

The Early Efficacy of Topical Levocabastine in Patients with Allergic Conjunctivitis

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ABSTRACT

Background: We investigated the early efficacy of topical levocabastine, an H₁ histamine-receptor antagonist, in improving the clinical symptoms of allergic conjunctivitis.

Methods: Thirty-six patients with allergic conjunctivitis were enrolled. One drop of levocabastine was instilled in one eye and one drop of artificial tears in the contralateral eye. Clinical examinations were performed before, and 15 and 30 minutes after instillation. Symptoms of itching and signs of injection were assessed at each time point.

Results: Both levocabastine and artificial tears resulted in a statistically significant reduction in ocular itching. However, levocabastine was significantly more effective.

Conclusions: Although artificial tears had a positive effect in reducing symptoms of allergic conjunctivitis, by the washing out of allergens, levocabastine was more effective than artificial tears in controlling acute symptoms of allergic conjunctivitis, demonstrating that the selective H₁ histamine-receptor antagonist action of levocabastine is rapidly effective in a clinical setting.

KEY WORDS

allergic conjunctivitis, artificial tears, H₁ antagonist, histamine, levocabastine

INTRODUCTION

Allergic conjunctivitis is a common disease and is estimated to affect approximately 25% of the world population.¹ The primary symptom of allergic conjunctivitis is ocular itching; other signs include conjunctival hyperemia or redness, chemosis, eyelid swelling, ocular discharge, and lacrimation.² A wide range of treatments is currently available to the clinician. These include mast cell stabilizers, antihistamines and steroids. Steroids inhibit multiple mediator-induced allergic responses and are effective in controlling symptoms and signs of allergic conjunctivitis; however, possible complications including cataracts and intraocular pressure elevation limit their use. In contrast, mast-cell stabilizers such as cromolyn (cromoglycic acid) inhibit more specific actions such as mast-cell degranulation and mediator

release, however these drugs often require up to about a week to obtain satisfactory relief of symptoms. Artificial tears are also often used to wash out allergens from the conjunctival sac.

Oral antihistamines are effective in controlling symptoms such as itching but often induce side effects such as dehydration and drowsiness. Therefore, in patients with predominantly ocular symptoms, topical preparations are preferable. Levocabastine hydrochloride, a second-generation antihistamine, is a non-sedating, highly potent, selective H₁ histamine-receptor antagonist. A 0.025% suspension of levocabastine has been developed in Japan for the treatment of allergic conjunctivitis. In this study, we evaluated whether the early efficacy of levocabastine is superior to the wash-out effect of artificial tears. In this study, the early efficacy of 0.025% levocabastine ophthalmic suspension and that of artificial tears were

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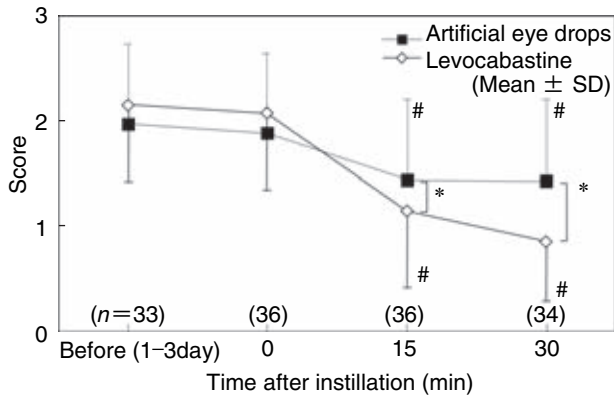


Fig. 1 Ocular itching in the early efficacy study. Though both artificial eye drops and levocabastine reduced ocular itching, levocabastine was more effective than artificial tears. ■ : artificial tears, ◇ : levocabastine. Values indicate means \pm SD, paired *t*-test ; * $p < 0.05$ (artificial tears vs. levocabastine), # $p < 0.05$ (vs. pretreatment levels).

compared.

METHODS

Thirty-six patients (10 men and 26 women; mean age, 41.0 ± 15.4 years; range, 20–73 years) with allergic conjunctivitis participated in the study. Patients were examined at the Kozuka Eye Center in Ehime, the Fujishima Eye Clinic in Niigata, or the Nakagawa Eye Clinic in Osaka. The studies were performed from August 2001 to March 2002.

Medical histories were recorded from all patients, and written informed consents were obtained. The following patients were excluded: 1) patients who had any ocular surface diseases other than allergic conjunctivitis, 2) patients who had used systemic or topical medications (e.g. steroids, nonsteroidal anti-inflammatory drugs, anticholinergics, immunosuppressives, mast-cell stabilizers, antihistamines) during the past week, 3) patients younger than 20 years, 4) women who were pregnant or potentially pregnant, and 5) patients who wore contact lenses.

Diagnoses were based on clinical symptoms and slit-lamp examination. Patients were asked to grade their baseline symptoms of ocular itching, conjunctival redness, and foreign body sensation on a scale of 0 to 3 (0 = none, 1 = mild, 2 = moderate, 3 = severe). Patients who had pre-treatment symptom grades that differed by more than 1 between their eyes were excluded from the analysis to reduce the bias caused by differences in symptom severity. Objective bulbar conjunctival injection was also graded on a scale of 0 to 3 (0 = none, 1 = mild, 2 = moderate, 3 = severe) based on slit-lamp examination. All the data are presented as means \pm SD.

