

Topical Fluorometholone Versus Diclofenac Sodium in Cases With Perennial Allergic Conjunctivitis

Zhiwei Li, M.D., Wei Chen, M.D., Yong Zhang, M.D., Vishal Jhanji, M.D.,
Zhaoshan Fan, M.D., and Guoying Mu, M.D.

Purpose: To compare the efficacy of diclofenac sodium (DS) 0.1% and fluorometholone (FL) 0.1% in patients with perennial allergic conjunctivitis. **Methods:** Fluorometholone 0.1% or DS 0.1% eye drops were topically administrated 4 times daily for 4 weeks in patients with perennial allergic conjunctivitis. Assessment was conducted with a 4-point rating scale (0=none, 1=mild, 2=moderate, and 3=severe) for 4 signs and 5 symptoms.

Results: Two hundred sixty-one patients were recruited. The demographics and baseline skin prick scores between both groups were comparable. Mean baseline scores in DS and FL group were 6.77 ± 2.24 and 6.34 ± 2.10 , respectively. The scores rapidly decreased to 3.28 ± 1.47 and 2.69 ± 1.44 on day 7. Diclofenac sodium expressed a slower effect compared with FL within the first 3 days of treatment ($P=0.01$).

Conclusions: The efficacy of topical FL and DS was comparable for the management of cases with perennial allergic conjunctivitis. However, FL led to a more rapid alleviation of signs and symptoms as compared with DS in early days after the initiation of treatment.

Key Words: Fluorometholone—Diclofenac sodium—Perennial allergic conjunctivitis.

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Perennial allergic conjunctivitis is a commonly encountered clinical entity. The clinical manifestations of allergic conjunctivitis are varied. If left untreated, some cases may progress to debilitating ocular symptoms and ultimately loss of best-corrected visual acuity. A persistent activation of mast cells and delayed-type hypersensitivity response are involved in perennial allergic conjunctivitis.¹ A variety of pharmacological treatment options are available for the management of allergic conjunctivitis, including antihistamines, mast cell stabilizers, nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids.² Although corticosteroids are effective in relieving symptoms and signs in cases with allergic conjunctivitis, their long-term use is associated with the occurrence of cataract and ocular hypertension.^{3,4} Topical NSAIDs are another group of agents that are widely used in

clinical practice. They provide comparable clinical outcomes while avoiding the potential side effects induced by corticosteroids.^{5–7} In this study, we compared the efficacy of 0.1% diclofenac sodium (DS) and 0.1% fluorometholone (FL) eye drops in patients with perennial allergic conjunctivitis.

METHODS

This study was conducted in three eye centers in Northern China: Central Area of Provincial Hospital affiliated to Shandong University, East Area of Provincial Hospital affiliated to Shandong University, and Tian'Jin Eye Hospital. Patients with symptoms of perennial allergic conjunctivitis for more than 6 months were enrolled. The Ethics Committee of all three hospitals approved the study protocol. The trial was performed in accordance with the tenets of the Declaration of Helsinki and National Drug Law of China.

Patients aged 18 years or older with a diagnosis of allergic conjunctivitis and a positive skin prick test (SPT) reaction to house dust mite (*Dermatophagoides pteronyssinus*) were included. We excluded patients with history of immunotherapy, systemic immunological disorders, giant papillary conjunctivitis, atopic keratoconjunctivitis, and vernal keratoconjunctivitis. All other topical therapies were discontinued at least 1 month before the study initiation.

After obtaining an informed consent, patients were prescribed DS 0.1% (Difei; Xingqi Pharmaceutical Co, Ltd, China) or FL 0.1% (Flumetholon; Santen Pharmaceutical Co, Ltd, Japan) eye drops 4 times daily for 28 days. The randomization codes for each subject had been sealed off into the each envelope respectively. An investigator took a numbered sealed envelope and gave it to the patients before obtaining the demographic data. The randomized information was not revealed to the investigators until the completion of the study. Follow-up was conducted on days 3, 7, 14, 21, 28, 42, and 56 after commencement of eye drops. The scoring system to evaluate the severity of conjunctivitis was adopted from our previous study.⁷ Two experienced clinicians (W.C. and Z.L.) evaluated the scores at all time points. A total eye score was calculated by adding up the scores of four objective signs: discharge, conjunctiva edema, eyelid edema, and conjunctival redness and five subjective symptoms: itching, burning sensation, tearing, foreign body sensation, and photophobia. The severity of 4 signs and 5 symptoms was assessed with a 4-point rating scale (0=none, 1=mild, 2=moderate, and 3=severe). The subjective or objective score ratio was calculated by dividing the subjective or objective scores at a specific time point by the baseline score. Patients with score more than 4 and persistent symptoms for 1 week were excluded from the study. These patients received

