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Research Article

A comparative study of fluorometholone (0.1%), cyclosporine-A (0.05%), Olopatadine (0.1%) topical drops as a monotherapy for vernal keratoconjunctivitis.

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Keywords

Vernal keratoconjunctivits, Olopatadine, Fluorometholone, Cyclosporine-A

Abstract

Aims and objectives: The aim of our study was to compared the efficacy and safety of Fluorometholone, Cyclosporine – A, Olopatadine topical drops as a monotherapy for vernal keratoconjuntvitis. **Material and methods:** The study included total of 45 diagnosed patients of VKCall less than 15 years of age. Patients were randomly divided in three groups A (Fluorometholone), B (Olopatadine) and C (Cyclosporine-A) with 15 patients in each group. Grading of signs and symptoms was done based on the scoring system. Follow up of the patients was done weekly for four weeks and subsequently monthly up to third month**. Result:** Symptomatic relief attained at the end of first week was comparable in the three groups i.e. 86.67% (Group A), 80% (Group B) and 80% (Group C). At the end of third month recurrence was seen in 46.67% in Group B and 20% in group C and no recurrent case in Group A. **Conclusion:** Viewing our observation in the light of currently available literature we conclude that Fluorometholone is a superior drug for monotherapy in VKC. Cyclosporine due to cost factor and can be reserved for special cases like steroid responders and patients with prominent conjunctiival signs like giant papillae. Olopatadine as a monotherapy is consistently ineffective. Although there is a need of further studies introspecting the safety and consistency of a sequential or combined therapy of fluorometholone and cyclosporine considering the limitations of both the drugs.

Introduction

Vernal keratoconjunctivitis (VKC) is a chronic, recurrent bilateral seasonal allergic condition that affects children between age groups of 5 to15 years mainly in temperate areas.(1, 2) The disease may involve the cornea and can be sight threatening. Pollen grains, fungus, pet saliva, dust, smoke and environmental pollutants are main causes of allergy. The symptoms of ocular allergy are outcome of binding of allergen with IgE on mast cell. This binding in turn leads to mast cell degranulation and release of mediators of allergy (histamine, IL3, IL4, IL5and IFN-g). Mast cells appear to play a pivotal role in the disease pathogenesis. The mast cells increase in cases of VKC and also elevated IgE levels are noted in tears of patients with allergic conjunctivitis. (3, 4) Immunologically it is both Type-I and Type-IV hypersensitivity reaction .(5)Various treatment modalities are available for the disease. Steroids, antihistaminic, mast cell stabilizers immunomodulators are the various groups of drugs tried over the times. (6) But still in the current scenario the search for ideal topical medication to treat VKC is still on. Studies are available in literature comparing immunomodulators with steroids, antihistaminic with mast cell stabilizerand so on. But studies comparing the three major groups of drugs simultaneously are not available in literature. In our study we have compared the three drugs olopatadine, fluorometholone and cyclosporine-A All the three drugs belong to different classes. Olopatadine is both a mast cell stabilizer as well as selective H1 antagonist while Cyclosporine a specific T cell inhibitor and Fluorometholone a low potency steroid.

Aims and objectives:

Our aim was to compare the three drugs Fluorometholone, Cyclosporine-A, Olopatadine topical drops as a monotherapy for vernal keratoconjunctivitis based on relief of clinical features. We also compared long term control of the disease and recurrence rate during the course of the treatment.

Materials and Methods:

We took a group of 45 patients all less than 15 years of age and all were diagnosed case of vernal keratoconjunctivitis .Patients were randomly divided into three groups with 15 patients in each group .After a wash out period of one week group A was started on Fluorometholone drops, group B on Olopatadine drops and group C on Cyclosporine-A.

Grading of signs and symptoms was done based on the scoring system. The scoring used in the study was a three point scale. We included the three major symptoms of itching (I), redness (R) and watering /ropy discharge (D) in the study. The absence of any of these symptom was graded as 0,minimal symptom was graded as 1 and obvious was graded as 2.The signs included were conjunctival (C) and corneal signs.(Co)Absence was graded as 0,small papillae with limbal thickening and punctuate corneal staining was graded as 1 while presence of giant papillae horners strantas dots and shield ulcer was graded as 2.(Table 1). Follow up of the patients was done weekly for four weeks and subsequently monthly up to third month. On each follow up visit signs and symptoms were assessed according to the scoring system. Complete slitlamp examination, fluoresein staining of cornea and intraocular pressure record was done on each visit.

