Comparison of the therapeutic efficacy of 0.1% olopatadine hydrochloride and 0.025% ketotifen fumarate in allergic conjunctivitis

Aims: To study whether 0.1% olopatadine hydrochloride (OHCL) is more effective and safer than 0.025% ketotifen fumarate (KF) in the management of allergic conjunctivitis. **Methods:** 83 patients with the sign (hyperemia) and symptoms of allergic conjunctivitis (i.e., tearing, itching and photophobia) were randomized (stratifying by age and sex) 1:1 to receive either 0.1% OHCL or 0.025% KF (one drop in each eye every 12 h). Signs and symptoms were scored before and after 2 weeks of drug therapy using a four-point scale (range: 0–3) while side effects were scored 30 min and 2 weeks after treatment initiation. A composite score of signs and symptoms was defined by adding all measures of signs and symptoms and then subtracting the week 2 sum from the pretreatment sum. **Results:** Both drugs reduced signs and symptoms of allergic conjunctivitis at 2 weeks from baseline. The treatment with 0.1% OHCL was more effective compared with 0.025% KF, as the mean (SD) composite score of 6.3 (±1.3) for the OHCL group was significantly higher than that of 4.3 (±1.7) for the KF group ($p < 0.001$, two-sided t-test). KF reduced the mean scores of hyperemia, tearing, itching and photophobia by 64, 63, 55 and 81%, respectively, while OHCL reduced these by 96, 97, 88 and 96%. Relative significant efficacy was achieved for hyperemia, tearing and itching ($p \leq 0.001$) but not for photophobia ($p = 0.315$). No adverse events were observed in the OHCL group while 30% of patients in the KF group showed mild stinging or foreign body sensation after instillation of the first dose. **Conclusion:** 0.1% OHCl is more effective and safer (in the short term) than 0.025% KF in the management of allergic conjunctivitis.

KEYWORDS: allergic conjunctivitis ■ efficacy ■ ketotifen fumarate ■ olopatadine hydrochloride

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Allergic eye disease affects approximately one-fifth of the world's population [1]. The most disabling effects are due to the clinical manifestations, with some patients having seasonal exacerbations of their symptoms, whereas others have symptoms that are present throughout the year [1]. The number of people affected by allergic conjunctivitis (AC) is increasing day by day along with environmental pollution. Approximately 30% of the US population has some form of allergy [2] and up to 40% of the US population have experienced ocular symptoms at least once in their lifetime, with a peak of symptoms in the months of June and July [3]. Similarly, seasonal AC affects 15% of the UK population: in spring when the predominant airborne allergen is tree pollen and in summer when the predominant allergen is grass pollen, or in fall when the predominant allergen is weed pollen [101]. There are no accurate statistics regarding the incidence of AC in Bangladesh. However, it may vary from 15 to 30%. The predominant allergens in Bangladesh are tree pollen, animal dander, grass pollen and wood pollen, and the main allergy season is spring and summer.

Allergic conjunctivitis is a typical hypersensitivity reaction mediated by IgE in response to environmental antigens [4]. Mast cells play an important role in the pathogenesis of AC. Binding of specific antigens on mast cells in the conjunctiva leads to mast cell degranulation and the release of histamine and other allergic and inflammatory mediators [5]. Histamine is the principal mediator, which is responsible for the major signs and symptoms of AC including ocular itching, redness, tearing and lid swelling in ocular allergy. If mast cell activity is not blocked, symptoms such as itching and red eye will continue.

The pharmacotherapy of AC consists of several classes of drugs: H_1 receptor blockage, mast cell stabilizers, dual-acting agents, NSAIDS and corticosteroids. Topical histamine H_1 receptor antagonists are the primary means of treating ocular allergic disorders due to their rapid treatment of itching and redness. Recently antihistaminic agents with mast cell stabilizing properties have been described. This dual action controls the signs and symptoms during the acute phase (antihistaminic action) and also prevents long-term mast cell degranulation [4].