From the Department of Ophthalmology (Z.L., Y.Z., Z.F., G.M.), Provincial Hospital, Shandong University, Ji'nan, China; Tian'Jin Eye Hospital (W.C.), Tianjin, China; and Department of Visual Sciences and Ophthalmology (V.J.), The Chinese University of Hong Kong, Hong Kong, China.

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Address correspondence to Guoying Mu, M.D., Department of Ophthalmology, Provincial Hospital, Shandong University, No.324, Jing 5 Road, Ji'nan, Shandong Province, China; e-mail: mguyeyes@163.com

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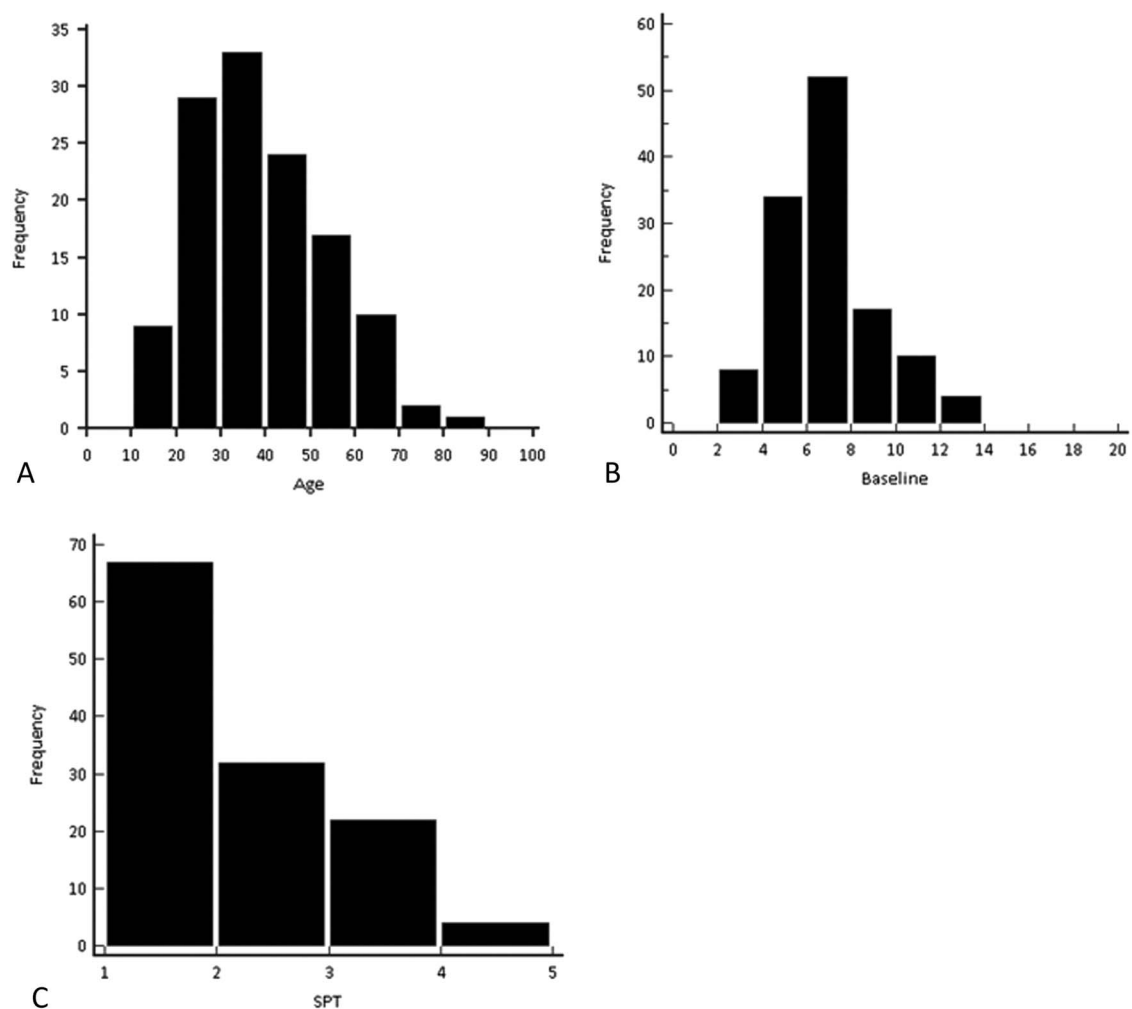


