

CASE REPORT

OPEN ACCESS

Full open access to this and thousands of other papers at <http://www.la-press.com>.

The Use of Topical Tacrolimus 0.1% Skin Ointment for Anterior Segment Conditions: A Case Series

Poorna Abeysiri, Nicholas R. Johnston and Anthony C.B. Molteno

Dunedin Eye Department, Dunedin Hospital, Dunedin, Otago, New Zealand. Email: nic_johnston@yahoo.com

Abstract: Tacrolimus (FK 506) is a macrolactam derivative with immunomodulatory and anti-inflammatory activity. Topical tacrolimus 0.03% has been used for inflammatory conditions of the anterior segment. This article adds to the literature on the off-license application of tacrolimus ointment, by describing the safe and effective use of the higher strength of 0.1% topical tacrolimus skin ointment in four patients. To our knowledge this is the first report of topical tacrolimus 0.1% ointment applied to the conjunctival sac for the treatment of atopic keratoconjunctivitis, vernal keratoconjunctivitis and the post-operative management of trabeculectomy and graft rejection in steroid responders.

Keywords: tacrolimus, anterior eye segment, topical administration, intraocular pressure, inflammation

Ophthalmology and Eye Diseases 2010:2 5–8

This article is available from <http://www.la-press.com>.

© the author(s), publisher and licensee Libertas Academica Ltd.

This is an open access article. Unrestricted non-commercial use is permitted provided the original work is properly cited.

Introduction

Tacrolimus (FK 506) is a macrolactam derivative with immunomodulatory and anti-inflammatory activity.¹ Produced by the fungus *Streptomyces tsukubaensis*, it suppresses T cell activation and IL-2 production by (Figure 1b) binding to an immunophilin and inhibiting the enzymatic activity of calcineurin.¹

Tacrolimus, in its topical form, has been established as a safe and effective alternative to topical corticosteroids because of its mild side effects and minimal absorption.¹ Initially approved as a skin applicant for the treatment of atopic dermatitis (AD) it has also been used with good effect in seborrhoeic dermatitis, psoriasis and allergic contact dermatitis.¹ Extensive testing has shown systemic absorption to be 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.²

Topical tacrolimus ointment is commercially available in two strengths 0.03% and 0.1%.³ Topical tacrolimus 0.03% skin ointment has been used effectively for inflammatory conditions of the anterior segment.⁴⁻⁷ This article adds to literature on the off-license application of tacrolimus ointment, by describing the use of the higher strength 0.1% topical tacrolimus (Protopic) skin ointment at our eye unit. The higher strength enables a low dosage frequency and has been a feasible and acceptable treatment to patients.

To our knowledge this is the first report of tacrolimus 0.1% ointment for the treatment of atopic keratoconjunctivitis (AKC), vernal keratoconjunctivitis (VK) and the post-operative management of trabeculectomy and graft rejection in steroid responders. The use of tacrolimus 0.1% ointment has been reported in atopic eyelid disease.^{8,9}

We present a case series of four patients of ages ranging from 7–52 years with vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC) and corneal graft rejection complicated by steroid resistance or steroid-induced intra-ocular pressure (IOP) rise, who were successfully treated with 0.1% topical tacrolimus applied to the conjunctival sac. Due to the severity of inflammation and problems with topical steroids, patients were commenced on 0.1% topical tacrolimus that we obtained from the hospital pharmacy under the New Zealand Medicines Act 1981



Figure 1a. Picture of upper lid tarsal plate in case one before tacrolimus ointment application.

for use of unapproved medicine.¹⁰ Each patient was only treated after informed consent as per Section 25 of the New Zealand Medicines Act 1981.

Case Reports

Case 1

A 7 year old boy with severe intractable VKC, giant papillae and a shield ulcer, resistant to topical steroids, presented with steroid induced raised IOP. He was treated with 0.1% tacrolimus ointment twice daily to the right eye (Figure 1a). Within a month his IOP had normalised and his giant papillae had resolved, his conjunctiva was white and his cornea only had a faint



Figure 1b. Picture of upper lid tarsal plate in case one after tacrolimus ointment application.



scar left. Due to residual giant papillae and discomfort in his left eye, he was left on a maintenance dose of tacrolimus 0.1% once daily (Figure 1b). He has remained free from recurrence for 3 years on tacrolimus once daily to both eyes with normal vision and IOP. He lives rurally and attends annually for review.

Case 2

A 39 year old with keratoconus, AKC and atopic dermatitis of the eyelids presented with glaucoma induced by long term topical skin steroids. He required bilateral sequential trabeculectomy. Post-operatively, topical steroids were substituted by 0.1% tacrolimus twice daily, at week four post operatively, due to steroid induced IOP rise. At follow up several weeks later he had minimal inflammation and normal IOP and the tacrolimus was tapered to once daily and stopped within a month. Nine years later he is maintaining normal vision and IOP in mid-teens with bilateral functioning blebs. His dermatitis and AKC are well controlled on short courses of topical tacrolimus twice daily during episodes of flare up. He attends annual review.

