Use of tacrolimus ointment (0.03%) for refractory VKC

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Abstract

We report a series of 8 children with severe vernal keratoconjunctivitis who presented to us over last two years. The mean age was 7.375 years. The mean vision was 0.375 OD and 0.3625 OS.

All these children were using topical steroids of varying strengths for more than two year. 2 out of 8 children had secondary glaucoma. The mean intraocular pressure was 21.75 $\pm$ 4.74 OD and 23.25 $\pm$ 6.25 mm of Hg OS. The highest IOP recorded was 28 mm Hg. All patients with glaucoma had early optic disc changes.

Topical steroids were stopped for all patients and they were started on topical tacrolimus eye ointment (0.03%) twice a day along with lubricants. Patients relative were counseled to avoid eye rubbing, ignore minimal redness of eyes and counseled against any form of steroids. All patients continued tacrolimus for 3 months. Tacrolimus ointment was stopped at 3 month and lubricants were continued. Follow up was done at 1st week, 3rd week, 6th week, 3rd month and monthly thereafter till 6 months.

At 6 months follow up all except one patient was discontinued of antiglaucoma medication.

Keywords: VKC, Tacrolimus.

Introduction

Allergic eye disease is a common problem seen by eye doctors worldwide. These may range from mild seasonal allergic symptoms to perennial resistant eye disease. Vernal keratoconjunctivitis is a chronic bilateral allergic eye disease which involves limbus and cornea occasionally. It is more common in children and young adults.[1]

Pathophysiology of VKC is complex and involves IgE-mediated disease (type I hypersensitivity) along with Th2 lymphocytes.[1] Medical management of VKC includes anti-histamines, mast-cell stabilizers, and non-steroidal anti-inflammatory drugs, topical steroids and immunomodulators such as cyclosporine and tacrolimus.[2] In recent times use of tacrolimus for refractory allergic eye disease has increased worldwide. Topical tacrolimus with concentrations of 0.02–0.1% in ointment form has successfully been used for treatment of atopic keratoconjunctivitis (AKC),[3-5] giant papillary conjunctivitis,[6] and VKC.[7,8] Topical preparations of tacrolimus include suspensions and ointment (0.03% and 0.1%)

In our study we retrospectively evaluated the documents of patients with VKC receiving tacrolimus since 2015 January. The clinical history, symptoms, signs and medicines were documented, tabulated and analyzed to study the effect of tacrolimus.

Materials and Methods

We recorded data of all children presenting to our centre with symptoms of Vernal Keratoconjunctivitis (VKC) over the last two years. All children were subjected to detailed history, ocular and systemic examination. Ocular examination included vision recording with slit lamp examination. Intraocular pressures were checked with Applanation tonometer (if Possible) or Perkins tonometer under sedation. Disc evaluation was done and documented. All steroid eye drops/ointments were stopped and topical tacrolimus eye ointment (0.03%) was started to be applied over the upper eye lids twice daily along with topical carboxy methyl cellulose (1%) lubricant four times a day. Patient's relatives were counseled to avoid eye rubbing, to ignore minimal redness of eyes and counseled against any form of steroids. All patients of tacrolimus follow up at 2 week interval as a standard protocol of the eye department till they receive tacrolimus. Efficacy of the treatment was analysed by evaluating the changes in patients' symptoms and signs, and need for additional medications. Signs noted were conjunctival hyperaemia, papillary hypertrophy, limbal hypertrophy and corneal involvement as per records.

Results

The mean age was 7.375 years. The mean vision was 0.375 OD and 0.3625 OS. All these children were using topical steroids of varying strengths for more than two year. 2 out of 8 children had secondary glaucoma. The mean intraocular pressure was 21.75 $\pm$ 4.74 OD and 23.25 $\pm$ 6.25 mm of Hg OS. The highest IOP recorded was 28 mm Hg. All patients with glaucoma had early optic disc changes.

