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ORIGINAL ARTICLE

EFFICACY OF OLOPATADINE HYDROCHLORIDE (0.1%) VERSUS KETOTIFEN FUMARATE (0.025%) OPHTHALMIC SOLUTION IN RELIEVING ITCHING IN ALLERGIC CONJUNCTIVITIS IN POPULATION OF PESHAWAR, PAKISTAN

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ABSTRACT

Background: Allergic conjunctivitis is a common hypersensitivity disorder that is prevalent globally. The objective of this trial was to compare the efficacy of Olopatadine versus Ketotifen ophthalmic solution in relieving itching in allergic conjunctivitis in population of Peshawar, Pakistan.

Materials & Methods: This RCT was conducted at Department of Ophthalmology, Khyber Girls Medical College, Peshawar, Pakistan from March 01, 2022 to June 30, 2022. One-eighty-six patients with allergic conjunctivitis with itching score of 2-3 and aged 5-65 years were randomly allocated to two groups; 93 to experimental/Olopatadine and 93 to control/Ketotifen group. Itching was graded as; no itching zero, mild itching 1, moderate itching 2 and severe itching 3. Pre-treatment itching score was measured. Experimental group used Olopatadine Hydrochloride 0.1% b.i.d., while control group used Ketotifen Fumarate 0.025% q.id., both for six-weeks. Post-treatment presence of itching was measured as 0-1 as itching relieved and 2-3 as not relieved. Sex, age groups, pre-treatment itching score and presence of itching were described by count and percentage. Hypothesis was verified using McNemar chi-square test.

Results: Experimental/Olopatadine group included 58 (62.37%) men and 35 (37.63%) women, while control/Ketotifen group included 55 (59.14%) men and 38 (40.86%) women. There were 78 (83.87%) patients in age group 5-35 years and 15 (16.13%) in age group 36-65 years in each group. Pre-treatment itching score was 2 in 40 (43.02%) and 3 in 53 (56.98%) patients in experimental group, and 2 in 42 (45.16%) and 3 in 51 (54.84%) patients in control group. Itching was relieved in 77 (82.80%) in experimental/Olopatadine group, and in 67 (72.04%) patients in control/Ketotifen group. Experimental/Olopatadine showed statistically significantly higher efficacy than control/Ketotifen (p-value .0139).

Conclusion: The efficacy of Olopatadine Hydrochloride 0.1% b.i.d. was higher than Ketotifen Fumerate 0.025% ophthalmic solution q.i.d. in terms of itching relief in allergic conjunctivitis.

KEY WORDS: Olopatadine Hydrochloride; Ketotifen Fumarate; Allergic Conjunctivitis.

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1. INTRODUCTION

1.1 Background: Ocular allergy is a common hypersensitivity disorder that affects 15-20% of the population in developed nations.[1] Epidemiological surveys have shown that up to 35% of US population is suffering from ocular allergies; although the true prevalence may be more.[2] Allergic eye disease represents a spectrum of disorders, comprising of Seasonal and Perennial Allergic Conjunctivitis and Vernal and Atopic Kerato-conjunctivitis. Allergic conjunctivitis is mainly type-I hypersensitivity

reaction with some additional element of type-IV hypersensitivity.[3]

The symptoms consist of watering, redness, chemosis and itching.[4] These are activated by release of active substances by Mast cells, including Histamine, thus increasing the secretion of tears, stimulating blood vessels dilation and irritating nerve endings.[5]

Patho-physiology of ocular allergy is a cascade of events coordinated by mast cells. Mediators that take part in allergic conjunctivitis are Exotoxins, T-cells, Cytokines, Histamine, Prostaglandins, and Platelet-activating factor.[6]

Commonly used treatments for allergic conjunctivitis are topical and oral drugs that decreases symptoms such lacrimation and itching of eye, chemosis of conjunctiva and lid edema. Various classes of drugs either individually or in combination are used to control symptoms of allergic conjunctivitis. These are Mast Cells stabilizers and anti-histamines. Combined preparations of anti-histamine and vasoconstrictor (Antazoline with Xylometazoline), dual action anti-histamine and mast-cells stabilizers (Azelastine, Ketotifen, Olopatadine) and oral anti-histamines such Diphenhydramine and Loratadine are also prescribed in different settings.[7]

1.2 Research Problem, Knowledge Gap & Rationale: We don't know whether the efficacy of Olopatadine is same as Ketotifen ophthalmic solution in relieving itching in allergic conjunctivitis in population of Peshawar, Pakistan. This unawareness is our research problem. No study could be retrieved regarding this problem for our population. It was our knowledge gap. To fill this gap and to solve this problem is rationale of our trial.

