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A clinical study of the efficacy of topical corticosteroids on dry eye

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Abstract: Objective: To evaluate the effect of topical corticosteroid for treatment of moderate or severe dry eye. Methods: Sixty eyes of 30 patients with moderate or severe dry eye, who were not sensitive to artificial tears, were treated with 0.1% fluorometholone eye drops. Subjective symptom and objective tests were used to evaluate the efficacy of treatment before and after application of 0.1% fluorometholone eye drops for 1 week and 1 month. Side effects were also evaluated. Results: After 1 week of treatment, subjective symptoms were improved in all dry eye patients; objective tests were improved in all dry eye patients 1 month after treatment, and the difference was significant. Conclusion: Topical corticosteroid drops can rapidly and effectively relieve the symptoms and signs of moderate or severe dry eye.

Key words: Dry eye, Treatment, Corticosteroids
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INTRODUCTION

Dry eye is a common ocular surface disease with various clinical manifestations. Some mild or episodic symptoms are easily controlled with an ocular lubricant. Long-term application of artificial tears is not effective for some patients, especially those with severe symptoms. It has been confirmed that dry eye is related to the inflammation of ocular surface, is based on immune response and induced by many cytokines (Stern *et al*., 1998; Zoukhri, 2006; Gao *et al*., 2004; Nagelhout *et al*., 2005). Corticosteroid is an effective anti-inflammatory drug widely used to control eye inflammation. In this study, we evaluated the efficacy and safety of using topical corticosteroids for treating moderate or severe dry eye.

PATIENTS AND METHODS

Cases

Between Aug. 2004 and Oct. 2005, 30 patients (60 eyes) with moderate or severe dry eye received treatment, 9 patients (18 eyes) were male and 21 patients (42 eyes) were female. The mean age was 42.39±7.58 (years±*SD*) (range: 24 to 58). Criteria used for the diagnosis of dry eye included: presence of fluorescein staining of the cornea in areas where the epithelium has been disrupted, 5-min Schirmer test showing less than 5 mm strip wetting and break-up time (BUT) less than 10 s. The baseline demographics of the patients are listed in Table 1.

Table 1 Baseline demographics of 30 patients

	All eyes (*n*=60)
Age (years)	42.4 (24~58)
Gender	
Male	*n*=18
Female	*n*=42
Symptom (score)	6.95±1.11
Hyperemia of conjunctiva (score)	2.42±0.75
BUT (s)	4.20±1.75
Cornea fluorescein staining (score)	5.49±2.03
Schirmer test I (mm/5 min)	4.03±1.85
Intraocular pressure (IOP) (mmHg)	12.75±2.86

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Methods

1. The symptoms were scored according to the detailed history

The main symptoms included ophthalmocopia, foreign body sensation, dry, burning sensation, ophthalmalgia, photophobia, and so on.

The method to score is as follows:

0 score: no symptom; 1 score: less than 3 times a week, relieved after rest; 2~4 scores: between 1 and 5 scores; 5 scores: occur frequently, affect daily activities, relieved after drug use; 6~8 scores: between 5 and 9 scores; 9 scores: occur continuously, affect daily activities seriously, relieved only after drug use.

2. Hyperemia of conjunctiva evaluation according to slitlamp

0 score: no hyperemia of conjunctiva; 1 score: mild hyperemia of conjunctiva; 2 scores: moderate hyperemia of conjunctiva; 3 scores: severe hyperemia of conjunctiva.

3. Break-up time (BUT)

A strip of fluorescein is applied in the lower eyelid fornix and then removed. The patient is asked to blink three times and then look straight forward, without blinking. The tear film is observed under cobalt-blue filtered light of slitlamp microscope and the time that elapsed between the last blink and appearance of the first break in the tear film is recorded with a stopwatch (a break is seen as a dark spot in a sea of blue).

4. Cornea fluorescein staining inspection

The cornea can be divided into 4 quadrants: supranasal, infranasal, supratemperal and infratemperal quadrant. In each quadrant, the degree of cornea fluorescein staining can be scored into 4 levels.

0 score: negative staining; 1 score: pointed staining, less than 5 points; 2 scores: pointed staining, more than 5 points; 3 scores: filament staining or piece staining.

So the total score of the cornea fluorescein staining is from 0 to 12.

5. Tear secretion test (Schirmer test I): The Schirmer value was recorded as the strip was wetted for 5 min in millimeters.

6. Visual acuity

7. Intraocular pressure detection with non-touch ophthalmotonometer.

Pharmaceutics

The artificial tear used for investigation was 0.1% Hialid (Santen Pham company, Japan) and the corticosteroid was 0.1% flurometholone (Santen Pham Company, Japan). One drop each time, 4 times a day.

Statistical analysis

All data in our study were analyzed with the one-way ANOVA procedure of SPSS 10.0 software (SPSS Inc.), $P<0.05$ represented significant difference.

RESULTS

After the additional application of corticosteroid eye drops to patients who had already used artificial tears, all the patients had fewer symptoms as early as one week later. The average value of the symptom score was (6.95±1.11) before treatment, (4.08±1.09) one week after treatment ($P<0.05$), (2.75±0.93) one month after treatment ($P<0.05$). Hyperemia of conjunctiva was relieved obviously one month after the treatment ($P<0.05$). The mean value of BUT before treatment was (4.20±1.75) s and (6.32±1.95) s one month after treatment ($P<0.05$). The mean value of cornea fluorescein staining was (5.49±2.03) before treatment and (1.29±0.83) one month after treatment ($P<0.05$). The mean value of Schirmer test I was (4.03±1.85) mm/(5 min) and (6.83±1.97) mm/(5 min) one month after treatment ($P<0.05$). The mean value of intraocula pressure (IOP) was (12.75±2.86) mmHg before treatment, (12.85±2.96) mmHg one month after treatment. There was no statistically significant difference between two groups ($P>0.05$) (Table 2).

