A Forced Choice Comfort Study of Olopatadine Hydrochloride 0.1% versus Ketotifen Fumarate 0.05%

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ABSTRACT.

Purpose: **To compare the ocular comfort of two ophthalmic anti-allergic agents: olopatadine hydrochloride 0.1% and ketotifen fumarate 0.05%.**

Subjects and Methods: **In a double-masked, multi-centered, randomized trial, 80 subjects were asked to make a 'forced choice' based on ocular comfort between one drop of olopatadine hydrochloride 0.1% instilled in one eye and one drop of ketotifen fumarate 0.05% instilled in the contralateral eye. At one site, the incidence of adverse reactions was also reported.**

Results: **All subjects (100%) selected olopatadine as the more comfortable formulation. One site (n=35) reported a 49% incidence of moderate burning and a 49% incidence of mild burning after ketotifen instillation. One subject (2% of population) at this site experienced no ocular discomfort with ketotifen. There were no reports of discomfort associated with olopatadine instillation.**

Conclusion: **Olopatadine is a more comfortable ophthalmic preparation than ketotifen.**

Key words: ophthalmic anti-allergic agents – olopatadine hydrochloride – ketotifen fumarate.

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Introduction

Over the past several years, new topical ocular agents have been developed to treat the signs and symptoms associated with allergic conjunctivitis, and studies have been conducted to compare the efficacy and safety profiles of these agents. A significant component of the safety profile of any new ophthalmic solution is its ocular comfort. Patients naturally prefer agents that are not only effective in reducing the signs and symptoms of ocular allergy, but are also comfortable to use. Furthermore, studies have shown that the more comfortable solutions are used with better compliance. A well-formulated ophthalmic anti-allergic agent should not only perform its active function, such as binding to histamine receptors and/or stabilizing mast cells, but it should also provide vehicle-derived benefits. Volume expansion with an inert solution dilutes the tears, providing a beneficial cleansing of the ocular surface. Enhancement of the barrier function of the tear film also minimizes the exposure of the ocular surface to environmental allergens.

To further investigate the acceptability of two new ophthalmic anti-allergic agents, and specifically, the comfort of their respective formulations, a multi-centered study using a 'forced choice' model, in which the patient had to choose which formulation he/she preferred, was completed. Olopatadine hydrochloride 0.1% (Alcon Laboratories, Inc.) is a novel mast cell stabilizer/antihistamine combination that has a significantly higher H_1 receptor affinity than many other topical agents (1). Ketotifen fumarate 0.05% (CIBA Vision) is a mast cell stabilizer/antihistamine. Both have been recently introduced as ophthalmic products with promising anti-allergic activities.

Subjects and Methods

In a double-masked, multi-centered (two sites: n=35, n=45), randomized trial, 80 subjects received one drop of olopatadine hydrochloride 0.1% in one eye and one drop of ketotifen fumarate 0.05% in the fellow eye. Beginning with the right eye, drops were instilled into the inferior cul-de-sac. Subjects were asked to choose which medication was more comfortable. Adverse event information was collected secondarily at one of the two sites.

Results

All subjects (n=80) chose olopatadine as more comfortable than ketotifen (Fig. 1). The site that collected adverse event information (n=35) reported moderate burning in 49% (n=17) and mild burning in another 49% of patients (n=17) in the ketotifen eye only (Fig. 2). Only one patient (2% of the population) reported no burning after ketotifen instillation. Burning with ketotifen instillation was also noted at the second site, but its exact incidence was not reported.

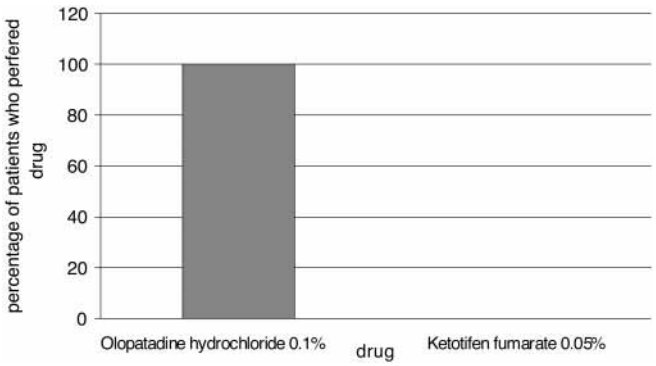

Fig. 1. Percentage of subjects (n=80) who preferred olopatadine (100%) versus those who preferred ketotifen (0%).

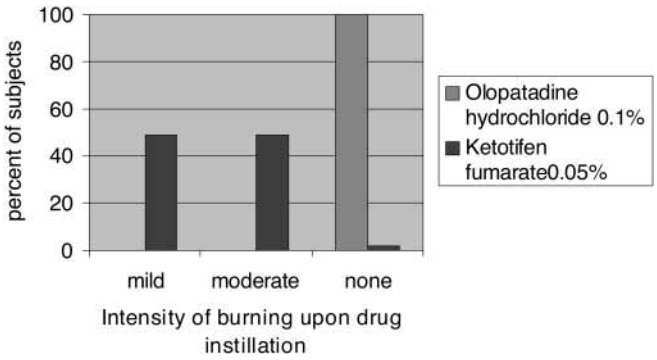

Fig. 2. Adverse events (moderate burning, mild burning or no burning) reported after ketotifen or olopatadine instillation. There were no reported adverse events with olopatadine (n=80).

Discussion

This very simply designed study was completed to answer the question as to which new anti-allergic ophthalmic solution, olopatadine or ketotifen, was more comfortable. The response was quite powerful: one hundred percent of subjects preferred olopatadine to ketotifen. Furthermore, the incidence of stinging that was reported at one site also showed dramatic differences between the two preparations: olopatadine instillation was never associated with burning, while ketotifen had a 98% incidence of burning after instillation.

While this information may appear to be only superficially relevant, optimizing the comfort of an anti-allergic preparation could significantly increase compliance, particularly since formulations of this class of drugs have been notoriously uncomfortable in the past (i.e., the first generation antihistamines). The comfort of ophthalmic drugs such as these anti-allergics, which may be taken for relatively long periods of time during the allergy season, is becoming an increasingly important parameter for drug acceptability with today's emphasis not only on drug efficacy, but on quality of life factors as well.

While the focus of this study did not encompass other subjective parameters, increased ocular comfort is certainly known to lead to better compliance and better control of the disease (1). It is known that the most efficacious drugs are those that will be used appropriately. Subjects who use drops as directed will attain longer, more continuous control of the disease than found with the sporadic and hesitant use of a medication that causes burning upon instillation. For a condition such as ocular allergy, which often requires only symptomatic control, it is inappropriate to replace one symptom, itching, with another, burning.

From the pharmacoeconomic perspective, additional costs are potentially associated with the use of ketotifen. Subjects who suffer from ocular allergy most likely will not use an agent that causes further discomfort. The discomfort caused by ketotifen could cause a subject to seek an alternative therapy from his physician, needlessly adding the costs of additional visits and medication.

The results of the present study complement those of a comparative efficacy clinical trial that has recently been completed on olopatadine and ketotifen in which olopatadine was shown to be significantly more efficacious in controlling itching and hyperemia (2).

Conclusion

The ophthalmic formulation of olopatadine is more comfortable than that of ketotifen. This increased comfort should lead to better subject compliance and therefore, better control of the disease.

References

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