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Comparative Evaluation of Efficacy of Olopatadine 0.1% Ophthalmic Solution and Epinastine 0.05% Ophthalmic Solution in Cases of Vernal Keratoconjunctivitis

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ABSTRACT

Background: The aim of the study is to compare the efficacy of olopatadine 0.1% Ophthalmic Solution And Epinastine 0.05% Ophthalmic Solution In patients of Vernal Keratoconjunctivitis. **Methods:** A total of 40 patients with signs and symptoms of vernal keratoconjunctivitis presenting in the outpatient department (OPD) of Regional Institute of Ophthalmology, IGIMS, Patna were enrolled in this study. They were divided in 2 groups : GROUP 1 : (comprised of 20 patients)These patients received Olopatadine 0.1% eye drop in one eye and the placebo (artificial tear)in other eye. GROUP 2 : (comprised of 20 patients). The symptoms (itching, foreign body sensation, swollen eyes, ropy discharge, photophobia etc) and signs(palpebral and bulbar conjunctival hyperaemia, conjunctival chemosis, limbal gelatinous thickening, papillae, muddy discolouration of conjunctiva, horner trantas spots etc) of VKC were graded in order of increasing severity from 0 to 4. **Results:** Statistically significant reduction in itching, ropy discharge, palpebral and bulbar hyperaemia was observed throughout the study but reduction in limbal infiltrate and papillary hypertrophy was statistically insignificant at day 14 while significant at day 28 &42 in both the groups. Adverse effects were observed in 2out of 20 patients (10%) in both the groups. Headache, dry eye and asthenia were observed in olopatadine treated group while red eye, headache, burning sensation and dry mouth were observed in epinastine treated group. **Conclusion:** Both olopatadine and epinastine ophthalmic solution were found to be effective in alleviating the clinical signs and symptoms of VKC as compared to placebo .However the improvement in clinical parameters particularly ocular itching, hyperaemia and limbal infiltrates were more in olopatadine treated group as compared to epinastine treated group.

Keywords: *Olopatadine, Epinastine, Vernal Keratoconjunctivitis*

INTRODUCTION

Vernal keratoconjunctivitis (VKC) is a bilateral, chronic, external ocular inflammatory disorder, mainly affecting patients in their first or second decade.[1-3] Although it is a rare allergic disorder in temperate regions, in many parts of Africa, Latin America and Asia VKC represents an important cause for hospital attendance, ranging from 3% to 6% of patients of all ages, rising to 33% and 90% in children and adolescents.[2,4-7] In large European and Asian case series boys appear to be affected more than girls.[1-4] Palpebral forms are more prevalent in Europe and the Americas, whereas mixed and limbal forms are more seen in Asia and Africa respectively, with some geographic variation.[8-14] VKC has a prominent seasonal variation in disease expression, but flare-ups during winter months can happen in a significant percentage of cases, leading to chronic, perennial disease after a few years.[11,14]

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Vernal keratoconjunctivitis is usually bilateral, although it can occasionally present unilaterally, at least initially.[3,15] Its predominant symptom is intense ocular itching, followed by lacrimation, mucous stringy discharge, severe photophobia, blepharospasm and foreign body sensation.

It can present as purely palpebral or purely limbal disease, but a range of mixed appearances exist.[10] The hallmark sign of palpebral VKC is papillary hyperplasia of the upper tarsal conjunctiva, ranging from papillae of 1 mm of diameter to typical giant or cobble stone papillae.[10] The dominating clinical sign in limbal VKC is infiltration of the limbal subconjunctival tissues forming nodules, sometimes accompanied by pannus of superficial neovascularisation of the peripheral cornea, making the limbus to appear thickened and opaque. They often are topped by chalky white excrescences, known as Horner-Trantas dots.[13] Increased spotty pigmentation of the interpalpebral exposed conjunctiva is common among patients from Africa and Asia, especially among very young children, but whether this sign is correlated to the disease activity is controversial.[8,10-12] In tropical regions corneal complications develop in 7% to 50% of patients with VKC presenting to a hospital facility.[9,16] During exacerbations of palpebral VKC, punctate epithelial keratopathy may develop, leading to macroerosion

