ORIGINAL ARTICLE

Comparison between Topical 0.025% Ketotifen Fumarate and Topical 4% Cromolyn Sodium for Symptomatic Relief of VKC

MUHAMMAD KHALID[1], ASAD MAHMOOD KHAN[2], NOOR UL HUDA ANSARI[3]

ABSTRACT

Aim: To compare the symptomatic relief of VKC between topical 0.025% ketotifen fumarate and topical 4% cromolyn sodium.
Methods: This comparative study was consisted on 746 patients with VKC symptoms and was conducted at Department of Ophthalmology, DHQ Hospital Sahiwal from January 2015 to June 2015.
Results: Mean age of patients in Group A was 16.85±4.99 years and mean age of in group B was 16.82±4.9 years. Symptomatic relief of VKC was seen in 215(71.67%) patients treated with Ketotifen Fumerate as compare to 162(54%) patients treated with Cromolyn Soduim. Significant (P=0.000) difference for symptomatic relief of VKC was seen between the both groups. More symptomatic relief of VKC was observed in male as compare to female.
Conclusion: This study shows ketotifen feumarate solution is effective in reducing signs and symptoms of VKC and preventing their recurrence. It has showed best efficacy in comparison with cromolyn sodium. So it can be taken first line drug in VKC.
Keywords: Ketotifen fumerate, cromolyn sodium, VKC, topical 0.025%

INTRODUCTION

Ocular allergies are the most common conditions affecting the external ocular adnexa throughout the world[1]. These allergies are type 1 hypersensitivity reactions which are mediated by Ig-E antibody in response to various environmental allergens such as pollens, mites, molds, dust, grass, weeds and animals dander[2,3].

Vernal Keratoconjunctivitis (VKC) is a bilateral, recurrent disorder in which ig-E and cell mediated immune mechanism play key role[2]. It initially affects the body and usually found in first decade of life (mean age 7 years); about 95% cases remit by the late teens and the reminder develops atopic keratoconjuctivits.[2] it usually occurs at the onset of hot weather and subsides during winter[2]. In temperate regions about 1/3 of patients have associated atopy and 2/3 have a family history of atopy[2]. Symptoms are intense itching associated with lacrimation, a foreign body sensation, photophobia, burning and thick muciod discharge[2].

Mast cells play a major role in pathogenesis of vernal keratoconjuctivitis[2]. When a specific allergen bonds to the sensitized mast cell in conjunctiva it causes degranulation of mast cells and inflammatory mediators are released i.e. histamine, prostaglandins, leukotrienes, PAF of all, histamine is responsible for symptoms of vernal keratoconjuctivitis predominantly[3]. Most common agents for symptomatic relief of vernal keratoconjuctivitis are mast cell stabliziers, antihistamine, steroids and ciclosporins[4].

Commonly used topical agents in vernal keratoconjuctivitis include anithistamines, mast cell stabilizers, immunosuppressive drugs and corticosteroids[5]. Newer, more selective therapeutic strategies like leukotriene receptor antagonists, antichemokine receptor antibodies and specific marcobiomolecules are under evaluation[5].

A study was planned to evaluate the symptomatic relief of VKC with the use of ketotifen fumarate 0.025% and cromolyn sodium 4%. Results of this study may guide us, which one drug has better safety and efficacy profile.

MATERIAL AND METHODS

This comparative study was consisted on 746 patients with VKC symptoms and was conducted at Department of Ophthalmology, DHQ Hospital Sahiwal from January 2015 to June 2015.An approval was taken from institutional review committee and written informed consent was taken from every patients.

Patients with symptoms of intense itching, pain, redness, lacrimation, photophobia, foreign body sensation and with signs; conjuctival chemosis, hypertrophy, hyperemia, papillae, mucous deposition on papillae, puntate epithelial erosion on slit lamp examination were considered as a case of vernal keratoconjuctivitis. Symptoms were graded as present or absent according to history and after complete slit lamp examination. The absence or

[1]Assistant Professor Ophthalmology, Sahiwal Medical College Sahiwal
[2]Assistant Professor Pharmacology, PM C, Faisalabad
[3]Assistant Professor Pharmacology, QAMC, Bahawalpur
Correspondence to Dr. Muhammad Khalid,

presence of symptoms was used as a mean of determination.

Patients having age 8 to 25 years either male or female and were not using any topical medicine for VKC were excluded from this study. Patients with glaucoma, diabetic retinopathy, corneal ulcer and ocular hypertension were excluded from the study. All the patients were randomly divided into two groups A and B.

Ketotifen fumarate was advised to the patients of Group A 1 drop BD and cromolyn sodium was advised to the patients of Group B Q.I.D. Weekly, follow-up of the patients was done and final outcome was determined at 28th. Efficacy of the both drugs were noted in pre-designed proforma in term of present or absent of VKC symptoms. The disappearance of the symptoms of the disease was considered as resolution of the disease. Demographic data of all the patients were also noted in the proforma.