All patients were treated with one drop of levocabastine (Livostin[®] Eye Drops 0.025%, Santen Phar-

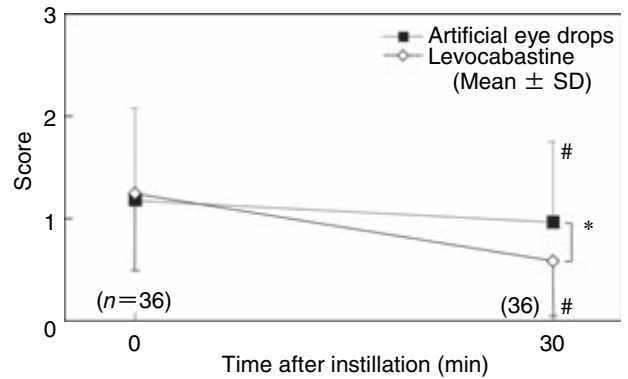


Fig. 2 Objective bulbar conjunctival injection in the early efficacy study. Levocabastine was more effective in reducing bulbar conjunctival injection than artificial tears. ■ : artificial tears, ◇ : levocabastine. Values indicate means \pm SD, paired *t*-test ; * $p < 0.05$ (artificial tears vs. levocabastine), # $p < 0.05$ (vs. pretreatment levels).

maceutical, Osaka, Japan) in one eye, and one drop of artificial tear (Soft Santear[®], Santen Pharmaceutical) in the contralateral eye. In order to avoid evaluation bias, neither the patients nor examiners were notified of the laterality of the eye drops. Symptoms and signs were re-evaluated at 15 and 30 minutes after instillation.

Statistical Analysis—Paired *t*-tests were used to assess the differences in symptoms before and after treatment, and between levocabastine and artificial tears. *P* values of less than 0.05 (two-tailed) were considered to indicate statistically significant differences.

RESULTS

Although both levocabastine and artificial tears significantly reduced ocular itching compared with pretreatment levels, at 15 and 30 minutes ($p < 0.001$), levocabastine was significantly more effective than artificial tears ($p = 0.001$ at 15 minutes and $p < 0.001$ at 30 minutes) (Fig. 1). Levocabastine reduced conjunctival redness at both 15 and 30 minutes ($p < 0.001$) compared with pretreatment levels, while artificial tears reduced conjunctival redness only at 30 minutes ($p = 0.023$). Levocabastine was also significantly more effective in reducing conjunctival redness than artificial tears ($p < 0.001$ at 15 and 30 minutes). Levocabastine also significantly reduced foreign body sensation in the eye compared with pre-treatment levels at 15 ($p = 0.001$) and 30 minutes ($p < 0.001$). Treatment with artificial tears did not significantly reduce foreign body sensation. Levocabastine was clearly more effective than artificial tears in reducing foreign body sensation at both 15 ($p = 0.005$) and 30 minutes ($p = 0.001$). Although both levocabastine ($p < 0.001$) and artificial tears ($p = 0.017$) significantly reduced bulbar conjunctival injection at 30 minutes, levo-

cabastine was more effective than artificial tears ($p < 0.001$) (Fig. 2). No adverse events were observed during this study.

DISCUSSION

In this study, artificial tears had a positive effect in reducing symptoms of allergic conjunctivitis. Allergic conjunctivitis is often complicated by dry eye and this relationship has been studied in many studies.^{3,4} Although artificial tears do not specifically treat allergy, they augment the tear film, effectively "washing" the ocular surface. This mechanism is useful for removing or reducing the concentration of allergens or proteins that induce inflammation from the ocular surface. Instillation of just one drop was sufficient to bring about this positive effect in our study. This suggests that more frequent instillation or washing with greater volume of artificial tears might be even more effective in improving the signs and symptoms of allergic conjunctivitis.

In this study, we also compared the early efficacy of artificial tears and levocabastine in the same patient by instilling one drug in one eye and the other drug in the other eye. By this method, we excluded bias arising from subjectivity of the patients' evaluation of symptoms and responses to the drugs.⁵ In our study, topical levocabastine was more effective than artificial tears in reducing ocular itching, conjunctival redness, and foreign body sensation, and also in reducing bulbar conjunctival injection assessed by slit-lamp examination. These results demonstrated that the selective H₁ histamine-receptor an-

tagonist action of levocabastine is rapidly effective in a clinical setting. The reduction of itching and vessel permeability caused by histamine release by levocabastine led to the decreased level of symptoms and signs observed in this study.

In conclusion, our study demonstrated that both artificial tears and levocabastine were effective in reducing acute symptoms of allergic conjunctivitis. Levocabastine however was significantly more effective than artificial tears demonstrating that the selective H₁ histamine-receptor antagonist action of levocabastine is rapidly effective in a clinical setting.

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