



Study of Clinical Features and Management of Vernal Keratoconjunctivitis

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Introduction

Vernal Keratoconjunctivitis is a recurrent, bilateral interstitial inflammation of the conjunctiva, of periodic seasonal incidence, self limited character and unknown etiology. It is characterised by flat- topped papillae, usually on the tarsal conjunctiva resembling cobble stone in appearance, a gelatinous hypertrophy of limbal conjunctiva, either discrete or confluent and a distinctive type of keratitis. It is associated with itching, redness of eyes, lacrimation and a mucinous or lardaceous discharge usually containing eosinophils. The term 'vernal' is derived from the Greek meaning 'occurring in the spring'. It has predilection for warm rather than cold climates with frequent family and personal history of atopic disease, a higher than 2:1 frequency in males over females, an early onset, with remission by the late teens and a hereditary predisposition with exogenous factors, such as climate, season, allergen exposure, determining the likelihood and severity of this. The pathogenesis of VKC is probably multifactorial. The histopathologic and immunopathologic characteristics of the tissues had led some

authorities to conclude that VKC is not a pure type 1 Gell and Coombs hypersensitivity reaction, but rather a combination of both type 1 and type 4 reactions. The predominant symptom of VKC is profound itching. Other symptoms are excessive tearing, mucus production, photophobia and burning and foreign body sensation. The classic sign of palpebral VKC is giant papillae or cobblestone in upper tarsal conjunctiva. Inflammation of bulbar conjunctiva is variable, but a ropy, lardaceous thread almost invariably can be found in inferior fornix¹. Keratitis and shield ulcers are sight threatening complications.² There is an association of keratoconus in VKC patients.³ Other risks are of cataract and glaucoma due to steroids. VKC may cause significant complications and lead to loss of vision.

Currently available drugs to treat VKC include antihistamines, mast-cell stabilizers, corticosteroids, immunomodulators. VKC requires long term treatment in many cases. Topical steroids are the mainstay of treatment for moderate to severe forms of VKC. Steroids, however, cannot be administered for a long period. Injudicious and prolonged use of topical steroids may lead to

glaucoma, cataract and secondary infections. The risk of steroid induced ocular complications in VKC is particularly high in children who are the most commonly affected age group.

This study was undertaken to stress upon the importance of clinical manifestations, management of VKC and to prevent the complications of the disease and those secondary to its long term medication.

Material and Methods

The present study is a hospital based prospective study. It was carried out on 160 patients with symptoms of allergic conjunctivitis attending the outpatient department of Ophthalmology of Mamata Medical College, Khammam, Telangana from January 2013 to December 2016.

All patients with history of itching, photophobia and mucous discharge were included in the study.

Using a pre-formed proforma, history was obtained from each patient with special attention to characteristic symptoms, duration of symptoms, occurrence of symptoms, whether seasonal or perennial, family and personal history of allergy and past treatment. Patients underwent a detailed clinical examination, unaided visual acuity was determined separately for each eye. The BCVA was recorded after refraction, slit lamp

examination with fluorescein staining, tonometry and fundus examination.

Patients were divided into mild, moderate and severe category based on signs and symptoms. Patients with mild grade were treated with sodium cromoglycate 4% eye drops QID alone and those with moderate were put on Fluoromethalone 0.1% eye drops QID and Olopatadine hydrochloride 0.1% eye drops BD and those with severe grade were put on Prednisolone 1% eye drops QID and Olopatadine hydrochloride 0.1% eye drops BD.

Those with uncontrolled severe VKC after treatment with steroid were put on Cyclosporine 2% eye drops QID and Tacrolimus 0.03% eye ointment BD for 4 weeks.

Effectiveness of different modalities of treatment noted. Patient reviewed once in fortnight and period of follow up ranged from a minimum of 3 months to 4 years.

