Original Article

Comparative Study of Olopatadine Hydrochloride 0.1% and Emedastine difumarate 0.05% Comparing their Clinical Efficacy and Adverse Effects in Allergic Conjunctivitis

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ABSTRACT

Objective: To assess the efficacy and adverse effects of 0.1% Olopatadine hydrochloride (OHC) and compare them to 0.05% Emedastine difumarate (ED) in the treatment of allergic conjunctivitis.

Study Design: Prospective and comparative study

Place and Duration of Study: The study was conducted at Islam Teaching Hospital, Islam Medical College, Sialkot from February 2013 to June 2014.

Materials and Methods: 74 adult patients including 35 male patients aged 21- 47 years (Average 32.39) and 39 females aged 20 - 42 years (Average 31.8) some with a history of systemic allergic manifestation (e.g. asthma, dermatitis, or bronchitis) along with sign and symptoms of allergic conjunctivitis were enrolled in the study. At the time of induction, manifestations of allergic conjunctivitis (mucous discharge, itching, conjunctival congestion, chemosis, and watering) were present. Patients were allocate at random to either of the 2 groups, A and B. The patients in the Group A, (n = 36) received OHC and those in the Group B (n = 38) were treated with ED. The dose in Group A was one drop in both the eyes 12 hourly. Group B received one drop in both the eyes 6 hourly. The study was started on the first patient visit, when after the diagnosis; the drug was administered. Patients from both the groups were re-evaluated half an hour, forty eight hours, seven and fourteen days later. Efficacy and side effects in both the groups were assessed. The severity of signs and symptoms were assigned a score from 0 - 3. The results were analysed using independent sample T test.

Results: At the start of the study, cumulative score of the patient's sign and symptoms was calculated, with a mean value of 7.31 for group A and 7.38 for group B. There was no significant statistical disparity between the groups (p = 0.88). The cumulative scores at the end of study on day fourteen were 0.72 for group A and 1.0 for group B. This was also statistically not significant (p = 0.15) but Olopatadine was noted to be more effective.

The side effects of both the medicines were similarly assessed with cumulative scores calculated at each follow up. In group A, there were minimal side effects with mean cumulative score on the final visit was 0.25 in group A and 0.54 in Group B, with statistically significant (p = 0.015) difference.

Conclusion: Olopatadine was discovered to have better efficacy (not statistically significant) and less adverse effects (statistically significant) than Emedastine.

Key Words: Olopatadine, Emedastine, Allergic Conjunctivitis

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INTRODUCTION

Allergic conjunctivitis (AC) is an immune mediated ocular surface disorder that disturbs nearly one fourth of population at large[1,2]. Of the various causes of conjunctivitis, allergy is the most common aetiology, responsible for 15% to 40% of the presentations with conjunctivitis[3]. The incidence rises in spring and summer[4]. Allergic conjunctivitis is the inflammatory response of the conjunctiva to environmental antigens such as animal dander, pollen, and dust etc. Redness and itching are the most consistent symptoms[3]. AC is an immune mediated disorder. It is a "Type I hypersensitivity reaction" to pollen and other antigens, arbitrated by IgE as indicated by accompanying eosinophilia, and results from a sequence of biological reactions[5]: a) atmospheric allergens cause sensitization; b) activation of mast cells by IgE and subsequent

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release of mediators; c) inflammation of the conjunctiva with prevalence of eosinophils; d) production of cytokines, and e) exaggerated production of mucous.