All the collected data was entered in SPSS version 18 and analyzed. Mean and SD was calculated for age and frequencies were calculated for categorical data. Chi-square test was used as test of significance to compare the proportion of relief of symptoms between the two groups. P. value ≤ 0.05 was considered as significant.

RESULTS

Total 746 patients with VKC symptoms were selected for this study. Mean age of patients in Group A was 16.85±4.99 years and mean age of in group B was 16.82±4.9 years. Mean hospital stay in group A was 10.65±3.012 and in group B was 9.84±3.356.At the day 28, as shown Table 1 in group A out of 373 patients symptomatic relief of VKC was found in 272(72.92%) and in group B symptomatic relief was found in 207(55.5%) patients. Group A showing significantly higher symptomatic relief as compare to group B.

As shown in table No.2 in group A, out of 373 patients there were 223(59.79%) patients were male and symptomatic relief for VKC symptoms was found in 187(83.86%) patients. Female patients were 150(40.21%), out of which VKC symptomatic relief was found in 85(56.67%) patients. In group B out of 373 patients 198(53.08%) were male and 175(46.92%) were female, symptomatic relief for VKC was found in 142(71.72%) and 65(31.14%) in male and female respectively. In both groups symptomatic relief for VKC symptoms significantly is higher in male patients as compared to female patients.

As shown in table 3, patients were divided into two age groups. In group A 177(47.45%) patients fall in age group 8-16 years and symptomatic relief for VKC was found in 120(67.80%) patients. In age group 17-25 yeas there was 196(52.55%) patients and symptomatic relief for VKC was found in 152(77.55%) patients.

In group B, out of 373 patients there were 185(49.6%) patients in age group 8-16 years and symptomatic relief for VKC symptoms was found in 97(52.43%) patients, 188(50.4%) patients belong to age group 17-25 years and symptomatic relief for VKC was found in 110(58.5%) patients. In both study groups, insignificant (P=0.034, 0.238) association between age and symptomatic relief of VKC symptoms was seen.

Table 1: Comparison of symptomatic relief of VKC symptoms between the both study groups

Groups	Present	Absent	Total
Ketotifen Fumerate (n=373) Group-A	101 (27.08%)	272 (72.92%)	373 (50%)
Cromolyn Sodium (n=373) Group-B	166 (44.5%)	207 (55.5%)	373 (50%)

P value 0.000

Table 2: Relation of gender with symptomatic relief of VKC symptoms

Gender	Present	Absent	Total
Group A (p value 0.000)			
Male	36(16.14%)	187(83.86%)	223(59.79%)
Female	65(43.33%)	85(56.67%)	150(40.21%)
Group B (p value0.000)			
Male	56(28.28%)	142(71.72%)	198(53.08%)
Female	110(62.86%)	65(31.14%)	175(46.92%)

Table 3: Relation of age with symptomatic relief of VKC symptoms

Age(Yrs)	Present	Absent	Total
Group A (p value 0.034)			
8-16	57(32.20%)	120(67.80%)	177(47.45%)
17-25	44(22.45%)	152(77.55%)	196(52.55%)
Group B (p value0.238)			
8-16	88(47.57%)	97(52.43%)	185(49.6%)
17-25	78(41.5%)	110(58.5%)	188(50.4%)

Table 4: Relation of duration of disease with symptomatic relief of VKC symptoms

Duration	Present	Absent	Total
Group A (p value 0.000)			
6-10 days	12(6.67%)	168(93.33%)	180(48.26%)
11-15 days	89(46.11%)	104(53.89%)	193(51.74%)
Group B (p value0.002)			
6-10 days		120(63.16%)	190(50.94%)
11-15 days	96(52.46%)	87(47.54%)	183(49.06%)

As shown table 4, duration of severity of symptoms was divided in to two groups 6-10 days and 11-15 days in both groups. In group A, 180(48.26%) fall in 6-10 days groups and symptomatic relief was found in in 168(93.33%) patients, 193(51.74%) patients was found in group of 11-15 days and symptomatic relief for VKC was

found in 104(53.89%) patients. In group B 190(50.94%) patients were found in 6-10 days group and relief of VKC symptoms were found in 120(63.16%) while group 11-15 days consisted on 183(49.06%) patients and symptomatic relief of VKC were found in 207(55.5%) patients.

DISCUSSION

VKC is a common, prevalent and clinically significant IgE mediated hypersensivity response. VKC is an immunopathological disease in which the number of mast cells in substantiapropria increase. Activation of mast cells by IgE bound receptor cross linking by allergen promotes the release of several mediators such as histamine, prostaglandins and cytokinase, all of which contribute to the symptoms of VKC. The mast cell is considered to play a pivotal role in producing symptoms and signs of VKC[6]. Current therapy of VKC focuses on modulation of the immune system and pharmacologic inhibition of the chemical mediators involved in the immune response. Mast cell stabilizers and antihistamines are two of the most commonly used groups of therapeutic agents. They stabilize the mast cell membranes by preventing calcium influx across the mast cell membranes, thereby preventing mast cell degranulation and mediator release. The new antihistamines have been demonstrated to be capable of affecting several phenemonea of the allergic inflammation[6].

