

# Efficacy of topical application of 0.03% tacrolimus eye ointment in the management of allergic conjunctivitis

Ajit Kumar Hazarika,  
Prodip Kumar Singh

Department of Ophthalmology, Sikkim Manipal Institute of Medical Sciences, Central Referral Hospital, Sikkim, India

**Address for correspondence:**

Dr. Ajit Kumar Hazarika, Department of Ophthalmology, Sikkim Manipal Institute of Medical Sciences, Central Referral Hospital, 5<sup>th</sup> Mile, Tadong, Gangtok - 737 102, Sikkim, India.  
E-mail: ajitkharika@gmail.com

## Abstract

**Background:** Allergic conjunctivitis is commonly observed eye diseases in Sikkim, India due to the abundance of seasonal pollens, environmental pollutants, and house dust. We evaluated the efficacy of topical 0.03% tacrolimus eye ointment in the management of simple allergic conjunctivitis. **Materials and Methods:** A prospective observational study was designed consisting of 41 patients with refractory simple allergic conjunctivitis, whose condition responded very poorly to conventional anti-allergic eye drops (azelastine, olopatadine, chlorpheniramine maleate, sodium chromoglycate). Simple allergic conjunctivitis cases were diagnosed and followed up evaluating both subjective and objective findings (itching, photophobia, tearing, chemosis, conjunctival congestion, tarsal papilla, and eyelid edema). Existing ocular treatment was discontinued at enrolment and 0.03% tacrolimus ointment was applied into the conjunctival sac of the affected eyes twice daily for 4 weeks followed by a 2 weeks washout period. Patients were followed up at the end of 1<sup>st</sup> week, 4<sup>th</sup> week, and at 7<sup>th</sup> week (2 weeks washout period). **Results:** Symptoms of simple allergic conjunctivitis (itching, tearing and photophobia) were significantly reduced at the end of 1<sup>st</sup> week. Signs such as conjunctival chemosis, congestion, tarsal papillae, and eyelid edema were effectively treated in all cases at the end of 1<sup>st</sup> week. At the end of 4<sup>th</sup> week, all cases were fully cured and none of the patient had any recurrences up to 7<sup>th</sup> week. Mean score at 1<sup>st</sup> day ( $9.6 \pm 3.27$ ) was significantly ( $P < 0.0001$ ) reduced by 7<sup>th</sup> day ( $1.35 \pm 1.19$ ) of treatment. **Conclusion:** Topical application of tacrolimus ointment is an excellent alternative to anti-allergic and steroids eye drops for the treatment of simple allergic conjunctivitis as it significantly reduces recurrences.

**Key words:** Simple allergic conjunctivitis, tacrolimus, topical immunosuppressant

## INTRODUCTION

Allergic conjunctivitis is one of the most common benign external ocular conditions encountered in general ophthalmic practice<sup>[1]</sup> and is estimated to affect 20% of the population worldwide.<sup>[2]</sup> Occasionally, a severe chronic form can be debilitating which can impair vision when

the corneal surface is disrupted.<sup>[1-4]</sup> Treatment is usually based on eye drops containing antihistamines, mast cell stabilizers or dual action agents, which are often insufficient necessitating the addition of steroids.<sup>[1,3-5]</sup> However, steroids increase the risk of glaucoma, cataract, and secondary infections when used for the long duration. Tacrolimus also known as FK 506 is a macrolide derivative with anti-inflammatory and immunomodulatory activity. Tacrolimus is produced by the fungus *Streptomyces tsukubaensis* can suppress the T cell activation and interleukin-2 production by binding to an immunophilin and inhibiting the enzymatic activity of calcineurin.<sup>[6]</sup> Here we evaluated the efficacy of topical application of 0.03% tacrolimus eye ointment in conjunctival sac for the treatment of patients with intractable simple allergic conjunctivitis refractory to conventional anti-allergic medicines.

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## MATERIALS AND METHODS

This prospective observational study was conducted at the Department of Ophthalmology Sikkim Manipal Institute of Medical Sciences during the period of March to August 2014. The study included 41 patients with refractory simple allergic conjunctivitis, whose condition had responded poorly to conventional anti-allergic eye drops. Existing ocular treatment was discontinued at the enrolment [Table 1]. 0.03% tacrolimus ointment was applied into the conjunctival sac of affected eyes twice daily for 4 weeks followed by a 2 weeks washout period. Conjunctivitis severity was recorded with composite subjective and objective findings at each visit. Patients were followed up in the 1<sup>st</sup>, 4<sup>th</sup>, and 7<sup>th</sup> week. Simple allergic conjunctivitis cases were diagnosed and followed up evaluating subjective and objective findings at baseline, 1<sup>st</sup> week, 4<sup>th</sup> week, and after washout period (7<sup>th</sup> week). The study conformed to the Helsinki Declaration and Institution Ethical Committee approved the study. All the participants were motivated, explained, ensured strict confidentiality, and then informed consent was taken from each participant.

### Diagnostic criteria

Patients were diagnosed on following subjective and objective findings at baseline; (1) itching (2) photophobia (3) tearing (4) conjunctival chemosis (5) conjunctival congestion (6) tarsal conjunctival papilla, and (7) eyelid edema [Table 2].