Table 1: Scoring system

Abbreviation	Sign/symptom	0	1	2
I	Itching	absent	minimal	obvious
R	Rednss	absent	minimal	obvious
D	Discharge/watering	absent	minimal	obvious
C	Conjunctival sign	absent	Small papillae/limbal thickening	Giant pappilae/limbal thickening with HT dots
Co	Corneal sign	absent	Punctate staining	Shield ulcer

Observation:

The pretreatment scores of the three groups were comparable. (Table 2) The scores of group A (Fluorometholone) on each follow up visit when compared to the baseline scores showed a decline on every follow up. The graph shows a steady decline due to improvement of each symptom score on every visit. (Table 3, Figure 1) The scores of group B (Olopatadine) showed initial decline for one week representing improvement in symptoms .That phase was followed by a plateau phase representing that the symptoms were static. On final visits at end of second and third month there occurred recurrence of symptoms. The graph showed an initial decline up to one week followed by a plateu phase ie the curve remained flat and in last phase due to recurrence of the disease the graph rose back to the pretreatment level. (Table 4, Figure 2)The scores of group C (Cyclosporine A) showed an initial decline similar to the other two groups representing initial improvement in disease followed by static symptom scores .Finally there was a rise in symptom score due to disease recurrence but not to the pretreatment level unlike group B .The pattern of graph shows an improvement for few weeks initially followed by rise at final follow up but not to baseline level. (Table 5, Figure 3). Symptomatic relief attained at the end of first week was comparable in the three groups i.e. 86.67% (Group A), 80% (Group B) and 80% (Group C).($p>0.01$) At the end of second month, recurrence in group B was 33.3%, and in Group C was 20% while no recurrent case was seen in Group A. At the end of third month recurrence was seen in 46.67% in Group B and 20% in group C. The difference was statistically significant. ($p<0.001$) (Table 6)

Table 2: Baseline scores in the three groups

Sign/symptom	A	B	C
I	22	20	25
R	24	26	20
D	12	08	14
C	24	25	23
Co	0	2	1

Table 3: Post treatment scores group A at every follow up visit

Sign/symptom	baseline	1 week	2week	3 week	4 week	2 month	3 month
I	22	10	10	8	6	4	4
R	24	8	6	7	4	4	2
D	12	7	6	5	5	1	1
C	24	22	22	20	16	10	10
Co	0	0	0	0	0	0	0

Graph 1: Graph showing response of treatment in group A

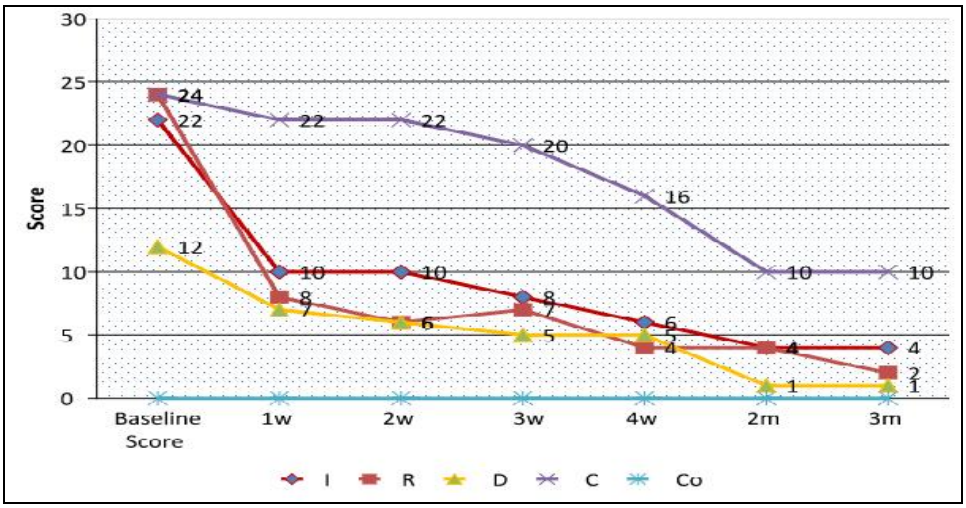

Table 4: Post treatment scores in group B at every follow up visit

Sign/symptom	baseline	1 week	2 week	3 week	4 week	2 month	3 month
I	20	10	10	9	7	18	20
R	26	16	17	16	15	20	23
D	8	8	7	6	8	7	7
C	26	22	24	23	20	25	26
Co	2	2	2	2	1	1	2