and sight threatening shield ulcers.[13,17] Generally, a shield ulcer is differentiated from an infective corneal ulcer by its transversely oval shape, and its location in the centre of the superior third of the cornea, but superinfection can occur. Limbal disease can induce stem cell deficiency, that leads to compromised corneal surface, characterised by corneal vascularisation, chronic stromal inflammation, persistent epithelial defects and ingrowth of conjunctival epithelium onto the corneal surface.[18]

Diagnosis is mainly based on the typical clinical VKC signs. So far only a few laboratory tests are used to confirm the disease. The eosinophils usually found in conjunctival scrapings of patients with VKC support the diagnosis, but their absence does not exclude it.[11,13] Total and specific immunoglobulin E (IgE) determination in tears and serum and skin prick tests can provide additional evidence, but there is a high variability in IgE levels, and skin tests may not always be positive among VKC cases, especially in Africa.[8,11,13] Limbal and palpebral forms do not differ in IgE levels in serum or tears.

Vernal keratoconjunctivitis treatment options vary. Often the first step in the management of allergic conjunctivitis consists of avoidance of the offending allergens, however, this is often impractical. Artificial tears used as diluents and the use of cold compresses have also been employed with a limited amount of efficacy. Clinicians often prescribe topical anti-allergic agents (e.g., antihistamines, mast cell stabilizers, and combination antihistamine/mast cell stabilizers) to manage the manifestations of the disease during allergy season. These agents have varying efficacy, safety, and comfort profiles.[21]

The most recent class of topical anti allergics used in the prevention and treatment of VKC combines both antihistamine and mast cell stabilization. The first available agent in this class was Olopatadine which has become the mainstay of therapy for allergic conjunctivitis.[25,26] Olopatadine is indicated for the treatment of all signs and symptoms of allergic conjunctivitis.[27] This formulation was first approved in United States in 1996 and unlike some other ocular antiallergics originally developed for rhinitis, olopatadine was initially developed for ophthalmic use. This agent combines the benefits of a H1 selective antihistamine and human ocular mast cell stabilizer that inhibits the release of histamine and other pro-inflammatory mediators26. This dual mode of activity provides relief within minutes, a duration of effect up to 12 hours and long-term control.[26] Many studies have shown that olopatadine administered twice daily for the treatment of allergic conjunctivitis is effective, well tolerated, and safe in adults and children.[27]

Another addition to the anti allergy market is Epinastine. Epinastine first received approval for rhinitis treatment in 1981 and has been commercially available in Europe and Japan as an antihistamine for rhinitis under the product names and formulations Alesion (0.2% oral liquid), Flurinol (2 mg tablets), and Talerc (10 mg tablets).[28,29] In October 2003, it was approved in the US for treatment of allergic conjunctivitis. Epinastine is a direct H1 receptor antagonist and inhibitor of histamine release from the mast cell. Epinastine is indicated for the prevention of itching associated with allergic conjunctivitis.[29] The anti-itching efficacy of epinastine compared to vehicle was shown at 15 min post dose and 8 hours post dose in the CAC model.[30]

Aim:

To compare the efficacy of olopatadine 0.1% Ophthalmic Solution And Epinastine 0.05% Ophthalmic Solution In patients of Vernal Keratoconjunctivitis