FIG. 1. Distribution of age (A), baseline scores (B), and skin prick test value (C) of involved patients. Two hundred sixty-one patients were enrolled at baseline. The age ranged from 18 to 81 years (38 ± 15 years). Scores at baseline ranged from 3 to 13 (6.55 ± 2.17).

other treatments, including high-frequency application of corticosteroid eye drops. Intraocular pressure (IOP) was measured at each follow-up, and the measurement on day 28 was used as a marker for long-term effect of drugs on IOP.

Statistical analysis was performed with SPSS (version 19.0.0 for windows). Analysis of variance test was used to compare the ratio of average scores of two groups on each follow-up. $P<0.05$ was considered statistically significant.

RESULTS

Two hundred sixty-one patients were enrolled at baseline. The age ranged from 18 to 81 years (38 ± 15 years). The scores at baseline ranged from 3 to 13 (6.55 ± 2.17) (Fig. 1). One case in

DS group withdrew from study on day 2 because of the subconjunctival hemorrhage, and another case in DS group withdrew on day 19 because of exacerbating eye redness. Three cases in FL group and 5 cases in DS group withdrew on day 7 because of persistently high scores. No significant difference in age, sex, baseline scores, and SPT scores was observed between both groups (Table 1). The age and scores harvested at baseline followed a normal distribution.

The average scores in DS and FL groups decreased from 6.77 ± 2.24 and 6.34 ± 2.10 to 3.28 ± 1.47 and 2.69 ± 1.44 , respectively, on day 7 (Fig. 2A). The decline in scores was slow in both groups after 7 days of treatment. The overall score ratio ($P=0.01$) and the subjective score ratio ($P=0.03$) were higher in DS group compared with FL group on day 3 (Fig. 2A,B). No difference was

TABLE 1. Preoperative Scores for Severity of Conjunctivitis and Skin Prick Test Scores in Diclofenac and Fluorometholone Groups				
Group	M/F	Age (Range), yr	Baseline Scores (Range)	Skin Prick Test Scores (Range)
Diclofenac sodium	66/63	39±14 (18–81)	6.77±2.24 (3–12)	1.79±0.90 (1–4)
Fluorometholone	64/68	38±15 (18–70)	6.34±2.10 (3–13)	1.63±0.85 (1–4)