Graph 2: Graph showing response of treatment in group B

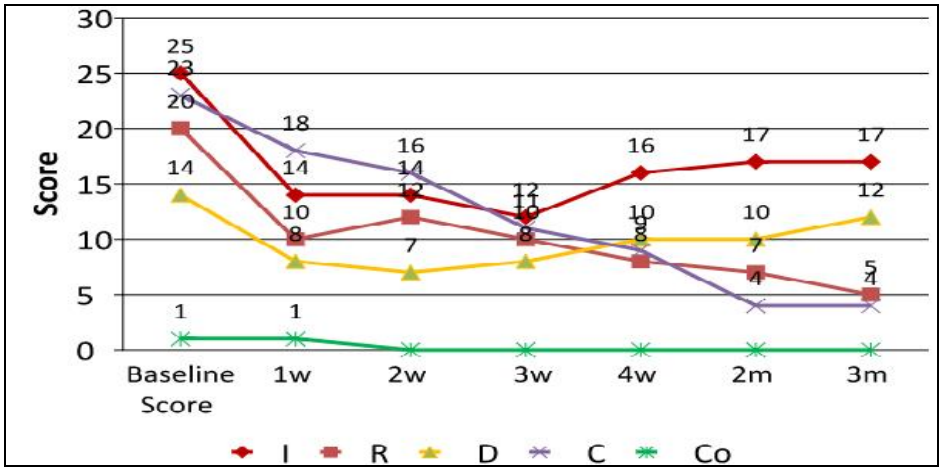

Table 5: Post treatment scores in group Cat every follow up visit

Sign/symptom	baseline	1 week	2 week	3 week	4 week	2 month	3 month
I	25	14	14	12	16	17	17
R	20	10	12	10	8	7	5
D	14	8	7	8	10	10	12
C	23	18	16	11	9	4	4
Co	1	1	0	0	0	0	0

Graph 3: Graph showing response of treatment in group C

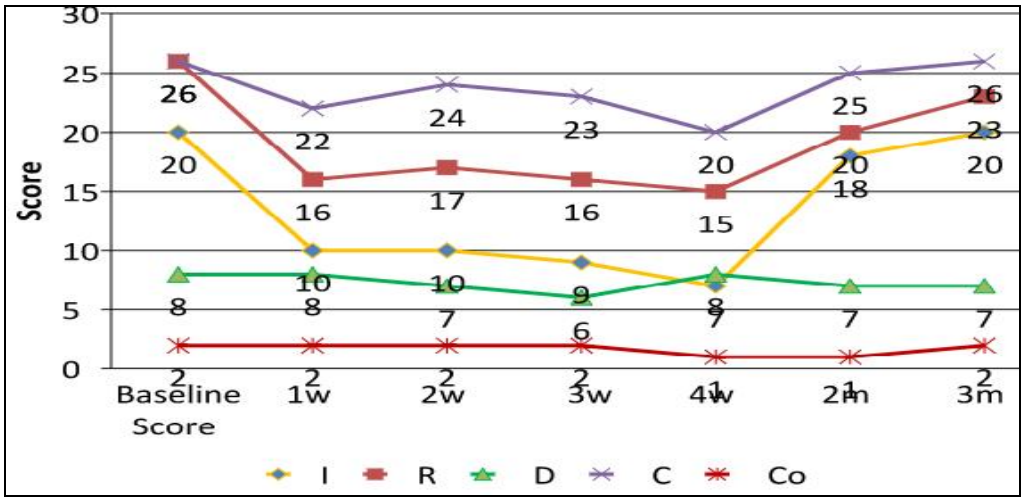

Table 6: Result calculated in percentage

Response	1 week	2 week	3 week	4 week	2 month	3 month
Group A improvement	86.67	86.67	80	93.33	93.33	80
Static	13.33	13.33	20	6.67	6.67	20
Recurrence	0	0	0	0	0	0
Group B Improvement	80	66.67	53.33	33.33	26.67	20
Static	20	33.33	46.67	46.67	40	33.33
Recurrence	0	0	0	20	33.33	46.67
Group C Improvement	80	86.67	80	66.67	53.33	46.67
static	20	13.33	20	20	26.67	20
Recurrence	0	0	0	13.33	20	33.33