1.3 Research Question: Is the efficacy of Olopatadine same as Ketotifen ophthalmic solution in relieving itching in allergic conjunctivitis in population of Peshawar, Pakistan?

1.4 Research Objective: The objective of this trial was to compare the efficacy of Olopatadine versus Ketotifen ophthalmic solution in relieving itching in allergic conjunctivitis in population of Peshawar, Pakistan.

1.5 Research (Null) Hypothesis: The efficacy of Olopatadine is same as Ketotifen ophthalmic solution in relieving itching in allergic conjunctivitis in population of Peshawar, Pakistan.

1.6 Significance: This trial will provide us with local statistics for the efficacy of Olopatadine versus Ketotifen Fumarate in the treatment of allergic conjunctivitis, which will help our clinicians for better treatment of this disease.

2. METERIALS AND METHODS

2.1 Design, setting & duration: This Randomized Controlled Trial was conducted at the Department of Ophthalmology, Khyber Girls Medical College, Peshawar, Pakistan from March 01, 2022 to June 30, 2022. The sample was collected form outdoor of Hayatabad Medical Complex, Peshawar. Written informed consent was taken from all patients/their guardians.

2.2 Sampling & randomization: All patients with allergic conjunctivitis (seasonal/perennial allergic conjunctivitis, seasonal/perennial rhino-conjunctivitis, Vernal Kerato-conjunctivitis, Atopic Kerato-conjunctivitis) with itching score of 2-3 and aged 5-65 years were eligible for inclusion. All patients with dry eyes, bronchial asthma, patients on any ocular medications or systemic anti-histamines, mast cell stabilizers, non-steroidal anti-inflammatory drugs or steroids in past two weeks were excluded from the trial. One-eighty six (186) patients were selected from ophthalmic outdoor and were randomly allocated to two groups by lottery method; 93 to experimental/ Olopatadine group and 93 to control/ Ketotifen group.

2.3 Conduct or procedure & intervention: All patients underwent detailed history and complete ophthalmologic examination by slit lamp. Itching was graded on a subjective scale of 0-3; no itching was scored zero, mild itching 1, moderate itching 2 and severe itching 3.[7] The data for children was collected from their parents/ guardians. Pre-treatment itching score was measured. Then experimental group was subjected to twice daily Olopatadine Hydrochloride (0.1%) eye drops, while control group was subjected to four times daily Ketotifen Fumarate (0.025%) eye drops, both for six weeks. At follow-up visit, post-treatment itching score was measured. For post-treatment analysis, itching score of 0-1 was treated as no itching (itching relieved) and itching score of 2-3 was treated as having itching (itching not relieved).

2.4 Data collection and analysis plan: Sex (male/ female), age groups (5-35 & 36-65 years) and pre-treatment itching score were three matching variables on categorical scales. Presence of itching was a research variable (No/ Yes) on nominal scale. All four were described by count and percentage. Hypothesis was verified using McNemar chi-square test[8-9] through an online calculator.[10]

3. RESULTS

The 93 patients in the experimental/ Olopatadine group included 58 (62.37%) men and 35 (37.63%) women, while 93 patients in control/ Ketotifen group included 55 (59.14%) men and 38 (40.86%) women; almost in similar proportion.

There were 78 (83.87%) patients in the age group 5-35 years and 15 (16.13%) in the age group 36-65 years in both the experimental and control groups.

Pre-treatment itching score was 2 in 40 (43.02%) and 3 in 53 (56.98%) patients in experimental group, while it 2 in 42 (45.16%) and 3 in 51 (54.84%) patients in control group, almost similar.

Table 1: Efficacy of Olopatadine versus Ketotifen ophthalmic solution in relieving itching in allergic conjunctivitis in population of Peshawar, Pakistan

Groups		Experimental/ Olopatadine group (n1=93)		Columns Total	∑X2	d.f.	p-value
		Itching relieved	Itching not relieved				
Ketotifen/ Control group (n2=93)	Itching relieved	63	04	67	4.500	1	.0339
	Itching not relieved	14	12	26			
Rows Total		77	16	93 pairs	H_0 rejected at α .05		

Out of 93 patients in experimental/ Olopatadine group, 77 (82.80%) patients had itching relieved and 16 (17.20%) patients had itching not relieved. Out of 93 patients in control/ Ketotifen group, 67 (72.04%) had itching relieved and 26 (27.96%) had itching not relieved.