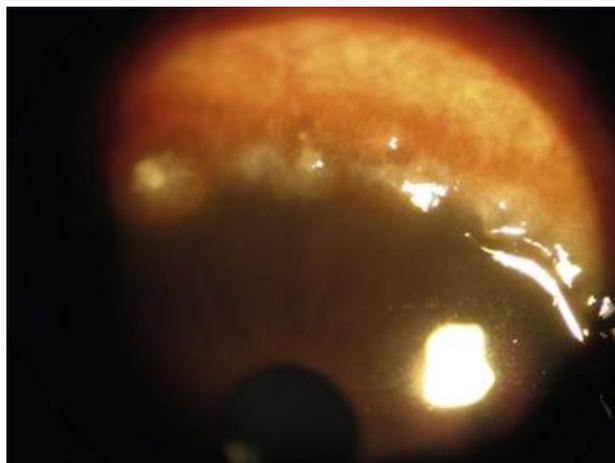
Observations and Results

160 patients with symptoms of allergic conjunctivitis were studied over a period of 4 years from Jan 2013 to Dec 2016.

Majority of the patients presented in age group of 10-16 years, mean age was 14 years. Males were predominantly affected. Seasonal occurrence of symptoms was common. Itching was the predominant symptom. Palpebral form was most common followed by bulbar and mixed form.



Papillary hyperplasia with cobblestone appearance in VKC



Gelatinous thickening around limbus in VKC

Characteristics	Type	No. of Cases	%
Age related distribution	3-9 years	40	25
	10 – 16 years	64	40
	17 – 23 years	36	22.5
	24 – 30 years	20	12.5
Gender	Male	132	82.5
	Female	28	17.5
Periodic variation	Seasonal occurrence	120	75
	Perennial occurrence	40	25
VKC association with allergic disease	Patients with history of allergic disorder	22	13.7
	Patients without history of allergic disorder	138	86.2
Incidence of symptoms	Itching	160	100
	Redness	92	57.5
	Photophobia	42	26.2
	Ropy discharge	58	36.2
	Burning Sensation	32	20
	Watering	23	14.3
Disease Pattern	Palpebral	78	48.75
	Bulbar	42	26.25
	Mixed	40	25

Treatment Group	No. of Cases
I] Topical Steroids+ Olopatadine hydrochloride 0.1% e/d	70
Prednisolone 1% e/d	20
Fluoromethalone 0.1% e/d	50
II] Sodium Cromoglycate 4% e/d alone	90

Treatment group	No. of cases	Improved Cases	Uncontrolled cases
Steroids	70	65	5
Non-Steroids	90	84	6
Total	160	149	11

Bulbar form of the disease was found to be sensitive to sodium cromoglycate alone but took longer time to achieve control. The response of pulse steroid therapy was usually dramatic with reduction of symptoms within days.

All patients except 11 showed good control over a period of one month. Among 11 patients who were not under control, 5 patients belonged to steroid + olopatadine group, 6 belonged to sodium cromoglycate group.

3 cases of 5 which were uncontrolled after treatment with steroid and olopatadine 0.1% e/d were treated with 2% cyclosporine e/d four times a day and 2 cases were treated with Tacrolimus 0.03% ointment BD for 4 weeks and improvement was noted in all 5 cases.

Among 65 patients who had good control at the end of one month, topical corticosteroids were gradually tapered and withdrawn and were asked to continue topical olopatadine 2 times daily and sodium cromoglycate 4% e/d 4 times daily respectively.

Many non-complaint patients belonging to sodium cromoglycate group came back with recurrent attacks next season as compared to those on olopatadine.

In this study, even after 4 weeks of therapy with low dose of topical corticosteroids no patient showed significant intraocular pressure rise. No other significant side effects noted in patients on low dose of topical corticosteroids during the study period. Of the 5 patients treated with topical 2% cyclosporine and tacrolimus 0.03% , the only side effect noted was burning sensation and tearing soon after administration of drugs.

Discussion

Vernal keratoconjunctivitis is a bilateral, chronic, external ocular inflammatory disorder, mainly affecting patients in their first or second decade representing an important cause for hospital attendance.

Male predominance was noted in our study with 82.5% males being affected with VKC and incidence in females being 17.5%. Similar results

were obtained by Baryishak Y.R, Zavaro et al study showed incidence of 73% males being affected by VKC⁴. Mean age affected was found to be 13.75% (range 3-30 yrs) . Similar results were observed by Bisht et al in his study, the mean age as 14.3 years (range 7 – 30 years⁵. The notable difference between sexes and the resolution of the disease with puberty are features that have persistently suggested that hormonal factors play a part in development of VKC (Bonini et al)⁶.