Mast cells have a major role in this pathophysiology[6]. These cells' action not just contributes to the progression of this acute hypersensitivity reaction but also plays an important role in the metabolic regulation of response of connective tissue succeeding this occurrence in the form of fibrosis. After the exposure to allergen, in both, acute and chronic phase, one of the key features is the appearance of inflammatory cells (neutrophils, lymphocytes, and eosinophils) in lacrimal secretion within nearly six to twenty four hours. Histamine is the main mediator, responsible for the sign and symptoms associated with allergic conjunctivitis[7,8]. Key signs comprise conjunctival hyperaemia, conjunctival chemosis, watering, mucous production, and papillae. Major and frequent presenting complaints comprise of itching, watering, blurry vision photophobia and foreign body perception. Itching is the hallmark of AC. AC can be managed with local anti-allergic drugs such as anti-histamines. These may be solo or in formulation with α-adrenergic drugs[9]. The management of allergic conjunctivitis has markedly evolved in recent times[10-13]. The vast array of treatment options provides opportunities for more individualized therapy, but at the same time also leaves the physicians and patients confused over which option to adopt[14]. Antihistamines delivered topically are the most favoured option for the management of allergic conjunctivitis[15]. These agents inhibit the effect of histamine on H_1 receptor. Emedastine difumarate (E.D) 0.05% is an antagonist with very selective and more potent H_1 receptor affinity when compared to levocabastine and other agents like ketotifen[16]. The latest type of topical agents for management of allergic conjunctivitis have the dual - effect, a strong antihistaminic activity that provides rapid relief and mast-cell stabilization that are responsible for extended respite[9]. Drugs such as Olopatadine, bepostatine, epinastine and azelastine are counted in in this group. Amongst this group Olopatadine hydrochloride (O.H.C) inhibits stimulation of eosinophils, macrophages and neutrophils, hence reducing liberation of platelet-activating factors, leukotrienes and other mediators of inflammation[14]. O.H.C 0.1% has a fast onset of action, initiating within a few minutes and lasting for hours, hence allowing a twice daily dose. It has potent, choosy antihistaminic and mast cell stabilizing activity[17].

MATERIALS AND METHODS

The study was conducted at Islam Teaching Hospital, Islam Medical College, Sialkot from February 2013 to June 2014. This was randomized double blind prospective study with active treatment concurrent control[18].

74 patients were included in the study, of these, 11 had a history of systemic manifestations of allergy, which included Allergic rhinitis, asthma, and dermatitis. Patients using any drugs at the time of the study were excluded as were those who had undergone ocular surgery in recent past. Females in whom pregnancy could not be ruled out were also excluded. All the patients were exhibiting clinical features of allergic conjunctivitis (Figure 1).

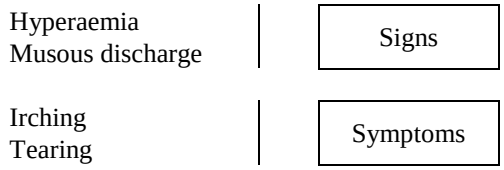

Figure No.1: exhibiting clinical features of allergic conjunctivitis

These symptoms and signs were classified in 4 grades: "Grading for Hyperemia: 0, Absent; 1, Mild: little dilatation of blood vessels, pink color, distributed in quadrants; 2, Moderate: moderate size dilatation of blood vessels, generally red color, generalized and randomly located in conjunctiva; 3, Severe: Numerous generalized dilatation of blood vessels, red color with or without chemosis. Grading for Mucous discharge: 0 , Absent 1; Mild: small mucous conglomerates, preferably concentrated in the inferior cul- de-sac; 2, Moderate: Bigger mucous conglomerates in the inferior conjunctival cul-de-sac, producing discomfort generally in the morning; 3, Severe: Big mucous conglomerates in cul-de-sac with discharge in palpebral edges and at the caruncle level, accompanied with sticky eyes in the morning. Grading for Itching: 0, Absent; 1, Mild: infrequent, with tendency to scratch or rub the eyes; 2, Moderate: constantly there, with tendency to scratch or rub the eyes; 3, Severe: continuous, frequently rubbing the eyes; Grading for Tearing: 0, Absent; 1, Mild: infrequent; 2, Moderate: perceived by patient, felt as discomfort; 3, Severe: permanent and commonly accompanied by drying of the eyes and palpebral edges".

Subjects were separated into 2 groups (A and B) comprising of 36 and 38 members respectively. The first group (Group A) was treated with 0.1% Olopatadine hydrochloride (OHC) and the second group (Group B) comprised those who received Emedastine difumarate 0.05% (ED). Every subject was administered a single drop in each eye every twelve hours, in group A and 6 hourly in group B. At the initial visit, the patients sign and symptoms were recorded and the first drop of medication was instilled in both the eyes. Patients were then re-evaluated after an interval of thirty minutes and any adverse effect / discomfort was noted as well as any improvement in the sign and symptoms. The next visits were after 48 hours, 1 week and 2 weeks respectively.