Table 1:

S. No	Age	OD Vision	OS Vision	IOP OD	IOP OS
1	6	0.3	0.3	18	18
2	7	0.3	0.3	20	19
3	8	0.3	0.3	20	18
4	6	0.5	0.5	17	17
5	9	0.5	0.5	18	19
6	9	0.5	0.5	26	26
7	7	0.3	0.25	24	28
8	7	0.3	0.25	14	14
Mean	7.375	0.375	0.3625	19.625	19.875
Std Dev	1.1877	0.1035	0.1157	3.8522	4.7037

Discussion

VKC is a chronic disease and frequently requires topical steroids over varying length of time. Side effects of long term topical steroids include cataract and glaucoma. The problem is compounded due to younger age group of VKC patients, difficulty in assessment of IOP in young children and injudicious use of over the counter available high potent steroids.[9,10] Topical tacrolimus ointment (0.03%) is well established drug being used since last few years for non-responsive ocular allergic diseases. Well documented case series has shown usefulness of tacrolimus in post adenoviral subepithelial infiltrates,[11] atopic eye disease,[4,5] superior limbic conjunctivitis[12] and refractory VKC.[13,14]

In our study, 8 patients being treated with tacrolimus (0.03%) were included. 6 out of 8 patients received tacrolimus for 3 months. 2 patients received tacrolimus for 7 months. Conjunctival application of the drug was avoided in view irritation and burning reported in literature due to drug. All the patients complained of redness and itching due to VKC in the initial 2 weeks, however the symptoms subsided after one month. All the patients remained symptom free at 3 months. At 3 rd month tacrolimus was stopped and all patients were started olopatadine eye drops twice daily. 2 patients reported recurrence of symptoms after stopping of tacrolimus and were restarted on tacrolimus at next follow up (15 days after stopping Tacrolimus). Range of follow up is 4 to 8 months (mean 5.75 months).

Barot R[15] et al studied the role of tacrolimus 0.1% ointment in their prospective case series of 36 patients with allergic ocular disease. Tacrolimus was found to be effective and almost 90% of patients were weaned off steroids. Transient burning sensation was reported in 36% of patients due to conjunctival application of the ointment. In our study this side effect was not observed as tacrolimus was applied over the lids.

Fukushima A[16] et al in their prospective study of 1436 patients of refractory allergic conjunctivitis examined the role of 0.1% tacrolimus eyedrop suspension and found favorable response. 50% patients were weaned off steroids. Giant papillae and corneal lesions were also reduced by tacrolimus eye drop use.

In our study 2 patients were receiving timolol for control of IOP which was an indication of starting tacrolimus. Both patients did not require timolol eyedrop after 3 month use of tacrolimus. They did not have recurrence of allergic symptoms till 6 month follow up.

In our study all patients were given tacrolimus for 3 months and then put on olopatadine eyedrops. 2 patients reported recurrence and tacrolimus was restarted for additional 3 months. Maximum period of tacrolimus application was 6 months. Maximum period of use of topical tacrolimus has been up to 42 months in patients with AKC.[3,5] Due to its local immunosuppressive effects, topical tacrolimus may potentially be associated with activation of herpes simplex dendritic keratitis[17] and development of molluscum contagiosum.[5] Further studies are required to evaluate the long-term safety of this medication. In our study, all patients had perennial disease and after starting treatment with tacrolimus they did not use additional medications such as anti-histamines or mast cell stabilizers. Total length of tacrolimus treatment required may be titrated as per severity of disease, potential side effects and clinical profile of the patients. It may be possible to discontinue or taper tacrolimus in patients with less severe disease, with or without addition of less potent agents during the time of year when ocular allergy is quiescent.

The main limitation of our study is the small sample size, lack of control group and retrospective data. However, since all patients had already received conventional treatment along with topical steroids signifies the response obtained due to tacrolimus. Future studies are needed to study the long term efficacy of tacrolimus, and compare the results of commercially available two strengths of topical tacrolimus ointment (0.03% and 0.1%).

In our study, we found good results with Tacrolimus and no side effects of tacrolimus were reported.

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