Among these drugs, new multiple action agents like Ketotifen fumarate is histamine H1-receptor antagonist, as well as mast cell stabilizer. In addition, in vitro and animal studies have shown that Ketotifen fumarate inhibits the activation and chemotaxis of eosinophils into the conjunctiva, which is an important step in late phase of immune response[6].

Cromolyn sodium, as a mast cell stabilizer is effective and safe in the treatment of VKC, buttopical steroids which are often required, increase the chance of bacterial keratitis, cataract, and glaucoma, so we decided to perform this study in order to investigate and compare the effect of the topical Ketotifen fumarate with Cromolyn sodium in moderate VKC[7]. The control of VKC symptom with Ketotifen fumarate 72.92% is better as compare to cromolyn sodium 55.5%. A study of Shoja MR[6] conducted in Iran reported symptomatic relief of VKC with Ketotifen fumarate as 61.5% which is comparable with my study. Another study of Australia[7] reported better control of VKC symptoms as 49.5% which is lower than my study. Ganzet et al[8] also documented a higher cure rate of ketotifen fumerate. Abelson MB also reported significant VKC control with Ketotifen fumerate[9]. Clinical trials demonstrated that ketotifen eye drop was efficacious and safe, providing a rapid onset and long duration of action[10].Leonardi's[11] study showed that investigators assessment of response rates for Ketotifen fumerate was superior to Cromolyn which is similar to our study. In term of efficacy, Ketotifen fumerate was numerically superior to Cromolyn for the majority of the individual symptoms score[12]. In contrast to our study at Canada Ketotifen reported to be cause slight discomfort after installation as compare to other anti-allergic drugs but even then its efficacy is not in doubt[13].

CONCLUSION

This study shows ketotifen feumarate solution is effective in reducing signs and symptoms of VKC and preventing their recurrence. It has showed best efficacy in comparison with cromolyn sodium. So it can be taken first line drug in VKC. Symptomatic relief of VKC symptoms with ketotifen fumarate 0.025% is significantly better than the use of cromolyn sodium 4%. Better symptomatic relief of VKC was seen in male as compare to female. So it can be taken as first line drug for the symptomatic relief of VKC symptoms.

REFERENCES

1. Ketelaris CH. Ocular: allergy: implications for the clinical immunologist. Ann Allergy Asthma-Immunol. 2003;90(6 suppl 3):23-7.
2. Kanski JJ. Clinical ophthalmology-a systematic approach. 6th edition Butterworth Heinemann Elsevier; 2007
3. Apple DJ, Rabb MF. Robbins and Cotran pathologic basis of the disease. 7th ed. Elsevier Saunders;2007
4. Ehlers JP, Shah CP. The wills eye manual. 5th ed. Lippincott Williams and Wilkins;2008.
5. Messmer EM. Therapeutic options in vernal keratoconjunctivitis; ophthalmologe 2009 June;106(6);577-61.
6. Shoja MR, Besharaty MR. Comparison of efficacy and safety of topical Ketotifen with Cromolyn sodium in the treatment of Vernalkeratoconjunctivitis. *Journal of Research in Medical Sciences*.2005;10(2):87-92.
7. Kidd M, McKenzie SH. Efficacy and safety of ketotifen eye drops in the treatment of seasonal allergic conjunctivitis. *Br J Ophthalmol*.2003;87(10):1206-11.
8. Ganz M, Koll E, Gausche J, Detjen P, Orfan N. Ketotifenfumarate and olopatadine hydrochloride in the treatment of allergic conjunctivitis: a real-world comparison of efficacy and ocular comfort. *Adv Ther*.2003;20(2):79-91.
9. Abelson MB, Chapin MJ, Kapik BM, Shams NB. Efficacy of ketotifenfumarate 0.025% ophthalmic solution compared with placebo in the conjunctival allergen challenge model. Arch Opthalmol2003;121(5):626–30.
10. Gomes PJ, Welch DL, Abelson MB. Evaluation of the efficacy and safety of Ketotifen in the allergen challenge model.Eur J Ophthalmol 2003 Mar; 13(2):128-33.
11. Leonardi A, Busca F, Tavolato M, Secchi AG. The anti-allergic effects of a chlorphiniramine sodium-chlorp combination compared to ketotifen in the conjuctivachallege model. Eur J Ophthalmol 2003 Mar;13(2):128-33.
12. Greiner JV, Minno G. A placebo-controlled comparison of ketotifenfumarate and nedocromil sodium ophthalmic solutions for the prevention of ocular itching with the conjunctival allergen challenge model. ClinTher 2003Jul;25(7):1988-2005.
13. Artal MN, Luna JD, Discepola M. A Forced Choice Comfort Study of Olopatadine Hydrochloride 0.1% versus Ketotifen Fumarate 0.05%. *Acta Ophthalmol. Scand*.2000;78:64-65.