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Ketotifen fumarate (KF) and olopatadine hydrochloride (OHCL) have dual actions that offer a combination of these two mechanisms [6,7].

As a combination of mast cell stabilizer and antihistamine, KF has been used for treatment of AC with some minor adverse effects and OHCL is a relatively newer drug with the same mode of action but a better safety profile. Olopatadine is a potent antihistamine with high affinity for H_1 receptors. It is the only compound that inhibited the release of histamine from human conjunctival mast cells without causing degranulation. However, KF showed significant membrane disruption of mast cells and corneal epithelial cells, indicating degranulation potential [8]. A study based on cultured conjunctival cells of rabbits *in vitro* revealed that KF showed greater nuclear degenerations of the conjuctival cells than OHCL [9]. A recent review showed that OHCL is a safe, comfortable and effective medication for the treatment of seasonal and perennial AC [10]. An ophthalmic solution of olopatadine was approved in the USA for the treatment of seasonal AC in December 1996, in Japan in December 2000 and in the EU in February 2002 [11].

Although the efficacy and tolerability of these two agents have been demonstrated by many clinical studies [10,12–16], there are few studies that have compared them. On the other hand, findings of the comparative studies, conducted abroad, were somewhat conflicting. For example, Berdy *et al.* reported from an US trial that OHCL was 43% more effective than KF [17]. Similarly, Aguilar reported from an Argentinean study that OHCL controlled AC symptoms and signs more rapidly and to a greater extent than KF [4]. However, a randomized controlled trial in Turkey did not find any significant difference between these two active treatments [7,18]. By contrast, Ganz *et al.* and Hida *et al.* reported in randomized US and Brazilian trials, respectively, that the responder rate was higher for KF than for OHCL on day 21 [19,20]. Although, the reasons for these conflicting results are unclear, differences in study population or design may be the reason.

Bangladesh is a developing country and hence the general population in Bangladesh cannot afford a more expensive product. Moreover, there is only minimal governmental funding of medical care in Bangladesh. Therefore, it is important to have cheaper products such as OHCL/KF that are less than TK. 100 (<GBP£1) per vial. To the best of our knowledge, the only Bangladeshi study conducted in this area was the study of therapeutic response of lodoxamine and sodium chromoglycate on vernal keratoconjunctivitis [21]. The main reason for the lack of drug research in Bangladesh is the scarcity of funding. Occasionally some researchers take the initiative and study some marketed drugs for practical reasons. This study was conducted to choose between two low cost drugs for AC in the context of Bangladesh as physicians have to make a choice on a daily basis. As such the primary objective of this study is to find out whether OHCL is more effective compared with KF in the management of AC. The secondary objectives are to compare the therapeutic safety of these two drugs in AC, and to present a summary review of the comparative efficacy and safety of these two drugs for the treatment of AC.

Patients & methods

Sample size

Aguilar found that complete control of all evaluated signs and symptoms ranged from 80 to 87.5% of patients in their 0.1% OHCL group and 60 to 70% patients in their 0.05% KF group after 1 week of treatment [4]. Therefore, we assumed that the treatment with 0.025% KF for a 2-week period would decrease the signs and symptoms by 65%. We considered that if the decrease in signs and symptoms in the 0.1% OHCL-treated group is 90% or higher, 0.1% OHCL would be considered superior to 0.025% KF in the management of AC. To detect a 25% difference in efficacy between these two treatment modalities, a two-sided t-test showed that a minimum sample size of 41 in each group was needed with 81% power at the 5% level of significance. To accommodate for loss to follow-up, five more patients were recruited into each group to give a total sample size of 92.