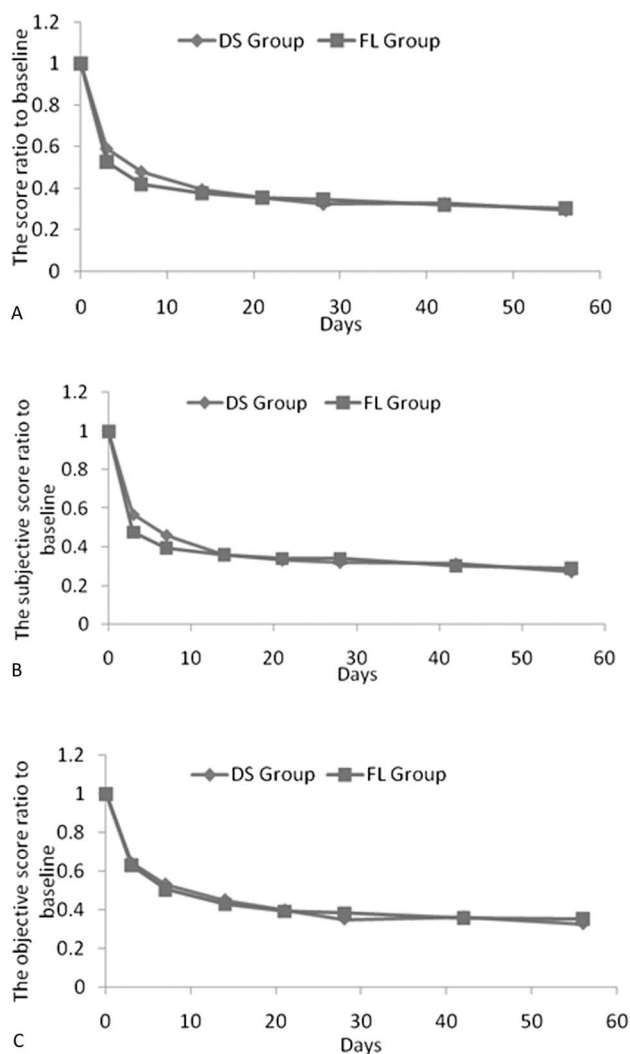


FIG. 2. Change in mean scores in diclofenac sodium (DS) and fluorometholone (FL) groups. Scores decreased rapidly in the beginning, followed by slow decrease in the following weeks (A); subjective score ratio in DS group was higher than FL group on day 3 ($P=0.03$) (B); score ratio (ratio of actual score to baseline score) on day 3 was higher in DS group compared with FL group ($P=0.01$). There was no difference in objective score ratio in both groups (C).

observed in the objective score ratio in both groups at all time points (Fig. 2C).

The IOP decreased by 0.2 mm Hg in DS group and increased by 0.5 mm Hg in FL group by the end of 28 days. However, no significant difference of IOP before and after therapy was obtained because of the small variation of IOP value.

DISCUSSION

In this study, we found that DS 0.1% eye drops has a comparable efficacy with FL in treating cases with allergic conjunctivitis. There were no significant adverse effects noted with any of the drugs.

Although the exact mechanism of anti-inflammatory activity of diclofenac is not entirely known, the primary mechanism is believed to be through the inhibition of prostaglandin synthesis

and bacterial DNA synthesis.⁸ The existing literature does not contain much information about the exact mechanism of action of diclofenac in cases with allergic conjunctivitis. Several studies have shown that the treatment with NSAIDs, including diclofenac, is effective in controlling the symptoms of patients affected by allergic rhinoconjunctivitis by directly reducing the biosynthesis of prostaglandins and indirectly reducing the production of leukotrienes.⁹ Another study showed that DS was better at day 3 and 7 compared with ketorolac in cases with seasonal allergic conjunctivitis.¹⁰ The authors suggested that NSAIDs might be effective for treating allergic conjunctivitis because of their ability to inhibit prostaglandin synthetase. Compared with diclofenac, corticosteroids have potent anti-inflammatory activity with a wider target spectrum including inhibition of cyclooxygenase¹¹ and phospholipase A2.¹² This can partly explain the more rapid relief of subjective score ratio in FL group, as observed in our current and previous study.⁷

In our study, there was no difference in the objective scores between the two groups at any time point, whereas the subjective scores in diclofenac group were higher than that in FL group on day 3. Our previous study using another NSAID, pranoprofen, also revealed a similar time curve.⁷ Figus et al.¹³ compared the efficacy of cromolyn sodium/chlorpheniramine maleate, diclofenac, epinastine, FL, ketotifen, levocabastine, naphazoline/antazoline, and olopatadine in cases with allergic conjunctivitis. The authors reported that efficacy of epinastine, ketotifen, and olopatadine in the treatment of allergic conjunctivitis was comparable with FL. They used topical diclofenac 0.1% and FL 0.2% using a twice-daily dose. The basal mean score for signs and symptoms of inflammation decreased significantly in their study, whereas the improvement for symptoms and signs at 1 month after treatment initiation in FL group was more significant than the diclofenac group. This may be attributed to a higher strength of FL (0.2%) used in their study compared with our study (0.1%).

The cases in FL eye drops had a 0.5 mm Hg increase in IOP as observed on day 28. Although the measurements could not be made on a specific time point during the day, there was no significant difference of IOP changes in two groups; the potential elevation in IOP induced by FL application should be considered in choosing the drugs during clinical practice.

Overall, this study found a comparable effect of DS and FL in cases with allergic conjunctivitis and a better response of symptoms in the early days after treatment initiation. A possible treatment protocol for these cases can consist of combination therapy with DS and FL for the first 3 days to obtain a rapid relief of symptoms followed by a maintenance usage of DS to get an acceptable clinical outcome with less possibility of steroid-induced side effects; however, the comparable efficacy of this combined treatment to DS or FL alone is still to be evaluated in the future studies.

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