Pulse steroid therapy was found to be a safe and effective method of management of VKC. Topical corticosteroids are the most effective treatment for moderate to severe forms of VKC because of their broad and early interference with the inflammatory cascade.

Sodium cromoglycate, a non-toxic mast cell stabiliser with anti-inflammatory activity has proved effective in the treatment of VKC^{7,8}. Bulbar form of the disease was found to be sensitive to sodium cromoglycate alone. Dahan and associates observed improvement in 90% subjective and 58% objective signs of bulbar form of the disease treated with sodium cromoglycate⁹. Olopatadine 0.1% is a selective H1 antagonist with mast cell stabilizing properties. Olopatadine hydrochloride 0.1% e/d were used along with steroids in patients and proved beneficial for long term treatment. Corum et al reported that 2 months treatment with olopatadine hydrochloride 0.1% relieves the signs and symptoms of VKC¹⁰. Cyclosporine A is effective in controlling VKC associated ocular inflammation by blocking Th2 lymphocyte proliferation and interleukin-2 production. It inhibits histamine release from mast cells and basophils through a reduction in IL-5 production and may reduce recruitment and effects of eosinophils on conjunctiva¹¹. 2% Cyclosporine e/d 4 times daily was found to be effective and safe in treatment of 3 cases of severe uncontrolled VKC. Study done by Pucci et al concluded that 2% cyclosporine eye drops 4 times a day represents a valid alternative to steroids in severe form of VKC¹².

Tacrolimus 0.03% ointment was shown to be effective in treating two cases severe uncontrolled VKC. Patients were treated twice daily for four weeks. Objective signs, subjective symptoms, giant papillae and corneal involvement were significantly improved. Tacrolimus has an immunomodulatory and anti-inflammatory activity. Tacrolimus suppresses Th2 lymphocyte activation, T helper cell-mediated B cell proliferation, and formation of cytokines¹³. Treatment with topical tacrolimus modulates the local immune response at the ocular surface and may theoretically increase the risk of infections¹⁴. There may be a particular concern about an increased risk of herpes simplex virus keratitis associated with topical tacrolimus¹⁵. There may be an increased risk of T cell lymphoma in atopic dermatitis patients treated with tacrolimus skin ointment¹⁶. Even after application of 0.1% topical tacrolimus, the risk of developing malignancy is extremely low¹⁴. The maximum blood concentration of tacrolimus following topical use was < 2ng/ml in selected cases of our patients. This was less than the high risk level (10ng/ml) at which systemic adverse drug reactions might occur¹⁷. The most frequent tacrolimus related adverse event was ocular irritation. A prospective double masked randomised comparative trial comparing the efficacy of 0.01% tacrolimus ointment with Cyclosporine A 2% showed that both were equally effective in the treatment of VKC¹⁸.

In a few patients with VKC, a systemic treatment may be required. Oral antihistamines can reduce the generalised hyper-reactivity but have little or no effect on VKC, while oral administration of Montelukast, an anti-leukotriene drug usually used in mild asthma, has been demonstrated to be effective in reducing signs and symptoms of VKC¹⁹. Omalizumab, an anti-Ig E recombinant, humanized, non-anaphylactogenic antibody, directed against the receptor- binding domain of IgE, may be used in VKC patients with high levels of total serum IgE²⁰.

Conclusion

VKC is a common form of allergic conjunctivitis in a tropical country like ours affecting young males below 16 years. Predominant features of VKC are its seasonal occurrence and itching. Palpebral form is the most common form of disease, followed by bulbar and mixed forms. Topical steroids have been shown to be effective in controlling ocular surface inflammation, but they should be used with particular caution due to their ocular side-effects. Olopatadine can be used for long term treatment. Topical sodium cromogylcate is effective in controlling bulbar form of disease. Grading of the severity of disease and periodicity of disease can be useful for deciding the appropriate line of management. Topical cyclosporine and tacrolimus ointment are useful steroid sparing agents that are underutilised and will help to safely control patients with moderate to severe VKC.

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