Patient recruitment

This randomized, double-blind, single-center trial was carried out during the period from 1 January 2007 to 31 December 2007 at the Department of Pharmacology and Therapeutics, Sylhet MAG Osmani Medical College (Bangladesh) with active collaboration of the Department of Ophthalmology of Sylhet MAG Osmani Medical College Hospital (SOMCH), following the declaration of Helsinki. Recruitment took place over the year to avoid seasonal variation of AC. The study was approved by the Sylhet MAG Osmani Medical College ethics committee. Patients attended the SOMCH outpatient department with various complaints, including ocular itching, hyperemia, dry eye, tearing, photophobia, eye pain, headache, mucus

discharge and lid edema. However, we diagnosed AC and selected patients based on the clinical sign (hyperemia) and symptoms (tearing, ocular itching and photophobia) as described in [4,22]. A clinical diagnosis of AC was made based on the abnormal clinical sign of hyperemia on slit lamp examination. No other methods of diagnosis were considered besides clinical signs and symptoms. For example, skin testing may have been useful to provide more accurate diagnosis but we chose to use signs and symptoms rather than skin testing mainly to reduce cost as the study was not externally funded. Exclusion criteria were associated with other systemic or ocular illness (bronchial asthma, eczema, dry eye, uveitis or infective conjunctivitis), history of ocular surgery, contact lens use, receiving systemic or topical ocular medication and pregnancy. We had to exclude some chronic AC patients due to the presence of other diseases such as bronchial asthma and eczema as they require other systemic and topical treatment besides treatment of AC and hence are likely to be lost to follow-up as they needed referral to other departments.

Treatment allocation & follow-up

Patients who were found to be eligible according to selection criteria were recruited in to one of the treatment groups (0.025% KF or 0.1% OHCL) according to a stratified randomization list based on age and sex. The objectives, nature, purpose and potential risk and benefits of all procedures used for the study were explained in detail to the patients and informed written consent was taken before randomization. Detailed history and clinical examination were performed in a prescribed data collection form. Almost one-fourth of the outpatients were not included in the study either owing to failure at screening or lack of consent to take part.

Patients received one drop in each eye every 12 h and patients were also counseled for proper administration of the eye drops. Study medications were provided in identical containers so that both patients and investigators remained blinded. Hyperemia, itching, tearing and photophobia were scored and recorded just before and after 2 weeks of drug therapy using a four-point scale (see Table 1). During drug therapy the patients were instructed to report to the ophthalmology outpatient department or to contact the chief investigator if any problem arose (e.g., foreign body sensation/stinging, headache, sedation, dry eye, worsening of symptoms/nonresponse to therapy). In addition, side effects were scored and recorded at 30 min and 2 weeks after treatment initiation based on a four-point scale according to Table 2.

Statistical methods

The primary objective of the trial was to assess the effectiveness of OHCL compared with KF. One way to compare OHCL and KF is to first subtract the week 2 measures from the week 0 (baseline/pretreatment) measures for each treatment before hypothesis testing. Therefore, a composite score of signs and symptoms was calculated to measure overall effectiveness by adding all the four measures of signs and symptoms (hyperemia, itching, tearing and photophobia) and then subtracting the week 2 sum from the pretreatment sum.

Overall effectiveness of OHCL compared with KF was tested based on composite score using a two-sided independent sample t-test at the 5% level of significance. However, an individual sign and symptom-specific parameter was tested at the 1.25% level following Bonferroni correction to adjust for multiple testing. Values were expressed as mean ± SD.

Table 1. Scoring of signs and symptoms of allergic conjunctivitis.

Signs and symptoms	Scoring of signs and symptoms of allergic conjunctivitis			
	Score 0: absent	***Score 1: mild***	***Score 2: moderate***	***Score 3: severe***
Hyperemia	Absent	Slightly dilated blood vessels, pink in color	More apparent vessel dilatation, vessel color is more intense, involves most of vessel bed	Numerous and obvious dilated blood vessels, color deep red
Tearing	Absent	Occasional, no complaints of discomfort	Frequent, patient felt as discomfort	Persistent and frequently accompanied by swabbing of the eye
Itching	Absent	Occasional itching, without tendency to scratch or rub the eyes	Frequent itching with tendency to scratch or rub the eyes	Continuous itching, frequently rubbing the eyes
Photophobia	Absent	Occasionally photophobic	Continuously photophobic	Eye responds with blepharospasm on exposure to light

Table 2. Scoring of side effects of drug (0.025% ketotifen fumarate and 0.1% olopatadine hydrochloride).