MATERIALS AND METHODS

All patients with vernal keratoconjunctivitis presenting in Outpatient Department of Regional Institute of Ophthalmology, IGIMS, Patna were included in our study with neither of the patients having a systemic or other ocular illness nor received systemic or ocular medications during last four weeks prior to study. A total of 40 patients with signs and symptoms of vernal keratoconjunctivitis presenting in the outpatient department(OPD) of Regional Institute of Ophthalmology, IGIMS, Patna were enrolled in this study. The patients were divided in 2 groups : GROUP 1 : (comprised of 20 patients)These patients received Olopatadine 0.1% eye drop in one eye and the placebo (artificial tear)in other eye.GROUP 2 : (comprised of 20 patients)These patients received Epinastine 0.05% eye drop in one eye and placebo(artificial tear) in other eye. The symptoms(itching, foreign body sensation, swollen eyes, ropy discharge, photophobia etc) and signs(palpebral and bulbar conjunctival hyperaemia, conjunctival chemosis, limbal gelatinous thickening, papillae, muddy discolouration of conjunctiva, horner trantas spots etc) of VKC were graded in order of increasing severity from 0 to 4.

Informed consent was taken from all the patients. In order to achieve better rates of compliance, patients were given 2months time table indicating control days and drop instillation times. Clinical signs & symptoms were evaluated at baseline (day0), day14, day 28and day42 of treatment. Data obtained were analysed by using student “t” test (paired and unpaired) for comparison.

RESULTS

The patients satisfying the inclusion criteria were categorised in single group and study was carried out

to evaluate the clinical efficacy of olopatadine 0.1% and epinastine 0.05% drops in reducing signs and symptoms of VKC. Each patient was receiving drug in one eye while placebo(artificial tear) in other eye.

In the study group,(37 out of40)92.5% of the patients were between 5-20yrs &(32)80% were male and(8) 20% were female,(33)82.5% were rural and (7)17.5% were urban & majority of them presented in the month of April to june(29 =72.5%) and in month of july to august(9=27.5%).Most of them were of Bulbar variety(57.5%) followed by Palpebral(25%) and Mixed variety(17.5%). 1out of 10(10%) cases of palpebral,6 out of 23(26%) cases of bulbar and 3 out of 7(42.86%)cases of mixed form were having corneal involvement indicating more corneal involvement in bulbar and mixed variety.

Table 1: Evaluation of Signs and Symptoms

Clinical features	Drugs	Day 0 mean score	Day 14 mean score	Day28 mean score	Day 42 mean score	% reduction in clinical features
A)Ocular itching	Olopatadine	3.2	2.1 p<0.01	1.2 p<0.01	0.4 p<0.001	87.5%
	Placebo	3.2	3.1 p>0.05	3 p>0.05	2.6 p>0.05	18.75%
	Epinastine	3.1	2.6 p<0.01	1.7 p<0.01	0.6 p<0.001	80.64%
	Placebo	3.1	3.0 p>0.05	2.9 p>0.05	2.5 p>0.05	19.35%
B)Ropy discharge	Olopatadine	2.9	2.1 p<0.01	1.3 p<0.01	0.6 p<0.001	79.3%
	Placebo	2.9	2.8 p>0.05	2.7 p>0.05	2.4 p>0.05	17.24%
	Epinastine	3.1	2.1 p<0.01	1.2 p<0.01	0.7 p<0.01	77.4%
	Placebo	3.1	3 p>0.05	2.9 p>0.05	2.6 p>0.05	16.13%
C)Palpebral hyperemia	Olopatadine	2.1	1.4 p<0.01	0.8 p<0.01	0.4 p<0.05	80.95%
	Placebo	2.1	2 p>0.05	1.9 p>0.05	1.5 p>0.05	28.57%
	Epinastine	2.1	1.7 p<0.01	1 p<0.01	0.5 p<0.02	76.19%
	Placebo	2.1	2 p>0.05	1.8 p>0.05	1.6 p>0.05	23.81%
D)Bulbar hyperemia	Olopatadine	2.5	1.8 p<0.01	1.2 p<0.01	0.4 p<0.01	80%
	Placebo	2.5	2.4 p>0.05	2.2 p>0.05	1.9 p>0.05	24%
	Epinastine	2.3	1.6 p<0.01	1 p<0.01	0.5 p<0.01	78.26%
	Placebo	2.3	2.2 p>0.05	2 p>0.05	1.7 p>0.05	26.08%
E)Limbal infiltrate	Olopatadine	2.2	2 p>0.05	1.7 p<0.01	0.7 p<0.01	68.18%
	Placebo	2.2	2.2 p>0.05	2.1 p>0.05	1.9 p>0.05	13.63%
	Epinastine	2.2	2 p>0.05	1.6 p<0.01	0.9 p<0.01	59.09%
	Placebo	2.2	2.1 p>0.05	1.9 p>0.05	1.7 p>0.05	22.73%
F)Papillary hypertrophy	Olopatadine	2.2	1.9 p>0.05	1.4 p<0.01	0.7 p<0.01	65.21%
	Placebo	2.2	2.1 p>0.05	1.9 p>0.05	1.7 p>0.05	22.71%
	Epinastine	2.2	1.9 p>0.05	1.3 p<0.01	0.8 p<0.01	63.64%
	Placebo	2.2	2.1 p>0.05	1.8 p>0.05	1.5 p>0.05	31.81%