Mc-Nemar chi-square test was applied to see the significance of difference of efficacy in terms of itching relief in experimental/ Olopatadine versus control/ Ketotifen group. With p-value of .0139 (less than alpha), the null hypothesis was rejected, showing statistically significantly higher efficacy for experimental/ Olopatadine group. (Table 1)

4. DISCUSSION

4.1 Efficacy of Olopatadine versus Ketotifen: In our population, out of 93 patients in experimental/ Olopatadine group, 77 (82.80%) patients had itching relieved and 16 (17.20%) patients had itching not relieved. Out of 93 patients in control/ Ketotifen group, 67 (72.04%) had itching relieved and 26 (27.96%) had itching not relieved. The efficacy of Olopatadine Hydrochloride (0.1%) twice daily was higher than Ketotifen Fumerate (0.025%) eye drops four times daily in terms of itching relief in allergic conjunctivitis.

Similar findings are reported by Sarker, et al.[11] from Sylhet, Bangladesh, who conducted a randomized, double-blind, single-center trial from January 2007 to December 2007 and concluded that Olopatadine hydrochloride 0.1% (n=40) is more effective than Ketotifen Fumarate 0.025% (n=43) in reducing itching score in allergic conjunctivitis.

Unlike our trial, Patel, et al.[12] from Karnataka, India carried out a randomized trial in 2017, which showed that mean itching score reduced significantly (p=.001) by both the Olopatadine 0.1% b.id. (n1=55) and by Ketotifen 0.025% q.i.d. (n2=54) (p=0.001) application at two weeks.

Contrary to our study, Varguez-Rodríguez from Spain reported in 2007 that both Olopatadine 0.1% 12-hourly (n1=20) and Ketotifen 0.025% 12-hourly (n2=20) achieved significant improvement in itching at two weeks and later on.[13]

Contrary to our results, Mortemousque, et al. also concluded that relief of itching was similar at one-month in preservative-free Ketotifen Fumarate 0.025% group (n1=38) and preserved Olopatadine hydrochloride 0.1% group (n2=37), both used twice a day. They conducted this randomized, investigator-masked clinical study in 2011 in France (6 centres) and Tunisia (4 centres) by including adults with seasonal allergic conjunctivitis.[14]

Opposite to our study, Ganz, et al, from Wisconsin, United States in a 3-weeks study found that Ketotifen fumarate 0.025% ophthalmic solution twice daily was superior to Olopatadine hydrochloride 0.1% ophthalmic solution twice daily in relieving the overall symptoms and signs of seasonal allergic conjunctivitis, including itching.[15]

Many studies including the Conjunctival Allergen Challenge (CAC) model have shown the efficacy of Olopatadine 0.1% in allergic conjunctivitis.[16-18] Aguilar et al.[19] reported that Olopatadine 0.1% showed higher efficacy in rapid resolution of the symptoms and signs of allergic conjunctivitis. Leonardi and Zafirakis[20] showed higher preference of patients for Olopatadine than Ketotifen. Lainer, et al.[21] in CAC studies reported that Olopatadine 0.1% 12-hourly had higher efficiency than Epinastine in the treatment of allergic conjunctivitis.

Abelson, et al.[22] reported similar efficacy for 12-hourly Olopatadine 0.1% and 24-hourly Olopatadine 0.2% in preventing eye itching in allergic conjunctivitis in Conjunctival Allergen Challenge study.

Guest, et al.[23] conducted this modelling study from the perspective of National Health Service, UK. They evaluated the economic impact of Olopatadine (Opatanol) as compared to branded Sodium Cromoglycate (Opticrom) and generic Sodium Cromoglycate in treatment of seasonal allergic conjunctivitis. Olopatadine use had an economic benefit to NHS over the other two drugs due to expected fewer GP visits.

4.2 Marwat's Logical Trajectory of Research Process: We in our project have incorporated this 8-steps logical flow; research problem, knowledge gap, research question, research objective, null hypothesis, data collection, data analysis and data interpretation, to give a clear and categorical organization to our manuscript. It has been devised by Dr. Muhammad Marwat from D.I.Khan, Pakistan (marwatmuhammad@gmail.com).[24-25]

5. CONCLUSION

The efficacy of Olopatadine Hydrochloride 0.1% twice daily was higher than Ketotifen Fumerate 0.025% ophthalmic solution four times daily in terms of itching relief in allergic conjunctivitis in our population.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	UA, MTK
Acquisition, Analysis or Interpretation of Data:	UA, MTK, AI, AU
Manuscript Writing & Approval:	UA, MTK, AI, AU

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.