Side effects	Scoring of side effect of drug			
	Score 0: absent	***Score 1: mild***	***Score 2: moderate***	***Score 3: severe***
Stinging or foreign body sensation	Absent	Stinging or foreign body sensation at instillation only and disappears rapidly	Stinging or foreign body sensation at instillation that persists but treatment does not need to be discontinued	Stinging or foreign body sensation at instillation and persisting to the point that treatment has to be discontinued
Headache	Absent	Present		
Sedation	Absent	Present		
Dry eye	Absent	Present		

Results

A total of 92 patients were randomized in this study as per the inclusion and exclusion criteria from patients with the signs and symptoms of AC who attended the ophthalmology outpatient department of SOMCH. Of the 92 patients, nine (three from the KF group and six from the OHCL group) failed to attend the week 2 visit and hence 83 patients (40 from the OHCL group and 43 from the KF) completed the study. The trial flow chart (CONSORT) is shown in Figure 1.

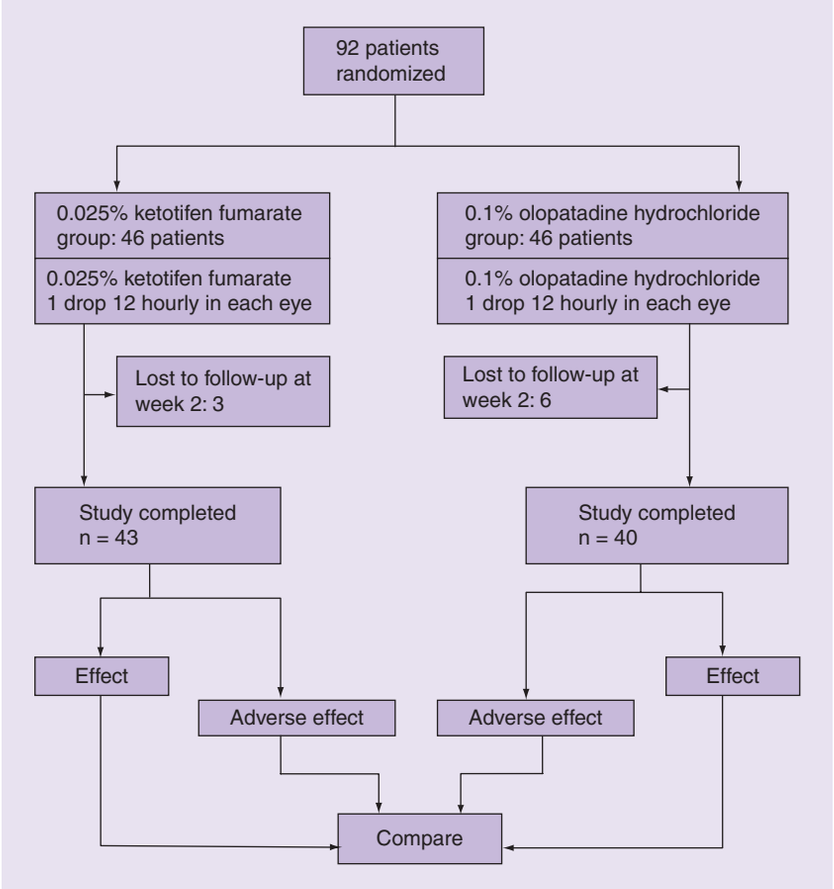

Figure 1. Trial flow chart.

The age range of the study subjects was 12–50 years. Mean age of the KF and OHCL groups were 28 ± 12 and 28 ± 11 years, respectively. In KF group 18 (42%) were male, while the OHCL group consisted of 18 (45%) male. There was no significant difference between the two treatment groups in terms of age and sex as the patients were randomized by stratifying in terms of age and sex (see Table 3). In addition, the two groups of patients did not differ in terms of their working place, dwelling place and food allergy.

