Original Article

Safety and efficacy of Lodoxamide in Vernal Keratoconjunctivitis

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Abstract

Objective: To observe the safety and efficacy of topical Lodoxamide eye drops in patients with diagnosed vernal keratoconjunctivitis (VKC).

Methods: This study was conducted at Department of Pharmacology and Therapeutics, BMSI, JPMC, Karachi in collaboration with Department of Ophthalmology, JPMC, Karachi, from April to October, 2009. A total of forty patients with diagnosed vernal keratoconjunctivitis were selected and enrolled consecutively from the out patient department (OPD) of Ophthalmology. Each patient received two drops of Lodoxamide eye drops topically in each eye four times daily. Patients were examined with a torch and slit lamp at baseline and follow-up visits.

Results: Out of 40 patients included, 39 completed the study and there was a significant effect of the drug on symptoms and signs of the disease. At the end of the study, 38 (97.4%) were cured, with few side effects. The cure criteria was based on patient's history of becoming symptom-free and resolution of ocular signs.

Conclusion: Topical lodoxamide eye drops, when used for treatment of VKC, are effective with fewer adverse effects.

Keywords: Vernal keratoconjunctivitis, Lodoxamide (JPMA 61:239; 2011).

Introduction

Vernal keratoconjunctivitis (VKC) is an ocular allergic disease, predominantly observed in children and young adults presenting with complaints of severe itching and photophobia accompanied by ocular discomfort and lacrimation, resulting in visual disturbances.[1,2] It is a chronic ocular allergy that affects mostly children and adolescents living in warm or hot climatic conditions.[3] VKC belongs to a group of ocular eye diseases classified as allergic conjunctivitis, other forms of this group are, seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), atopic keratoconjunctivitis (AKC), contact allergic conjunctivitis (CAC) and Giant papillary conjunctivitis (GPC).[4] The word 'vernal' is derived from the Greek language, which means 'occurring in spring', whereas keratoconjunctivitis denotes the involvement of both the cornea (-keratitis) and conjunctiva (-conjunctivitis).[5]

VKC was first described more than 150 years ago called with different names; these were conjunctiva lymphatica, spring catarrh and recurrent vegetative conjunctivitis.[3] This disease has a global distribution with widely varying incidence. It is less common in Northern Europe and North America and is more frequently seen in the African continent, Mediterranean countries, Central and South America and the Indian sub-continent.[6] In Mediterranean area and other temperate regions, the intensity of the disease increases in spring and summer and decreases in fall and winter.[7] A large number of patients have been reported from subtropical countries like Pakistan.[8] VKC primarily affects boys more than girls in the first decade of life around the age of 7 years. The male to female ratio observed is 2.3:1.[3] The onset of the disease is usually after age of 5 years and resolves around puberty, only rarely persisting beyond the age of 25 years.[8] There is a hereditary predisposition of atopy in about 75% of VKC patients, such as asthma, allergic rhinitis and eczema.[9,10] Clinical types of disease are palpebral, limbal and mixed types.[6] Signs of VKC are, chemosis or oedema of eyelids, ropy mucous discharge and giant papillae that give a cobblestone appearance.[11] These papillae are present either at upper conjunctiva or at the limbus, which are visible by slit-lamp examination after averting the upper lid. Cobblestone papillae are the hallmark of disease.[9]

There are many therapeutic options for treatment of VKC; these are topical steroids, antihistamines and mast cell stabilizers. Mast cell stabilizers are the gold standard for management because of their fewer side effects. From the group of mast cell stabilizers, lodoxamide is the most effective drug for controlling the early phase inflammatory process of the disease and alleviating severe vision disturbing signs and symptoms. Lodoxamide acts by stabilizing mast cell membrane by stopping Ca++ influx, thus preventing their degranulation.[12]

This study was undertaken to assess the efficacy and safety of topical Lodoxamide in patients with VKC.

Patients and Methods

The study was conducted at Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi in collaboration with Department of Ophthalmology, JPMC, Karachi, from April to October, 2009. All the patients attending the outpatients clinic and diagnosed with VKC were included after obtaining a written consent. The diagnosis of VKC was based on history and clinical examination performed with a torch followed by a slit lamp. The patients had either a mild, moderate or severe form of VKC and had not been treated earlier.

Patients with other types of allergic conjunctivitis were excluded. Those already on medication for the same complaint, were not enrolled in the study.

All the study patients received 2 drops of lodoxamide in each eye four times daily and during the study period no other treatment either oral or topical was given.

The follow up visits were carried out fortnightly at day 15, 30, 45, 60, 75 and last visit on day 90. All the patients were examined with a torch and then with slit lamp on each visit, for assessment of improvement in symptoms and signs.

Statistical Analysis was performed with the software SPSS ver 11.5 for data feeding and analysis. The results were given as number and percentages for qualitative variables and mean and standard deviation for quantitative variables.

