Original Article

Comparison of Fluorometholone 0.1% and Cyclosporine 0.05% in the Treatment of Vernal Keratoconjunctivitis

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ABSTRACT

Purpose: To compare the effectiveness of Fluorometholone 0.1% and Cyclosporine 0.05% in the treatment of vernal keratoconjunctivitis.

Study Design: Quasi experimental study.

Place and Duration of Study: Hayatabad Medical Complex, Peshawar from December 2020 to June 2021.

Methods: This study includes 104 patients divided into 2 groups. Patients in Group A were given topical Fluorometholone 0.1% while group B were given topical Cyclosporine 0.05%. Signs and symptoms were graded from scale 0-10 at the start of treatment and then at day 7,14 and 30. Drug was considered effective if the final score was equal to or less than 3 at day 30.

Results: Mean age of the patients was 9.96±2.722 years in group A and 10.02±2.790years in group B. Mean baseline score was 6.90±0.721 in group A and 5.87±0.768 in group B. In group A, 45 (86.5%) patients showed effectiveness while in group B, 36 (69.2%) patients showed effective results. Fluorometholone gave superior results as compared to Cyclosporine in patients with severe disease i.e., baseline score ≥ 6.Systemic allergic associations were noted in44.2% patients in group A and 36.5% patients in group B.

Conclusion: These findings suggest that Fluorometholone may be a preferable treatment option for vernal keratoconjunctivitis, particularly in cases of more severe disease. However, considerations regarding systemic allergic associations should also be taken into account when making treatment decisions.

Key Words: Fluorometholone, Cyclosporine, Vernal Keratoconjunctivitis.

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INTRODUCTION

Vernal keratoconjunctivitis(VKC) is a common allergic eye disease mainly affecting children and adolescents with seasonal recurrence.[1,2] VKC usually occurs before 10 years of age, lasts for 2-10 years and most of the times resolves by puberty. It is twice as common in males as compared to females.[3] Its prevalence is about 6-30% in general population and 30% in children alone or in association with allergic rhinitis.[4] Seasonal or episodic allergy patients are affected for only a few weeks or days, while those with perennial allergy have symptoms persisting throughout the year or their entire lifetime.[5] Vernal keratoconjunctivitis differs from seasonal and perennial allergic conjunctivitis as it is mediated by Th2 lymphocytes.[6] The main pathological mechanism is immunoglobulin E mediated; however, certain nonspecific hypersensitivity mechanisms may also be involved.[7] Chronic surface inflammation leads to more severe form of disease and is associated with eosinophilia and neutrophilia.[8] There are three forms of VKC: limbal, palpebral or tarsal and mixed. Major symptoms of VKC include watering, itching,

grittiness, photophobia, burning and foreign body sensation.[9,10]

Rarely, untreated VKC can lead to permanent visual loss.[11] Various treatment modalities are available for VKC like antihistamines, mast-cell stabilizers, corticosteroids and immune modulators. Topical corticosteroids provide quick relief but there is a potential of side effects with long term use such as secondary glaucoma, cataract and infections of ocular surface.[12,13] For the past two decades, immune modulators have emerged as a substitute for corticosteroids in allergic crisis control and maintenance of asymptomatic VKC patients because of fewer side effects and potent anti-inflammatory action.[14]

In the present scenario, search for an effective topical medication is still on for the management of VKC. This study is intended to evaluate the efficacy of topical Fluorometholone 0.1% in comparison to topical Cyclosporine 0.05% in treatment of patients of VKC. The data and results will help to improve patient care and better service delivery.

METHODS

A total of 104 treatment naïve patients with vernal keratoconjunctivitis were included in the study, using non probability consecutive sampling design. Sample size was calculated using Openepi, efficacy of topical Fluorometholone = 93.33%[15], efficacy of topical Cyclosporine = 66.67%[9], power of test = 90% and confidence intervalat 5%.Patients with history of contact lens, ocular trauma, glaucoma, uveitis or use of oral steroids were excluded. The participants were divided into 2 groups, first patient was randomly allocated to a group by lottery method and subsequent patients were alternatively assigned to groups by systematic sampling. Patients in group A were given topical Fluorometholone 0.1%, one drop in both eyes every two hours followed by prompt tapering while group B was given topical Cyclosporine 0.05%, one drop in both eyes four times a day. Data including name, age, gender, address and other allergic disorders were recorded in a predesigned proforma. Signs and symptoms were graded according to table 1 from scale 0-10 at the start of treatment and then at day 7,14 and 30. Drug was considered effective if the final score was equal to or less than 3 at day 30.

Data analysis was done using SPSS version 20. Frequency and percentages were calculated for categorical variables like gender, effectiveness of drug and other allergic associations like asthma, rhinitis or atopic dermatitis. Chi-square test was applied to compare the results between the two groups. Effect modifiers/confounders like age, gender and baseline score were controlled through stratification. Post stratification chi-square test was applied keeping $P \leq 0.05$ as significant.

RESULTS

In Group A, the mean age was 9.96 ± 2.72 years, and the mean baseline score was 6.90 ± 0.72. In Group B, the mean age was 10.02 ± 2.79 years, and the mean baseline score was 5.87 ± 0.77. In Group A, 29 patients (55.8%) were in the 5-10 years age group, while 23 patients (44.2%) were in the 11-15 years age group. In Group B, 33 patients (63.5%) were in the 5-10 year age group, while 19 patients (36.5%) were in the 11-15 years age group. Furthermore, in Group A, 35 patients (67.3%) were male, and 17 patients (32.7%) were female, whereas in Group B, 37 patients (71.2%) were male, and 15 patients (28.8%) were female. Systemic allergic associations were noted in 23 patients (44.2%) in Group A and 19 patients (36.5%) in Group B (Table 2).