Adverse reaction/intolerance was noted and graded according to the following criteria:

"Grading for Burning/ foreign body perception: 0, Absent; 1, Mild: mild burning/stinging or foreign body perception upon administration of drops; 2, Moderate: mild burning/ stinging or foreign body perception at instillation which persisted; 3, Severe: significant burning/stinging or foreign body perception at instillation that persisted to the point that therapy had to be withdrawn. Grading for Blurring of vision and dryness of eyes : 0, Absent; 1, Mild; 2, Moderate; 3, severe".

The symptoms and signs were assessed at before treatment and then thirty minutes, forty eight hours, seven days and fourteen days after commencement of therapy:

Statistics: The results were analysed using independent sample T test.

RESULTS

Members of group A (OHC) when evaluated half an hour after the first dose, showed an overall improvement in the symptoms. However, there was no improvement in the amount of discharge. 4 patients were excluded from the study on day 7 (due to no response), the rest completed the study. No adverse effect, except mild dryness, were witnessed (4 - 6%).

In Group B (ED), 6/38 of the subjects were excused from the study at day 7 of commencement of therapy because of the lack of a positive response. A further 3.13 % of the patients (1/32) missed further follow up. The patients reported mild side effects of stinging and burning as well as foreign body sensation at various points in the study; however, they were not strong enough to cause a withdrawal or discontinuation of therapy.

At the start of the study, pre-treatment cumulative score of the patients sign and symptoms was calculated, with a mean value of 7.31 for group A and 7.38 for group B. There was no significant statistical disparity between the groups (p = 0.88). The cumulative scores at the end of study on day fourteen were 0.72 for group A and 1.0 for group B. This was also statistically not significant (p = 0.15) but Olopatadine was noted to be more effective (Table 1).

Table No.1: Comparison of Cumulative score of sign and symptoms

.	Cumulative Score		p Value
	Group A (OHC)	Group B (ED)	
Pre-treatment	7.31	7.38	0.88
30 minutes	5.94	6.0	0.78
48 hours	4.28	4.45	0.78
7 days	2.25	2.51	0.63
14 days	0.72	1.0	0.15

The side effects of both the medicines were similarly assessed with cumulative scores calculated at each follow up. In group A, there were minimal side effects with no stinging/burning sensation or blurring of vision. The only side effect noted was mild dry eye in a small number of patients. The mean of cumulative score on the final visit was 0.25 in group A. Group B patients reported side effects including, stinging, burning, foreign body sensation as well as mild dry eye. However, none of these was severe enough to cause withdrawal of the drug or cessation of treatment. The mean cumulative score was 0.54. This was found to be statistically significant (p = 0.015) (Table 2).

Table No.2: Comparison of Cumulative score of adverse effects

	Cumulative Score		
	Group A (OHC)	Group B (ED)	p Value
30 minutes	0.25	0.81	< 0.001
48 hours	0.3[illegible]	0.81	0.004
7 days	0.[illegible]	0.74	0.012
14 days	0.[illegible]5	0.54	0.015

DISCUSSION

This is a novel study comparing clinical efficacy of Olopatadine hydrochloride 0.1% and Emedastine difumarate 0.05% and their adverse effects in allergic conjunctivitis

Olopatadine is a newer, dual action agent that exerts anti-histaminic and mast cell stabilizing effect. Several studies have found Olopatadine to be very well tolerated and these results are confirmed by the present study[19,20].

The most frequent and prominent side effect encountered in the group using Olopatadine was dry eye, but since the medication was preserved, it is not possible to say if the effect was directly due the active ingredient or the preservative, as the use of preserved eye drops is associated with a high incidence of dry eye symptoms[21].

Emastidine is a potent antihistamine that results in prompt resolution of symptoms and signs, but has been found to have several side effects, including stinging and foreign body sensation. This makes the drug less preferred by a lot of patients when compared with Olopatadine.

CONCLUSION

Olopatadine was discovered to have better efficacy (not statistically significant) and less adverse effects (statistically significant) than Emedastine.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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