THE EFFICACY OF TOPICAL TACROLIMUS OINTMENT 0.03% AS MONOTHERAPY FOR THE TREATMENT OF SEVERE CASES OF VERNAL KERATOCONJUNCTIVITIS

Nacima M. Elzitni and Samar A. Bukhatwa

ABSTRACT
Purpose The aim of this study was to evaluate the efficacy of Tacrolimus ointment 0.03% as monotherapy for the treatment of severe cases of Vernal Keratoconjunctivitis Setting DAR EL TAMUUS private ophthalmology clinic in Benghazi Libya Methods A prospective observational study of 32 eyes of 16 patients was carried out in the period from (01.01.2017) to (31.12.2017) All the patients attended DAR EL TAMUUS private ophthalmology clinic in Benghazi Libya, the clinical subjective ocular signs and the objective ocular symptoms of severe cases of vernal Keratoconjunctivitis were assessed. All patients were treated only with Tacrolimus ointment 0.03% applied to the conjunctival sac once at night in each eye for consecutive 8 weeks, where the signs and symptoms of vernal Keratoconjunctivitis followed prospectively at 1st week, 1st month, 2nd month, 3rd month, 6th month and 12th month. Result By the end of 8th weeks there was a dramatic relief in the total score of symptoms and signs from baseline were recorded at each visit and no need for further treatment up to the end of this study period 12th months. No relevant adverse effects were reported except mild burning sensation. Conclusion Tacrolimus ointment 0.03% was well tolerated and effective as monotherapy in reducing the signs and symptoms of severe cases of vernal keratoconjunctivitis and a valuable treatment option for this condition that may substitute for steroids treatment with its adverse effect.

Keywords: Tacrolimus ointment 0.03%, Vernal Keratoconjunctivitis, steroids treatment

Received: 05 August 2018
Accepted: 02 September 2018

INTRODUCTION
Vernal keratoconjunctivitis (VCK) is a chronic recurrent allergic inflammation of the conjunctiva affecting children and young adults. It shows more affinity towards males and is seen commonly in the hot, dry regions of the Middle East, Mediterranean basin, Africa, Japan and India. [1] Patients usually complain of severe itching, tearing, redness of the eyes, and photophobia. Clinically, it is characterized by the presence of papillary hypertrophy of the palpebral and/or the limbal conjunctiva, with conjunctival hyperemia, Horner Trantas dots, and mucous discharge. [2] The pathogenesis of VCK is multifactorial in which Th2 derived cytokines (IL-3, IL-4, IL-5 and IL-13) are increased; in addition, Th2 lymphocytes stimulate B lymphocytes leading to mast cell, eosinophil and neutrophil activation through IgE production. [3] VCK can be treated by topical antihistamines and dual action agents (e.g. olopatadine), but moderate to severe forms need to be treated with corticosteroids, which may often need to be taken for long periods of time. This is associated with visual morbidities such as glaucoma and cataracts. [4] This led to the use of drugs with potent anti-inflammatory effects and less steroid induced side-effects such as cyclosporine A and tacrolimus. Tacrolimus is an immunosuppressive effect than cyclosporine and better tolerance profile. It is a macrolide, isolated from the bacteria Streptomyces tsukubaensis. It acts by suppressing the activation of T-cells, the proliferation of B-cells, and the formation of inflammatory mediators (cytokines) especially interleukin2. [5] Studies had reported promising results in the treatment of VCK with tacrolimus; [6,7,8,9] and therefore this study was designed to evaluate the efficacy of Tacrolimus ointment 0.03% as monotherapy for the treatment of severe cases of vernal keratoconjunctivitis.