DISCUSSION

The etiology of dry eye is very complicated, tear film and ocular surface structures are interdependent of each other. Specifically, the cornea, conjunctiva, meibomian glands, goblet cells and lacrimal glands are intricately linked to one another via neural, hormonal and chemical feedback mechanisms. These constitute a "functional unit" for tear secretion (Stern *et al*., 1998; 2004; Mathers, 2000). Damage or alteration of any one structure may adversely affect the remaining components of this functional unit. Recent studies have found that dry eye disease often manifests as a chronic, low-grade inflammatory state of the

Table 2 Efficacy of corticosteroid eye drops treatment for patients after one week and one month

Clinical examination	Before treatment	One week later		One month later	
		Value	*P*	Value	*P*
Symptom (score)	6.95±1.11	4.08±1.09	<0.05	2.75±0.93	<0.05
Hyperemia of conjunctiva (score)	2.42±0.75	1.86±0.50	>0.05	1.05±0.29	<0.05
BUT (s)	4.20±1.75	5.85±1.69	<0.05	6.32±1.95	<0.05
Cornea fluorescein staining (score)	5.49±2.03	4.24±1.73	>0.05	1.29±0.83	<0.05
Schirmer test I (mm/5 min)	4.03±1.85	4.55±1.78	>0.05	6.83±1.97	<0.05
Intraocular pressure (IOP) (mmHg)	12.75±2.86	12.83±2.95	>0.05	12.85±2.96	>0.05

ocular surface (Caccavo *et al*., 2002; Johnson and Murphy, 2004). Inflammation of cornea and conjunctiva, primary or secondary to lacrimal gland disease, stimulates the expression of immune activation and adhesion molecules attracting and retaining inflammatory cells in the conjunctiva (Brignole *et al*., 2000; Pflugfelder, 2004). These inflammatory cells lead to apoptosis and diminished tear production (Mathers, 2000; Baudouin, 2001).

Artificial tears and punctual occlusion are often used in clinic without treatment of potential etiological factors. Patients who underwent punctual occlusion may experience diminished ocular surface sensation and a concomitant decrease in tear production (Yen *et al*., 2001). In recent studies, topical corticosteroids have shown promising results for treating dry eye. Steroids may help increase goblet cell density and reduce the accumulation of inflammatory cells within ocular surface tissues (Avunduk *et al*., 2003; Pflugfelder *et al*., 2004). Lee *et al*.(2006) and others reported ocular surface nerve growth factor (NGF) may play an important role in ocular surface inflammation processes associated with dry eye. Keratoconjunctivitis sicca patients showed elevated levels of tear NGF, which were decreased by treatment with 0.1% prednisolone.

In this study, corticosteroid could rapidly ameliorate the subjective symptoms among the patients with moderate or severe dry eye while no obvious effects were observed when using artificial tears only. It can significantly decrease the patient's complaints within one week. Meanwhile, all detected indexes such as cornea fluorescein staining, BUT, tear secretion test and so on were obviously improved one month after corticosteroid treatment. All of these suggested that rapid anti-inflammatory activity with high-performance of corticosteroid is very effective for patients with moderate or severe dry eye, which also provide evidence that non-specific immune inflammation is involved in the development of dry eye. Corticosteroid can ameliorate the symptoms and signs rapidly, however, prolonged use of corticosteroid have been associated with increased infection, IOP elevation, and cataract formation. In our experiment, increasing IOP and hormone-related complications did not occur in 1 month, suggesting that the application of topical corticosteroid for short-term was safe. Steroids that are less penetrating to the intraocular structures, can minimize hormone-related complications.

Cornea fluorescein staining was improved significantly in our research after corticosteroid treatment as early as the first week. Decreasing cornea fluorescein staining is due to the suppression of inflammation enabling normal function of ocular surface. With the deterioration of dry eye, there can be some filament and piece staining in the cornea. It has been confirmed in many clinical and elementary experiments that the inflammatory factors and the marks concerned are diminished after anti-inflammatory treatment, but the density of conjunctiva goblet cell is increased (Avunduk *et al*., 2003). The inflammatory factors are decreased and the integrity of ocular surface is improved after the application of corticosteroid, so the nerves of cornea and conjunctiva can be stimulated by blinking more effectively, the reflective secretion becomes normal, then the quality and quantity of tears are also improved, which supports the improved results of lacrimal gland secretion test in our experiment. We also found that some patient's vision were improved when the inflammation of ocular surface was relieved, which was mainly resulted from the diminishing of cornea fluorescein staining, the improvement of cornea clearing and the

increased stability of lacrimal film. In this study, slow elongation of BUT was observed after the application of corticosteriod and significant good effect was observed one month after treatment.

CONCLUSION

Dry eye is related to the inflammation of ocular surface, and immune-mediated inflammation plays an important pathogenic role. Corticosteroid is an effective anti-inflammatory drug, which can rapidly and effectively relieve the symptoms and signs of moderate or severe dry eye.

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