Regarding efficacy, in Group A, 45 patients (86.5%) exhibited effective results, while in Group B, 36 patients (69.2%) showed effectiveness (Table 3). The efficacies in both groups were further analyzed based on age and baseline score, as delineated in Table 4.

Table 1: *Grading of signs and symptoms.*

Abbreviation	Symptoms/signs	0	1	2
I	Itching	Absent	Minimal	Obvious
R	Redness	Absent	Minimal	Obvious
D	Discharge	Absent	Minimal	Obvious
C	Conjunctival sign	Absent	Small papillae /Limbal thickening	Giant papillae/limbal thickening with horner-trantas dots
Co	Corneal sign	Absent	Punctate staining	Shield ulcer

Table2: *Frequencies and percentages for allergic associations.*

	Group A (Topical Fluorometholone 0.1%)		Group B (Topical Cyclosporine 0.05%)	
Allergic Associations	**Frequency**	**Percent**	**Frequency**	**Percent**
Asthma	3	5.8%	2	3.8%
Rhinitis	12	23.1%	11	21.1%
Atopic Dermatitis	8	15.4%	6	11.5%
Total	23	44.2%	19	36.5%

Table 3: *Frequencies and percentages of efficacy.*

Treatment Groups	Efficacy	Frequency	Percent	P Value
Group A	Yes	45	86.5%	0.0334
	No	7	13.5%	
	Total	52	100.0%	
Group B	Yes	36	69.2%	
	No	16	30.8%	
	Total	52	100.0%	

Table4: *Stratification of efficacy with age groups and baseline score.*

Stratification variable			Efficacy		Total	P Value
			Yes	**No**		
Age Groups 5-10 Years	Treatment Groups	Group A	25 86.2%	4 13.8%	29 100%	0.066
		Group B	22 66.7%	11 33.3%	33 100%	
	Total		47 75.8%	15 24.2%	62 100%	
11-15 Years	Treatment Groups	Group A	20 87%	3 13%	23 100%	0.265
		Group B	14 73.7%	5 26.3%	19 100%	
	Total		34 81%	8 19%	42 100%	
Baseline Score ≤5 Score	Treatment Groups	Group A	26 89.6%	3 10.4%	29 50.6%	0.054
		Group B	26 81.2%	6 18.8%	32 49.4%	
	Total		52 85.2%	9 14.8%	61 100.0%	
≥6 Score	Treatment Groups	Group A	20 87%	3 13%	23 47.8%	0.292
		Group B	9 45%	11 55%	20 52.2%	
	Total		29 67.4%	14 32.6%	43 100.0%	

DISCUSSION

VKC is a complicated disease that affects people of all ages and has the potential for lifelong visual loss and a considerable decline in quality of life. However, there is currently no consensus on single treatment option, particularly in severe and refractory cases.[16] In our study, the results of Fluorometholone and Cyclosporine were comparable in patients with mild disease (baseline score ≤5). However in patients with severe VKC (baseline score ≥ 6), Fluorometholone was more effective (87%) than Cyclosporine (45%). Various studies have been carried out to compare steroids and immunomodulators in the treatment of VKC. Gupta et al conducted a study to compare the efficacy of topical cyclosporine and topical fluorometholone and found that there was a

progressive decrease in symptoms and sign scores from day 7 till day 30 in both groups.[12] The relief in symptoms and signs was more in fluorometholone group as compared to cyclosporine group when all the patients were included and analyzed (p=0.001). However when only patients with mild disease(total cumulative score 0-8) were analyzed, the improvement was similar in both groups (p=0.486). In fluorometholone group, there was a significant increase in intraocular pressure(positive linear trend of 14.23,p<0.0001) while no such significant increase in intraocular pressure was observed in cyclosporine group (statistically insignificant positive linear trend of 1.40, p=0.17).[12]

Ozcan et al, found that topical cyclosporine is an effective treatment option in the management of severe allergic conjunctivitis with a benefit as a steroid-sparing agent.[17]A concentration of 0.5% provides an optimum balance between efficacy and tolerance. One percent cyclosporin can be used in severe cases; however, concentrations up to 2% have been described in the literature.[18,19] In another study, the reduction in median values of signs and symptoms after the use of topical cyclosporine was found to be statistically significant. Moreover the need for topical steroids was also reduced.[20]

Similarly, the results of our study have also been supported by Baisakhiya S and Chaudhry M who compared fluorometholone (0.1%), cyclosporine A (0.05%) and olopatadine (0.1%) topical drops as a monotherapy for VKC.[15] They found that symptomatic relief attained at the end of first week was comparable in the three groups i.e. 86.67%(fluorometholone), 80% (olopatadine) and 80% (cyclosporine A) (p>0.01). However at the end of the second month, recurrence in olopatadine group was 33.3% and in cyclosporine A group was 20% while no recurrent case was seen in Fluorometholone group. So it was concluded that Fluorometholone is a superior drug for monotherapy in VKC.[15]

CONCLUSION

In the treatment of vernal keratoconjunctivitis, topical Fluorometholone gave superior results as compared to topical Cyclosporine in terms of efficacy. Further studies are needed to find a steroid sparing agent in the treatment of vernal keratoconjunctivitis in order to reduce the side effects of topical steroids.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board **(**322/HEC/B&PSC/2020**)**.

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Authors Designation and Contribution

Ahmed Usman Khalid; Registrar: *Concepts, Design, Data acquisition, Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing.*

Umaira Liaqat; Registrar: *Literature search, Data acquisition, Manuscript preparation, Manuscript review.*