Original Research Article

Efficacy of 0.03% tacrolimus eye ointment in refractive vernal kerato-conjuctivitis with corneal involvement

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Abstract

Aim: To study clinical efficacy of 0.03% tacrolimus eye ointment in refractive vernal keratoconjunctivitis (VKC) will) cornel involvement and proliferate lesion. **Methods:** Prospective observational study of 106 pts aged 7- 18yr (I2±5yrs). After taking history, total 8 clinical clinical signs and 5 symptoms were noted and graded. Patients were started with 0.03% tacrolimus eye ointment twice daily and followed up for 6 months. **Results:** Statistically significant improvement was seen in patients with conical involvement and giant papillary lesions ($p<0.001$).48 patients (4:3%) showed improvement after 1 month. After 6 months, 100 patients (95%) showed improvement in signs and symptoms. Only side effect observed was burning sensation (3 patients) that was relieved with lubricating drops. **Conclusion:** 0.03% Tacrolimus eye ointment was safe and effective in VKC cases resistant to anti-allergic/steroid/cyclosporine eye drop especially with proliferative lesions and corneal involvement.
Keywords : Tecrolimus, vernal keratoconjunctivitis, refractive.

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INTRODUCTION

Vernal keratoconjunctivitis (VKC) is a bilateral recurrent chronic allergic inflammatory disorder of ocular surface which is seasonally exacerbated mosily involving torsal and bulbar conjunctiva and in chronic and severe cases also shows cornoal involvement', mostly affecting children and young adults with male predominance. Previously its oliology was considered as classical igE mediated type 1 hypersensitivity reaction but now complex etiology involving T-lymphocytes are also involved[2]. The predominant eye symptoms are itching, ropy discharge, tearing, eye irritation, redness of the eyes, and to variable extent photophobia. Conjunctival signs include hyperernia and giant papillary cobblestone lesions in tarsal conjunctiva, in bulbar conjunctiva-congestion, gelatinous limbal membrane and Horner-Tranta's spots. Corneal lesions can range from punctuate epithelial erosions to shield ulcer, scarring and corneal plaques. Various treatment modalities had been tried ranging from topical antihislaminics, mast-cell stabilizers, NSAID, topical low and high potency steroids and cyclosporine[3-5]. Steroids in particular cannot be used for a long period because of their side-effects. Keeping this in mind; newer immunomodulating drugs like tacrolimus is being advocated for the management of VKC. This study aims at highlighting the role of tacrolimus in the management of VKC with corneal involvement and proliferate lesions.

MATERIALS AND METHODS

It is prospective observational study which includes consecutive 106 VKC patients attending Ophthalmology OPD of our hospital between July 2015 and May 2016. After taking history, total signs and symptoms score was noted. 0.03% Tacrolimus eye

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ointment was started in patients meeting inclusion criteria twice daily and studied for 6 months. Total of 8 clinical signs (Palpebral conjunctiva! hyperernia, follicles, papillae, giant papillae bulbar hyperemia, edema, Tranta's dot, corneal signs) and 5 symptoms (itching, foreign body sensation, tearing, discharge and photophobia) were graded as none, mild, moderate and severe. Baseline examination was done on day 0 using slit-lamp biomicroscope and then again after 1 month, 3 months and 6 months. Patients with clinical diagnosis of refractive VKC whose symptoms did not subside with antihistaminic/mast-cell stabilizer/topical steroids and patients who respond to steroid but develop steroid toxicity were included in this study. Patient having one useful eye, patients using contact lens, patients with any other active ocular inflammatory condition, patients with hypersensitivity reaction against the study medication were excluded from the study. Written informed consent.

Table 1: Comparison of symptom and sign grades at 0 (baseline) month and 6 months

Symptoms and signs	Grade 0		Grade 1(mild)		Grade 2 (moderate)		Grade 3 (severe)	
	At 0 Month	At 6 Month	At 0 Month	At 6 Month	At 0 Month	At 6 Month	At 0 Month	At 6 Month
Itching	-	81	20	15	56	5	30	5
Fb sensation	-	80	15	12	55	8	36	6
Tearing	-	77	12	11	48	10	46	8
Discharge	-	75	51	14	33	9	22	8
Photophobia	-	80	43	12	32	8	21	6
Conjuctival hyperemia	-	79	36	16	48	7	22	4
Follicles (n=74)	-	41	23	23	36	6	15	4
Papillae	-	51	21	22	28	23	57	20
Giant papilliae (n=56)	-	24	20	13	24	10	12	9
Bulbar hyperemia	-	86	24	9	34	7	44	4
Oedema (n=35)	-	18	19	11	13	5	3	1
Tranta Dots (n=55)	-	32	24	11	22	10	9	2
Corneal signs (n=66)	-	40	30	13	32	12	4	1

was obtained from the each of the participants (or from their legal guardians in cases of minors) before start of study medication. Institutional ethical committee permission was obtained before the start of the study.