A three-point scale of the following definitions: 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe was used for objective scoring. The same scale was used for follow-up. All patients were thoroughly examined for visual acuity, slit lamp examination of adnexa, anterior segment. Intraocular pressure (IOP) was measured and posterior segment examined by ophthalmoscopy. In this study, simple allergic conjunctivitis in males and females above 5 years of age were included [Table 3] and cases with pregnancy, lactation, history of herpetic eye disease, corneal transplant patients, high IOP, hypersensitivity to macrolides, ocular, and adnexal infections were exclude.

### Statistics

Data are represented as mean  $\pm$  standard deviation statistical analyses were performed using SPSS software version 16 (Statistical Package for the Social Sciences - IBM).  $P < 0.05$  was considered as statistical significant.

## RESULTS

Symptoms of simple allergic conjunctivitis (itching, tearing and photophobia) were significantly reduced at the end

**Table 1: Pretreatment medications**

Pretreatment anti-allergic medications	Number of cases (%)
Azelastine eye drop	11 (26)
Olopatadine eye drop	21 (51)
chlorpheniramine maleate eye drops	5 (12)
Sodium chromoglycate eye drops	4 (9)

**Table 2: Patient records and clinical scoring**

Clinical scoring		Score
Visits: 1 <sup>st</sup> /2 <sup>nd</sup> /3 <sup>rd</sup> /4 <sup>th</sup>		
Patient number: _____		
Hospital number: _____		
Name: _____		
Age: _____		
Sex: _____		
Religion: _____		
Date: _____		
Symptom and signs		
Itching		
Intense itching		2
Itching		1
None		0
Photophobia		
Intense photophobia		2
Photophobia		1
None		0
Tearing		
Excess tearing		2
Increased tearing		1
None		0
Palpebral conjunctiva hyperemia		
Dilatation of many vessels		2
Dilatation of several vessels		1
None		0
Chemosis		
Diffuse edema		2
Slight edema		1
None		0
Papillary reactions		
Mild		2
Few areas		1
None		0
Eyelid edema		
Present both lids		2
Present on one eyelid		1
None		0
Total score		

**Table 3: Age and sex distribution**

Age in years	Sex distribution		Total
	Male (%)	Female (%)	
5-10	4 (80)	1 (20)	5
11-19	5 (71)	2 (29)	7
20-40	12 (54)	10 (45)	22
41-60	4 (57)	3 (43)	7

of 1<sup>st</sup> week. Conjunctival chemosis, congestion relieved, tarsal papillae, and lid edema were successfully treated in all cases at the end of 1<sup>st</sup> week. At the end of 4<sup>th</sup> week, all cases were fully cured and patients were advice to discontinue 0.03% tacrolimus eye ointment. All patients

were re-examined at 7<sup>th</sup> week and none of the patients had any recurrences of allergic conjunctivitis. Mean score at the day was  $9.6 \pm 3.27$ , which was significantly ( $P < 0.0001$ ), reduced to  $1.35 \pm 1.19$  by 7<sup>th</sup> day.

The most common adverse reaction observed was a transient foreign body sensation (39%) followed by transient burning sensation in the eye (34%) and transient blurring of vision (26%) [Table 4]. However, these adverse reactions may be significantly reduced by using tacrolimus eye drops instead of tacrolimus ointment (as in this study).

## DISCUSSION

Ocular allergic disease is a common problem affecting about 20% of the population worldwide. 0.03% tacrolimus dermatologic ointment was reported to be effective in the treatment of intractable allergic conjunctivitis.<sup>[1]</sup> 0.1% topical tacrolimus (FK 506) ophthalmic ointment, was successfully used to treat vernal keratoconjunctivitis where in its lack of absorption from conjunctiva was favorable in achieving the therapeutic outcome.<sup>[3]</sup> The safety and efficacy of 0.03% tacrolimus were also reported in patients with severe atopic blepharoconjunctivitis, wherein once daily application on eyelids lead to clinical and cytological improvement of conjunctivitis.<sup>[4]</sup> In addition, 0.03% tacrolimus has been successfully used in the treatment of giant papillary conjunctivitis<sup>[5]</sup> and 0.1% topical tacrolimus skin ointment was effective in therapy of anterior segment inflammations (vernal keratoconjunctivitis and atopic keratoconjunctivitis) resistant to steroid therapy.<sup>[6]</sup>

We conclude that 0.03% tacrolimus eye ointment is very effective, safe, and well tolerated in treating refractory

**Table 4: Adverse effect of tacrolimus eye ointment**

Adverse effects	Number of patients (%)
Transient foreign body sensation	16 (39)
Transient burning sensation in the eye	14 (34)
Transient blurring of vision	11 (26)

simple allergic conjunctivitis. In comparisons to steroids, it does not increase IOP hence tacrolimus is an excellent alternative to anti-allergic and steroids eye drops. Moreover, the potential of 0.03% tacrolimus eye ointment to reduce the incidence of recurrences is desirable.

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