Treatment with 0.1% OHCL was found to be more efficacious compared with 0.025% KF in the management of AC as the mean (SD) composite score of 6.3 (±1.3) for the OHCL group was significantly higher than that of 4.3 (±1.7) for the KF group ($p < 0.001$). Since the overall effectiveness of 0.1% OHCL is significantly higher than that of 0.025% KF, we examined the effectiveness at the individual sign and symptom level.

The baseline/pretreatment mean scores (SD) of hyperemia, tearing, itching and photophobia were 1.93 ± 0.258, 1.07 ± 0.258, 2.40 ± 0.495 and 1.35 ± 0.573, respectively, in the KF group. After 2 weeks of treatment these mean scores reduced to 0.70 ± 0.887, 0.40 ± 0.66, 1.09 ± 0.527 and 0.26 ± 0.441, respectively. Thus, treatment with 0.025% KF reduced the mean scores of hyperemia, tearing, itching and photophobia by 64, 63, 55 and 81%, respectively (see Figure 2).

On the other hand, the baseline mean scores (SD) of hyperemia, tearing, itching and photophobia were 1.90 ± 0.304, 1.13 ± 0.607, 2.45 ± 0.677 and 1.27 ± 0.452, respectively, in the OHCL group. After 2 weeks of treatment these mean scores reduced to 0.08 ± 0.267, 0.03 ± 0.158, 0.33 ± 0.608 and 0.05 ± 0.221, respectively. Thus, treatment with 0.1% OHCL reduced the mean scores of hyperemia, tearing, itching and photophobia to 96, 97, 88 and 96%, respectively (see Figure 2).

Table 3. Participants' profile.

Characteristics	Total	KF (n = 43)	OHCL (n = 40)	p-value
Age: mean (SD), years	28 (12)	28 (12)	28 (11)	0.88†
Male (%)	36 (43)	18 (42)	18 (45)	0.83‡
Indoor work (%)	31 (37)	15 (35)	16 (40)	0.66‡
City dwelling (%)	34 (41)	19 (44)	15 (38)	0.66‡
Food allergy (%)	16 (19)	10 (23)	6 (15)	0.41‡

†Two sample t-test.
‡Fisher's exact test.
KF: Ketotifen fumarate; OHCL: Olopatadine hydrochloride; SD: Standard deviation.

For both treatments, the lowest observed reduction was in itching (55 vs 88%). While KF reduced photophobia most (81%), OHCL reduced tearing most (97%). 0.1% OHCL was significantly more efficacious compared with 0.025% KF in reducing the signs and symptoms of hyperemia ($p = 0.001$), tearing ($p < 0.001$) and itching ($p < 0.001$) (Table 4). Although the reduction in photophobia was 15% higher in the OHCL group than that of the KF group (96 vs 81%), it was not statistically significant ($p = 0.315$).

In our study no marked adverse effects; including problems with corneal epithelial integrity, were observed in either group over the observation period. Only mild stinging sensation was noted by 13 subjects (30%) of the KF-treated group after instillation of the first dose, which did not persist for more than a few minutes. Both treatment regimens were well tolerated, the drug-related adverse events reported in the KF-treated group were minor and transient.

Discussion

Allergic conjunctivitis hampers quality of life as patients with AC frequently present with symptoms of allergic rhinitis [23,24]. The goal of treatment for AC is to effectively resolve clinical signs and symptoms and improve quality of life. We conducted a double-masked randomized trial to find out whether OHCL is more effective compared with KF in the management of AC. In this trial, data from 83 patients with AC attending the ophthalmology outpatient department of SOMCH were analyzed. Out of 83 patients, 43 received 0.025% KF and 40 received 0.1% OHCL.