Table 2: Signs and Symptoms after 6 month follow up

Symptom and signs	At 1 month	At 3 months	At 6 months
Itching	49(46%)	69(65%)	101(95%)
Fb sensation	49(46%)	68(64%)	100(94%)
Tearing	47(44%)	68(64%)	103(97%)
Discharge	48(45%)	67(63%)	101(95%)
Photophobia	49(46%)	69(65%)	100(94%)
Conjuctival hyperemia	50(47%)	68(64%)	102(96%)
Follicles (n=74)	33(45%)	45(61%)	70(94%)
Papillae	44(42%)	66(62%)	101(95%)
Giant papillae (n=56)	24(44%)	34(62%)	47(85%)
Bulbar hyperemia	46(43%)	66(62%)	102(96%)
Oedema (n=35)	16(46%)	22(64)	34(97%)
Tranta's dot (n=55)	25(46%)	34(62%)	53(96%)
Corneal signs (n=66)	24(44%)	41(63%)	65(98%)
Mean	45%	63%	95%

Statistically significant improvement was seen in patients with corneal involvement and giant papillary lesions ($p<0.001$).Out of 106 patients around 48(45%), 67(63%), 100 patients (95%) showed improvement in symptoms and signs after application of 0.03% Tacrolimus ointment at 1st month, within 3rd month and within 6th month respectively(Table 1). Follicles were observed in 74 patients, giant papillae in 56 patients, edema in 35 patients, Tranta's dot in 55 patients and corneal signs in 66 patients. Only few side-effects were seen such as mild burning sensation seen in 3pts (2.5%) seen in 1st month which subsided in few weeks (Table 2).

DISCUSSION

Tacrolimus is a highly potent (100 times more than Cyclosporine A) immunomodulator agent-produced by

the fungus *Streptomyces tsukubaensis*. It suppresses T-celi activation, T helper cell-mediated B-cell proliferation, and formation of cytokines, especially interleukin-2. Initially approved as a skin applicant for the treatment of atopic dermatitis (AD) it has also been used with good effect in below quantifiable levels with no evidence of cancer risk or significant local side effects and only occasional reports of transient burning or pruritus at the application site.

Safer alternatives for topical steroids had been on especially in view of chronic and indolent nature of VKC. Fukusnima *et al*. used 0.1% tacrolimus in their study and placed it superior to cyclosporine in managing refractory VKC[10]. They reported significant reduction of total signs and symptoms including corneal lesions at one month after tacrolimus application. Burning sensation (transient) was the most commonly documented side effect in 3.20% (2.5% in our study). Results of 0.1 % tacrolimus in refractory VKC cited by Abaysiri *et al*. are similar to our study[11]. They concluded excellent safety profile of tacrolimus and efficacy as good as any high potency topical steroids. Improvement of comeal lesions had been reported (like our study) by Kheirkhah et al[12]. The major limitation of our study is small sample size and lack of control arm. 0.03% Tacrolimus eye ointment was found safe and effective in vernal keratoconjunctivitis cases resistant to anti-allergic /steroid/ cyclosporine eye drops especially with proliierative lesions and corneal involvement with mild side-effects of burning sensation which subsided within few weeks.

REFERENCES

1. Tacbara KF. Ocular complications of vernal keratoconjunctivitis. Can J Ophlhalmol 1999; 34: 88-92.
2. Bieiory L Frohrnan LP. Ailergic and immunologic disorders of the eye. J Allergy Clin Immunol 1992; 89:1-15.
3. BenEzra D, Peer J, Brodsky M. Cohen £. Cyclosporine eye drops for fie treatment of severe vernal keratoconjunctivitis. Am J Gphthsimol 19S6; 101:278-82.
4. Secchi AG, Tognon MS, Leonard"! A. Topical use of cyclosporine in the treatment of "vernal keratoconjunctivitis. Am J Ophthalrnol 1990; 110:. 641-5.
5. Bieik JH, Tabbara KF. Topical cycSosporine in vernal keratoconjunctivitis. Ophthalmology 19SV.98 :1679-84.
6. Savvada S, Suzuki G, Kawase Y, Takaku F. Novel immunosuppressive agent. FK506. *In vitro* effects on the cloned T cell activation. J Immunol 1987; 139:1797-1803.
7. Kobayashi C, Kanai A, Nakajima A, Okumura K. Suppression of corneal graft rejection in rabbits by a new immunosuppressive agent, FK-506. Transplant Proc 1989; 21:3156-8.
8. Nishi M, Herbort CP. Matsubara M, Morishita M, Nishimura M, Nieda M, et al. Effects of the immunosuppressant FK5Q6 on a penetrating keratoplasty rejection mode! in the rat. Invest Ophthalrnol Vis Sci 1993; 34; 2477-36.
9. Sloper CM, Powell RJ, Dua HS. Tacrolimus (FK506) in the management of high-risk corneal and limbal grafts. Ophthalmology 2001; 108: 1838-44.
10. Fukushima A, Ohashi Y, Ebinara N, et al. Therapeutic effects of 0.1% tacrolimus eye drops for refractory allergic ocular diseases with proliferative lesion or corneal involvement. BrJ Ophlhalmol. 2014:98:1023-7.
11. Abeysiri P, Johnston NR, Molteno ACB. The Use of Topical Tacrolimus 0.1% Skin Ointment for Anterior Segment Conditions: A Case Series. Ophthaimol Eye. Dis 2010; 2: 5-8.
12. Kheirkhah A, Zavareh M'K. Farzbod F, Mahbod M, Behrouz MJ. Topical 0.005% tacrolimus eye drop for refractory vernal keratoconjunctivitis. Eye (Lond). 2011; 25; 872-60.

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