Case 3

A 29 year old man underwent penetrating keratoplasty (PK) for KC. He had a post-operative steroid induced IOP rise and developed corneal graft rejection upon tapering of his steroids. He was treated with high frequency topical steroids and oral cyclosporine, his IOP's remained high on gutt brimonidine twice daily and acetazolamide three times a day. It was decided to try 0.1% tacrolimus twice daily as a steroid sparing agent to enable early tapering of steroids. He underwent complete resolution of the rejection episode with normalisation of IOP within six weeks of treatment. Unfortunately he required re-graft for failure a year latter.

Case 4

A 52 year old man with longstanding traumatic glaucoma successfully treated with a Molteno implant, underwent PK for corneal scarring. He had known steroid related IOP rise and was therefore commenced on adjuvant 0.1% tacrolimus twice daily at one month post-operatively and dexamethasone 0.1% was tapered and stopped over two and a half months. He has remained rejection free for 2 years

on tacrolimus once daily and attends for bi-annual review.

Discussion

We successfully treated severe steroid unresponsive VKC and AKC and corneal graft rejection and trabeculectomy surgery complicated by steroid induced IOP rise with commercially available 0.1% tacrolimus ointment applied to the conjunctival sac. We could find only one report on the ocular use of the higher strength in a patient with ocular cicatricial pemphigoid whose inflammation was successfully treated with 0.1% following initial tolerance testing using 0.03%.¹¹

A 30 g tube of 0.1% tacrolimus costs NZ\$136 and can be used until the manufacturer's expiry date. All patients tolerated treatment well with no side effects and once stable required annual or bi-annual review. We did not use 0.03% tacrolimus for tolerance testing as only the 0.1% could be sourced in our centre and no patients were intolerant of the higher strength. Nor did we experience non-response in our small number of cases.

We found 0.1% tacrolimus ointment applied to the conjunctival sac to have similar efficacy to high strength topical steroids but with negligible systemic or local side effects. In our practice it has a role for steroid resistant cases of VKC and AKC and as a steroid sparing agent for the management of corneal graft rejection and inflammation suppression post-trabeculectomy surgery in steroid responders. With modest cost, long shelf life and need for infrequent review, it appears an acceptable and feasible treatment.

Disclosures

The authors have no conflict or commercial interest in the findings.

No Financial Support was Received

This paper was presented in part at RANZCO Branch Annual meeting Nelson 14–17 May 2009.

References

1. Rallis E, Korfitis C, Gregoriou S, Rigopoulos D. Assigning new roles to topical tacrolimus. *Expert Opinion on Investigational Drugs*. 2007; 16:1267–76.
2. Rustin MH. The safety of tacrolimus ointment for the treatment of atopic dermatitis: a review. *British Journal of Dermatology*. 2007;157: 861–73.



3. Ngan V. Tacrolimus <http://dermnetnz.org/treatments/tacrolimus.html>. Created 2004.
4. Attas-Fox L, Barkana Y, Iskhakov V, et al. Topical tacrolimus 0.03% ointment for intractable allergic conjunctivitis: an open-label pilot study. *Current Eye Research*. 2008;33:545–9.
5. Dhaliwal JS, Mason BF, Kaufman SC, Dhaliwal JS, Mason BF, Kaufman SC. Long-term use of topical tacrolimus (FK 506) in high-risk penetrating keratoplasty. *Cornea*. 2008;27:488–93.
6. Joseph MA, Kaufman HE, Insler M, Joseph MA, Kaufman HE, Insler M. Topical tacrolimus ointment for treatment of refractory anterior segment inflammatory disorders. *Cornea*. 2005;24:417–20.
7. Kymionis GD, Goldman D, Ide T, et al. Tacrolimus ointment 0.03% in the eye for treatment of giant papillary conjunctivitis. *Cornea*. 2008;27:228–9.
8. Mayer K, Reinhard T, Reis A, et al. FK 506 ointment 0.1%—A new therapeutic option for atopic blepharitis. Clinical trial with 14 patients. *Klinische Monatsblätter für Augenheilkunde*. 2001;218:733–6.
9. Rikkers SM, Holland GN, Drayton GE, Michel FK, Torres MF, Takahashi S. Topical tacrolimus treatment of atopic eyelid disease. *American Journal of Ophthalmology*. 2003;135:297–302.
10. Medsafe. *Regulatory Issues: Unapproved Use of Medicines*. April 1998 [cited 28/11/2009]; Available from: <http://medsafe.govt.nz/profs/RIss/unapp.asp>.
11. Michel JL, Gain P, Michel JL, Gain P. Topical tacrolimus treatment for ocular cicatricial pemphigoid. *Annales de Dermatologie et de Venereologie*. 2006;133:161–4.

Publish with Libertas Academica and every scientist working in your field can read your article

“I would like to say that this is the most author-friendly editing process I have experienced in over 150 publications. Thank you most sincerely.”

“The communication between your staff and me has been terrific. Whenever progress is made with the manuscript, I receive notice. Quite honestly, I’ve never had such complete communication with a journal.”

“LA is different, and hopefully represents a kind of scientific publication machinery that removes the hurdles from free flow of scientific thought.”

Your paper will be:

- Available to your entire community free of charge
- Fairly and quickly peer reviewed
- Yours! You retain copyright

<http://www.la-press.com>