Allergan Inc., USA.

1.2 Subjects

Sixty subjects, male 9, female 51, with mean age of 45.89 years, who had symptoms and signs of dry eye attending our department, were enrolled in this prospective, stratified random sampling study. The average history period was 4.2 years (ranging from 6 months to 37 years). The subjective symptoms included foreign body sensation, ocular dryness, burning, pain or photophobia

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in eyes. The objective signs included less than 10 mm/5 min result in Schirmer's test (ST), tears breakup time (BUT) shorter than 10 s and positive corneal fluorescein staining. Dry eye syndrome was diagnosed when a subject had both subjective symptom(s) and any two objective signs, as mentioned above.

1.3 Methods

According to the age, severity and course, all subjects were divided into two parallel groups with 30 subjects (60 eyes) in each group. The two groups were similar in patient demographics and study parameters at baseline (table 1). One group received carbomer gel, and the other group received 1% CMC artificial tear. Subjects received the drops by themselves 3 to 4 times or more if needed per day for 3 months.

Table 1 The clinical data of subjects in two groups

Groups	Cases	Age (years)	Period (years)	ST (mm/5 min)	BUT (s)
Carbomer	30	46.7±2.3	6.7±1.2	5.12±1.28	6.23±1.58
CMC	30	46.6±2.1	6.2±1.2	5.48±1.12	6.56±1.42

At the first visit time, the precorneal residence time of these two drops was measured, respectively. The subjects' symptoms and signs were recorded before and after the treatment. The subjective symptoms were recorded as ocular dryness, foreign body sensation, burning sensation and pain. The objective signs included ST, BUT and corneal fluorescein staining. The efficacy was assessed by comparing the symptoms and signs prior to the study and after the treatment.

Efficacy variables were assessed according to 3 scales of the improvement of symptoms and signs. It was considered marked effective if subjective symptoms, such as foreign body sensation, ocular dryness, burning sensation or pain, disappeared, or corneal fluorescein staining became negative, or ST result prolonged to more than 10 mm, or BUT prolonged to more than 10 s. It was considered effective if subjective symptoms or objective signs improved, but less than the standard mentioned as above. It was considered ineffective without improvement of symptoms or signs.

1.4 Statistical Analysis

Statistical comparisons of the precorneal residence time of carbomer gel and 1% CMC were performed with *t*-test. Values were presented as $\bar{x}\pm s$. Analysis of the significance of efficacy difference between two groups was applied using Ridit analysis. Differences were accepted as significant when a $P<0.05$.

2 RESULTS

2.1 The Precorneal Residence Time of Carbomer Gel and 1% CMC

The precorneal residence time of carbomer gel and 1% CMC was (23.50±5.89) min and (9.07±3.09) min in right eyes, and (20.27±5.64) min and (8.87±3.18) min in left eyes, respectively. The precorneal residence time of carbomer gel was significant longer than that of 1% CMC ($P<0.001$).

2.2 The Improvement of Symptoms in Two Groups after Treatment

The improvement of symptoms, including ocular dryness, foreign body sensation, burning sensation and pain, in two groups after treatment was listed in table 2. Most of the primary subjective symptoms released after treatment in both carbomer gel group and 1% CMC group. As to release of each symptom, carbomer gel was more effective than 1% CMC ($P<0.01$).

2.3 The Improvement of Signs in Two Groups after Treatment

The improvement of objective signs, including ST, BUT, and corneal fluorescein staining, in two groups after treatment were listed in table 3. As to improvement of each objective sign, carbomer gel was more effective than 1% CMC group ($P<0.01$).

Table 2 Comparison of symptoms improvement in two groups after treatment

Effectiveness	Dryness		Foreign body sensation		Burning		Pain	
	Carbomer	CMC	Carbomer	CMC	Carbomer	CMC	Carbomer	CMC
Total eyes	60	60	60	60	38	36	38	36
Marked effective eyes	58	28	58	24	36	10	34	10
Effective eyes	2	32	2	28	2	10	4	14
Ineffective eyes	0	0	0	8	0	16	0	12

Table 3 Comparison of signs improvement in two groups after treatment

Effectiveness	ST		BUT		Fluorescein staining	
	Carbomer	CMC	Carbomer	CMC	Carbomer	CMC
Total eyes	60	60	60	60	60	60
Marked effective eyes	0	0	26	2	36	0
Effective eyes	24	4	0	0	24	6
Ineffective eyes	36	56	34	58	0	54

3 DISCUSSION

Because dry eye syndrome may cause impact on several common and important tasks of daily living, this condition is an important public health problem deserving increased attention and resources[14]. Although many factors are known to contribute to dry eye syndrome[3, 15-19], of the treatments available for dry eye, the common denominator seems to be tear substitutes, which are also called artificial tears. An artificial tear may target a specific tear film component, usually the aqueous but sometimes the lipid[20]. These agents typically aim to alleviate dry eye symptoms by temporarily bulking up the tear volume in the eye through instillation of a drop containing lubricating agents. It is vital for a tear substitute to provide the longest-lasting improvement of the symptoms and signs of dry eye as possible. Beyond the obvious benefits from a clinical perspective, this could afford less-frequent dosing for patients. But currently, the widely used artificial tears, such as 1% carboxymethyl cellulose[21] and 1.4% polyvinyl alcohol[7], encountered a major problem of the short-term effects due to quick disappearance quickly after instillation as the drop washes out of or is drained from the eye and thus needs frequent instillation.

One of the common methods of optimizing prolonged precorneal residence time is the use of polymers to increase solution viscosity. Carbomer is a water-soluble polymeric resin with a relative molecular weight of 4×10^6. It was reported that polyacrylic acid gel maintained the tear film in contact with the eye for an extended period[12, 13]. As shown in this study, the precorneal residence time of carbomer gel was significantly longer than that of 1% CMC. This is due to the higher solution viscosity of carbomer gel. Good thixotropic property of carbomer is helpful to maintain a proper viscosity and thus to avoid blurred vision. The long precorneal residence time of carbomer gel formed a protective shield over exposed and damaged corneal epithelial cells for longer periods of time. Afforded this protection, ocular surface cells may have the ability to perform self-repair. In addition, long precorneal residence time of carbomer gel promised more convenient instillation of no more than 4 times daily, while it was often 4 to 8 times daily with 1% CMC.

In a multicenter, single-masked, randomized, placebo-controlled study carried out on 123 patients with moderate-to-severe dry eyes, a 0.3% carbomer gel was proved safe and efficacious in improving a number of subjective symptoms of dry eyes[22]. Brodwall *et al*[23] and Bron *et al*[24] compared the safety and efficacy of 0.2% polyacrylic acid gel and 1.4% polyvinyl alcohol in the treatment of patients with dry eyes. The authors found that polyacrylic acid gel was as safe as and more effective than polyvinyl alcohol, and the daily frequency of instillation of polyacrylic acid gel was significantly less than that of polyvinyl alcohol. In our study, most of the primary subjective symptoms released after treatment in both carbomer gel group and 1% CMC group, but carbomer gel was more effective than 1% CMC in release of each symptom. The improvement of ST, BUT and corneal fluorescein staining were not as good as the release of symptoms in both groups. Carbomer gel was also more effective than 1% CMC in improvement of each sign.

Actually, most tear substitutes available nowadays provide only an initial offensive burst of lubrication and hydration and offer little or no protection lasting into the later rounds of the battle with dry eye. It is important that clinicians promote the development of artificial tears that offer sustained effectiveness in both the signs and symptoms of dry eye in future studies.

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