To improve quality of life it is important to get early relief from signs and symptoms of AC. Our trial found that the overall effectiveness of 0.1% OHCL is statistically significantly higher than that of 0.025% KF in reducing the sign and symptoms of AC 2 weeks after installation. Specifically, significant effectiveness was observed in reducing the signs and symptoms of hyperemia, tearing and itching but not photophobia. Although the reduction of photophobia was more than 15% higher in the OHCL group than the KF group, it was not statistically significant as the study was powered only to detect the reduction of 25% or higher. Berdy *et al.* compared the clinical efficacy of both drugs in the USA and found that OHCL reduced ocular itching more effectively compared with KF [17]. Similarly, Aguilar reported from an Argentinean trial that 0.1% OHCL controlled AC symptoms and signs (itching, hyperemia, mucous discharge and tearing) more rapidly and to a greater extent than 0.05% KF [4]. Varguez-Rodriguez *et al.* conducted a randomized trial in Mexico and found that OHCL was

Table 4. Difference between 0.025% ketotifen fumarate and 0.1% olopatadine hydrochloride in terms of mean scores of signs and symptoms.

Signs and symptoms	$KF_{(W0-W2)}$		$OHCL_{(W0-W2)}$		$OHCL_{(W0-W2)}$ - $KF_{(W0-W2)}$			p-value†
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SE*	*95% CI*	
Hyperemia	1.23	0.87	1.83	0.71	0.59	0.18	0.24–0.94	0.001
Tearing	0.67	0.47	1.10	0.50	0.43	0.11	0.21–0.64	<0.001
Itching	1.30	0.56	2.15	0.80	0.85	0.15	0.55–1.15	<0.001
Photophobia	1.09	0.61	1.23	0.58	0.13	0.13	0.13–0.39	0.315

Dose of one drop every 12 h in each eye in patients suffering from allergic conjunctivitis.
†p-value represents the difference between $OHCL_{(W0-W2)}$ and $KF_{(W0-W2)}$ and is based on the two-sample t-test.
KF: Ketotifen fumarate; OHCL: Olopatadine hydrochloride; SD: Standard deviation; SE: Standard error; W0: Week 0; W2: Week 2.