Results

Forty patients were enrolled for this study, 28 (70%) males and 12 (30%) females with a mean age of 14.7±0.96 years. Presenting complaints were itching (100%), photophobia (92.5%) and lacrimation (100%), whereas family history of atopy was reported by 34 (85%) patients. Thirty nine (97.5%) patients completed the study, while 38 were completely cured at the end of study. At day 30 of study, there was a significant decrease in signs like cobblestone papillae (87.5%) and ropy mucous discharge (96.6%), whereas itching, photophobia and lacrimation decreased remarkably (97.4%) at day 60 (Table-1). The cure rate at the end of study was 97.4%. The cure of disease was based on patient's history of becoming symptom-free and resolution of ocular signs. In 24 (60%) patients, no side effects of the drug were observed, while 10 (25%) patients complained of transient burning / discomfort after

Table-1: Percent changes in different signs & symptoms in vernal keratoconjunctivitis patients treated with lodoxamide from day 0 to day 90.

	Lodoxmide (n=40)	
	No.	%
Cobblestone papillae		
Day - 0	40	100.0
Day - 15	29	72.5
Day - 30	6	15.0
Day - 60	1	2.5
Day - 90	1	2.5
Ropy mucous discharge		
Day - 0	30	75.0
Day - 15	11	27.5
Day - 30	1	2.5
Day - 60	-	-
Day - 90	-	-
Itching		
Day - 0	40	100.0
Day - 15	39	97.5
Day - 30	21	52.5
Day - 60	1	2.5
Day - 90	-	-
Photophobia		
Day - 0	37	92.5
Day - 15	36	90.0
Day - 30	20	50.0
Day - 60	1	2.5
Day - 90	-	-
Lacrimation		
Day - 0	40	100.0
Day - 15	28	70.0
Day - 30	8	20.0
Day - 60	1	2.5
Day - 90	-	-

Cobblestone papillae, Ropy mucous discharge and Lacrimation were significantly decreases From day 0 to day 15 to day 90 ($p<0.05$). Itching and Photophobia were significantly decreases from day 0 to day 30 and day 60 ($p<0.05$).

Table-2: Adverse effects observed during the treatment with lodoxamide from day 15 to day 90.

Adverse effect in the Treatment of Lodoxamide	Day-15	Day-30	Day-60	Day-90
None	24 (60.0%)	35 (87.5%)	39 (100%)	39 (100%)
Transient burning/discomfort	10 (25.0%)	-	-	-
Blurred vision	1 (2.5%)	-	-	-
Dry eyes	2 (5.0%)	1 (2.5%)	-	-
Foreign body sensation	1 (2.5%)	1 (2.5%)	-	-
Eye pain	1 (2.5%)	1 (2.5%)	-	-
Edema	1 (2.5%)	1 (2.5%)	-	-

instillation of drops on day 15,which gradually subsided by day 30. At day 60 all the patients were free of any adverse effects. Other side effects observed during the study are shown in Table-2.

Discussion

VKC is a common ocular allergy prevailing in our society due to allergens like pollens, animal dander and industry fumes with hot weather intensifying the condition. Topical steroids are widely used in controlling the severe distressing symptoms as intense itching, photophobia and lacrimation. But the injudicious and prolonged use of topical steroids carries a high risk of steroid-induced cataracts, corneal thinning and super-infections with fungi, viruses and bacteria, and all of these conditions can potentially lead to blindness.[13] Keeping all these aspects in view, this study was conducted to evaluate the efficacy and safety of lodoxamide, a mast cell stabilizer being used topically as an ophthalmic solution since late 1990s.[14] The drug proved to be effective in controlling the early phase inflammation of VKC, which is due to the response of conjunctiva to environmental allergens like pollens, and industry fumes. Lodoxamide alleviated the signs and symptoms of disease i.e. itching, photophobia, lacrimation, ropy mucous discharge and cobblestone papillae, very effectively without any serious adverse effects. Though minor side effects like blurred vision, dry eyes, foreign body sensation and oedema were observed in 2.5% to 5% of cases. Whereas at the start of therapy, transient burning/discomfort was experienced by 25% of patients that subsided with continued use of the drug and disappeared at day 30 of study. A number of studies also observed beneficial effects of lodoxamide. Bonini et al.[15] reported that lodoxamide significantly controlled the ocular itching as compared to placebo. Avunduk et al.[16] observed the superiority of Lodoxamide against Cromolyn sodium in clinical improvement. This was assessed by symptoms and clinical score analysis which was more prominent in Lodoxamide-treated patients. Although sodium cromoglycate and nedocromil sodium are used for treating the symptoms and signs of VKC, Lodoxamide provides early relief with few adverse effects.

Conclusion

Topically used lodoxamide proved to be very effective in treating VKC with few adverse effects.

The limitations of this study were not having a control group, which would have made evaluation of the drug more valid.

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