Discussion:

Vernal keratoconjunctivitis is a seasonal allergic conjunctivitis which affects children in the age group of 5 to 15 years.). Boys are affected 2–4 times more frequently than girls. The notable difference between sexes and the resolution of the disease with puberty are features that have persistently suggested that hormonal factors play a part in the development of VKC (7).The disease is characterized by itching, redness, watering, foreign body sensation, photophobia, and thick mucoid stringy discharge. Morphologically the disease can present in three different forms bulbar, palpebral and mixed. The decreased vision occurs as a result of corneal complications in form of vascularization and scarring. The pathogenesis of ocular allergy is complex and multifactorial. Few studies have explored the genetic associations of allergic conjunctivitis and a clear familial predisposition to develop the disease has been demonstrated. (8)

In Our study the baseline demographic data like mean age, sex, type of the disease and seasonal variations were comparable in the three groups. There were 30 boys and 15 girls in the study each group had 10 boys and 5 girls. We have compared the efficacy and safety of fluorometholone (Group A), olopatadine (Group B), and cyclosporine-A (Group C). We found that at the initiation of therapy the symptomatic relief was seen in all the groups. Symptomatic relief attained at the end of first week was comparable in the three groups i.e. 86.67% (Group A), 80% (Group B) and 80% (Group C). ($p>0.01$).While on further follow up in group A (fluorometholone)sign and symptoms improved which is evident from the scores(table 2) and on final follow up at 3 months there was no case of recurrence or worsening of symptom. We noted IOP on every visit in all the three groups treated and found no significant elevation of IOP. In group B (olopatadine) sign and symptoms showed an initial improvement for 1-2 weeks and thereafter on further follow up the symptoms worsened and recurrence rate was 33.3% and 46.67% respectively at second and third month evident by the increase in the scores to almost baseline levels (table 3) In group C (Cyclosporine) the initial response to therapy was very effective in ameliorating the sign and the symptoms of the disease while later on follow up there was a recurrence of 20% cases at second and third .Cyclosporine was found to be significantly more effective in relieving symptom of tarsal papillae. There were no serious side effects of the three drugs except mild burning and stinging after initial application.

Gupta et al their study on comparison of Cyclosporine with fluorometholone found a rapid onset of relief of symptoms in subjects on cyclosporine. They also found that flourometholone did better on all the points as compared to cyclosporine in all the cases at one month and three month. Before that there was no difference between the response of the drugs in the two groups. They concluded that both drugs are safe as a therapy for disease. The limitation of fluorometholone being a rise in IOP. (9) Khalid FTabbara et al noted in their comparative study of fluorometholone versus nedocromil and concluded that fluorometholone is more effective in ameliorating signs and symptoms of the severe cases.(10) Altan A et al observed that Cyclosporine 0.05%is more effective and safe in the treatment of patients with VKC if patient is steroid resistant(11). Akpek et al showed that cyclosporine 0.05% has been found to be useful in the treatment of VKC and also an effective steroid sparing agent (12). However Daniell et al in their randomized double blind placebo controlled trial failed to show beneficial effect of 0.05% cyclosporine over steroid unlike observed by AltanA et al in their study (13). In a study done on efficacy of Olopatadine eyedrops in allergic conjunctivitis in Japanese population it was found to be a safe and effective drug for treatment of VKC. (14)A study done on South Indian population using combination therapy of dual acting agent ,NSAIDS and mild to moderate potency steroids concluded that dual acting agents (like Olopatadine) are effective in mild cases of VKC. Patients treated only with Olopatadine showed persistence of symptoms which were relieved on addition of steroids. While in moderate to severe cases steroid of varying potencies have to be used although with caution keeping in mind the potential side effects. (15)

Conclusion:

Viewing our observation in the light of currently available literature we conclude that Fluorometholone is a superior drug for monotherapy in VKC. Although careful monitoring of IOP should be done while patient is on therapy.. Cyclosporine due to cost factor and can be reserved forspecial cases like steroid responders and patients with prominent conjunctiival signs like giant papillae. Olopatadine as a monotherapy is consistently ineffective. Although there is a need of further studies introspecting the safety and consistency of a sequential or combined therapy of fluorometholone and cyclosporine considering the limitations of both the drugs.

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