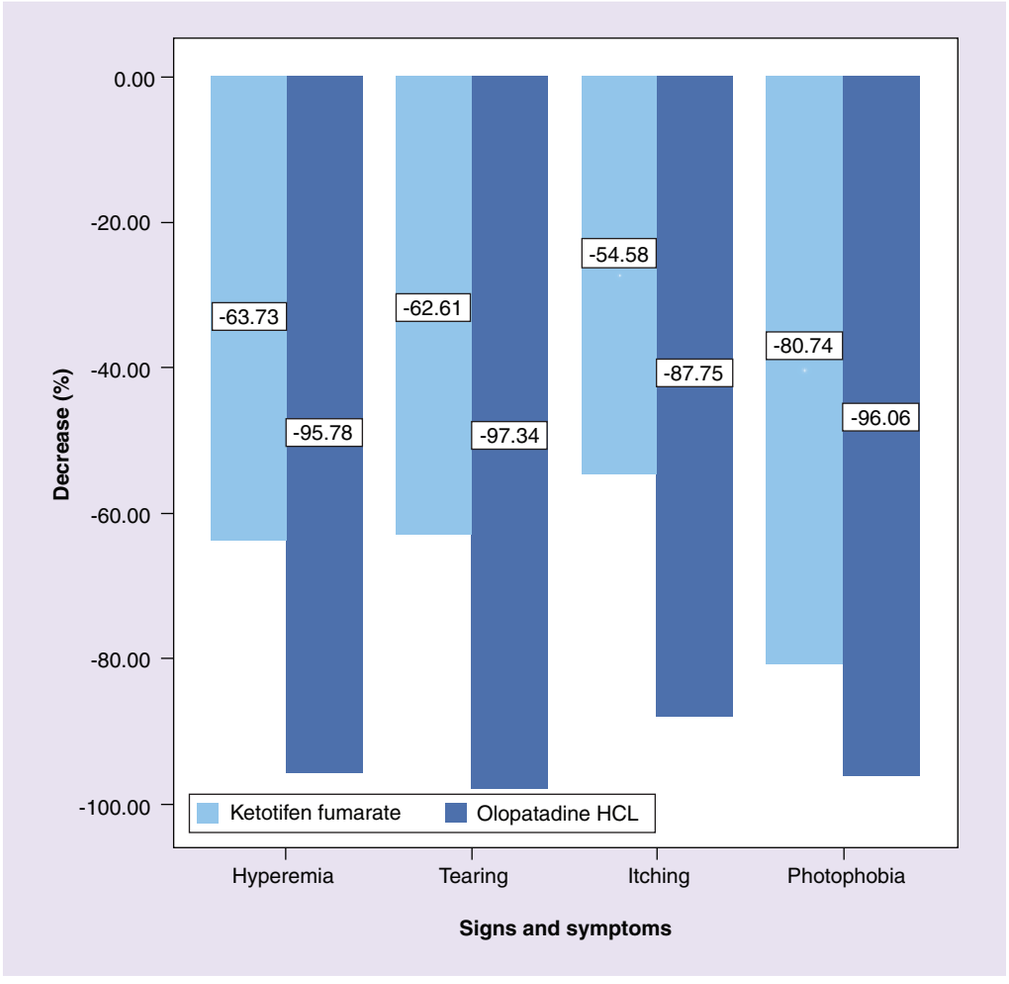

Figure 2. Comparison between 0.025% ketotifen fumarate and 0.1% olopatadine hydrochloride in terms of percentage decrease of scores within 2 weeks. Drugs were administered at a dose of one drop every 12 h on each eye in patients suffering from allergic conjunctivitis.

more effective than topical KF in improving itching, tearing and burning in AC [25]. In a recent review, superiority of OHCL compared with other topical allergic drugs was demonstrated by Leonardi and Quintieri [26]. Our trial confirms the findings of the previous trials regarding the relative efficacy of 0.1% OHCL over 0.025% KF. The survey of related trials and their conclusions is shown in Table 5.

Figus *et al.* reported from a recent Italian trial that the reduction of symptoms after 1 month of treatment is at least 75% in 70% of cases both for OHCL and KF but the 75% reduction for signs was obtained by KF only [27]. Avunduk *et al.* did not find any significant difference between these two active treatments in a randomized double-masked controlled clinical trial in Turkey [7]. However, their trials were likely to be underpowered as the total sample sizes were 40 and 39, respectively. By contrast, Ganz *et al.* [19] and Hida *et al.* [20] reported in randomized US and Brazilian trials, respectively, that the responder rate was higher with KF than with OHCL on day 21. The Brazilian trial was based on a sample size of 38 and the comparison was not made directly between the two groups using a statistical test. However, in the US trial, global efficacy ratings were also higher with KF, and severity scores for hyperemia and itching were significantly lower. The study was based on a sample size of 66; the results seem to conflict with common findings in the literature. We are uncertain why these results are discordant.

Aguilar reported that no intolerance reactions were observed in patients receiving OHCL [4]. However, approximately 23% of the patients in the KF-treated group had mild reactions of intolerance (stinging), which was not a cause to discontinue the treatment (see elsewhere for details on the safety of OHCL [28]). In our study, 30% of patients in the KF group

showed mild stinging or foreign body sensation after instillation of the first dose. The drug related adverse events reported in the KF group were minor and transient. No adverse events such as stinging sensation, headache, sedation or dry eye were observed in the OHCL group during the study period.

Leonardi and Zafirakis reported that a significantly greater percentage of patients (81%) selected OHCL when asked which medication they preferred, which they found more comfortable and more efficacious in reducing symptoms of allergy, in a large study of patient preference [5]. In a double-masked, multicentered, randomized trial by Artal *et al.,* subjects were asked to make a choice based on ocular comfort between one drop of 0.1% OHCL instilled in one eye and one drop of 0.05% KF instilled in the contralateral eye [29]. All subjects (100%) selected OHCL as the more comfortable formulation. Again our results confirm findings in the literature regarding the short-term safety and comfort of OHCL over KF.