METHODS
A prospective study conducted at Dar El Tamuis Private Ophthalmology Clinic in Benghazi Libya, during the period from the 1st January 2017 to the 31st December 2017. According to the tenets of the Declaration of Helsinki for research in human subjects, written informed consent was obtained from all the patients, or their legal representatives before inclusion in the study. In
### Table 1: Severity scores for signs of VKC

<table>
<thead>
<tr>
<th>Signs</th>
<th>Severity score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conjunctival hyperemia</strong></td>
<td>3 Impossible to distinguish individual blood vessels</td>
</tr>
<tr>
<td></td>
<td>2 Dilatation of many vessels</td>
</tr>
<tr>
<td></td>
<td>1 Dilatation of several vessels</td>
</tr>
<tr>
<td></td>
<td>0 None</td>
</tr>
<tr>
<td><strong>Papillae</strong></td>
<td>3 Giant papillae predominance on the upper tarsal conjunctiva</td>
</tr>
<tr>
<td></td>
<td>2 Thickened conjunctival surface with many papillae (some giant) on the upper tarsal conjunctiva</td>
</tr>
<tr>
<td></td>
<td>1 Prominent papillary reaction in the upper tarsal conjunctiva with thickening, impeding</td>
</tr>
<tr>
<td></td>
<td>0 Micropapillae of the upper tarsal conjunctiva</td>
</tr>
<tr>
<td><strong>Limbitis</strong></td>
<td>3 Horner-Trantas dots</td>
</tr>
<tr>
<td></td>
<td>2 Limbal hyperemia and papillae</td>
</tr>
<tr>
<td></td>
<td>1 Limbal hyperemia</td>
</tr>
<tr>
<td></td>
<td>0 No limbal inflammatory activity</td>
</tr>
<tr>
<td><strong>Keratitis</strong></td>
<td>3 Shield ulcer or corneal erosion</td>
</tr>
<tr>
<td></td>
<td>2 Exfoliation superficial punctate keratitis</td>
</tr>
<tr>
<td></td>
<td>1 Superficial punctate keratitis</td>
</tr>
<tr>
<td></td>
<td>0 None</td>
</tr>
</tbody>
</table>

addition official ethics approval was obtained from the Martyr Sohail Al Atrash Eye Hospital authorities. Only patients with severe VKC were included in this study. VKC was defined as the presence of chronic or recurrent conjunctivitis characterized by itching, photophobia, watering, and foreign body sensation in the presence of conjunctival hyperemia, keratitis, giant papillae on the upper tarsal plate and/or limbitis (gelatinous limbal infiltration or Horner-Trantas dots). Study exclusion criteria were cases with mild to moderate VCK, patients who had received systemic or sub-conjunctival corticosteroids, patients with a history of herpetic keratitis, glaucoma or ocular hypertension due to previous therapy, developmental cataract or any systemic illness. Complete ophthalmic examination was performed, including visual acuity, slit-lamp biomicroscopy, fluorescein staining, fundoscopy, and tonometry. A protocol for the scoring of signs and symptoms, which was modified from clinical trials with similar methods and objectives, was applied. \(^{10,11,12}\) Grading the severity of the symptoms of itching, lacrimation, photophobia and a foreign body sensation was done as follows: 0 (none), 1 for mild (occasional symptoms), 2 for moderate (frequent symptoms), and 3 for severe (constant symptoms). Also, the severity of the signs (conjunctival hyperemia, keratitis, giant papillae on the upper tarsal plate and/or limbitis) was evaluated and graded as follows: 0 (none), 1 (mild), 2 (moderate), and 3 severe.

Table 1 The whole evaluation was based on the examination of both eyes. All patients were treated only with tacrolimus ointment 0.03% (Astellas Pharma, Europe BV), patients were instructed to apply the ointment to the conjunctival sac once at night in each eye for eight consecutive weeks, and the signs and symptoms of vernal keratoconjunctivitis were then followed prospectively at the first week, first month, second month, third month, sixth month, and finally the twelfth month. Side effects of treatment were monitored by measuring visual acuity, intraocular pressure, presence of secondary infection, patient tolerance to the new treatment and other complications if any emerged. At the end of the second month, the change in the mean of total scores of signs and symptoms from baseline

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**Erratum**

The editors of Benghazi University Medical Journal wish to convey their apologies to the authors of the paper "Effect of Cavity Configuration on Postoperative Hypersensitivity of Posterior Composite Restorations" Nazema Betamar, Omar Zyo and Abdelghafar Farg for the misprint of the date of receipt and acceptance of their paper which should have been November 8 2017 and December 14 2017 respectively, and not with the year cited as 2018 as it appears in Vol.1 Winter 2018 page 19 of our journal.
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- Post INTACS/ICRS (Intrastromal corneal ring segment)
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