Both drugs have similar modes of action in stabilizing mast cell membrane and blocking H_1 receptors. However, OHCL is superior to KF in obtaining rapid and effective relief from the sign and symptoms of AC, with less adverse effects. Our trial also showed that the individual drugs reduced the signs and symptoms of AC from baseline, but this does not prove that the two drugs are separately effective unless compared with a placebo group. However, their individual efficacy have been well demonstrated in the literature via placebo-controlled trials [13,14,18].

Almost one-fourth of the outpatients did not take part in the study and we had to exclude some chronic patients due to the presence of diseases such as bronchial asthma and eczema. This may affect the generalizability of our trial findings, although our findings are not different from the findings in the literature.

Conclusion

0.1% OHCL is more effective and safer (in the short term) than 0.025% KF in the management of AC. Patients treated with OHCL had a good recovery of ocular hyperemia and symptoms attributed to AC with no reported adverse events and thus this offers a promising new strategy for the management of this disease. Moreover, less frequent doses with relatively low cost OHCL may lead to improved patient compliance. In clinical practice it may provide a useful treatment for AC patients who are unable to attain a satisfactory anti-allergic effect with other medication such as KF.

Table 5. Survey of related trials on 0.025% ketotifen fumarate and 0.1% olopatadine hydrochloride.

Place of trial	Trial design	Sample size	Conclusion	Ref.
USA	Randomized, double-blind	32	OHCL is more effective than KF in reducing the itching. OHCL caused less ocular discomfort than KF and was preferred by ~three-times as many patients as was KF	[18]
Argentina	Randomized	80	OHCL controlled allergic conjunctivitis and signs more rapidly and to a greater extent than KF. KF triggered mild reactions (stinging) in 23% of patients	[4]
Argentina	Randomized, double-masked	80	OHCL is a more comfortable ophthalmic preparation than KF	[29]
Greece and Italy	Randomized, double-masked	100	A significantly greater percentage of the patients preferred to use OHCL, and found it more efficacious and comfortable	[5]
USA	Randomized, double-masked	66	The responder rate was higher with KF than with OHCL on day 5 and day 21. Global efficacy ratings were higher with KF and severity scores for hyperemia and itching were significantly lower. Both drugs elicited comparable comfort ratings	[19]
Turkey	Randomized, double-masked	39	There was no significant difference between these two treatments	[7]
Mexico	Randomized	40	OHCL was more effective than topical KF in improving itching, tearing and burning in allergic conjunctivitis	[25]
Italy	Randomized, single-masked	240	OHCL and KF both obtained at least a 75% reduction in symptoms in 70% of cases, but a 75% reduction for signs was obtained by KF only	[27]
Bangladesh	Randomized, double-masked	83	OHCL is more effective and safer (in the short term) than KF in the management of allergic conjunctivitis.	[Sarker *et al.* Unpublished Data]

KF: Ketotifen fumarate; OHCL: Olopatadine hydrochloride.

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Executive summary

- 0.1% olopatadine hydrochloride (OHCL) is more effective than 0.025% ketotifen fumarate (KF) in the management of allergic conjunctivitis.
- OHCL is safer than KF in the short-term management of allergic conjunctivitis.
- Literature reviews show that generally OHCL is more effective and safer than KF in the management of allergic conjunctivitis with few exceptions.
- In clinical practice OHCL may be a useful treatment for allergic conjunctivitis patients who are unable to attain a satisfactory antiallergic effect with other medications such as KF.

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▪▪ **Compares all possible drugs for allergic conjunctivitis and unlike other articles performed correct statistical analysis by calculating the percentage reduction in signs and symptoms of allergic conjunctivitis.**

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