Table 2: Effect of Olopatadine 0.1% & Epinastine 0.05% ophthalmic solution on reduction of clinical features after 6 weeks of continuous treatment

Clinical features	Drug	
	Olopatadine	Epinastine
Itching	87.5%	80.64%
Ropy discharge	79.3%	77.4%
Palpebral hyperemia	80.95%	76.19%
Bulbar hyperemia	80%	78.26%
Limbal infiltrate	68.18%	59.09%
Papillary hypertrophy	65.21%	63.64%

Statistically significant reduction in itching, ropy discharge, palpebral and bulbar hyperaemia was observed throughout the study but reduction in limbal infiltrate and papillary hypertrophy was statistically insignificant at day 14 while significant at day 28 &42 in both the groups.

Olopatadine and Epinastine were observed to be almost equally effective in reducing sign and symptoms of VKC however percentage reduction in signs and symptoms of VKC particularly itching, hyperaemia and limbal infiltrate were more in olopatadine treated group.

Adverse effects were observed in 2out of 20 patients (10%) in both the groups. Headache, dry eye and asthenia were observed in olopatadine treated group while red eye, headache, burning sensation and dry mouth were observed in epinastine treated group.

DISCUSSION

The present study shows the efficacy of olopatadine and epinastine eye drop in alleviating the signs and symptoms of VKC by comparing these with placebo in 40 patients presenting with bilateral signs and symptoms in Regional Institute of Ophthalmology, IGIMS, Patna. Irrespective of age and sex they were divided in 2 groups consisting of 20 patients each.

It was found out that VKC is a disease of young adults most frequently between 5 to 20 years with preponderance in males with 80% male &20%

female in our study. Male predominance in VKC can be explained by their frequent outdoor activities leading to more exposure to allergens. Excessive exposure to allergens is also a notable cause for more VKC cases in rural than in urban population as reflected in our study with 82.5% patients from rural and 17.5% were from urban background. Duke elder(1965) stated that most striking point in the incidence of VKC is its seasonal character which points to the importance of heat, humidity and blossoming of flowers of certain plants. Vajpayee et al(1985)reported that bulbar variety is more common(75%) than palpebral (7.14%) and mixed (17.86%) variety which also corroborated with the findings in the present study of the bulbar variety (57.5%) followed by palpebral(26%) and mixed(17.3%) with itching and hyperaemia being the most constant features of the disease. Our study had some limitations of its being an environmental study differing from conjunctival allergen challenge (CAC) model. In order to minimise a large fluctuation of pollen, subjects of each season were selected in the same group and evaluated within the same season. As far as the effect of placebo on clinical parameters of VKC, it is well known that artificial tear preparations have diluting and flushing effect on allergen and inflammatory mediators present on ocular surface. Last problem related to the patient compliance was overcome by maintaining a dairy of drug instillations. B.Q.LANIERet all(2004) on their study on clinical efficacy of olopatadine versus epinastine ophthalmic solution in the conjunctival allergen challenge model came to the conclusion that olopatadine is significantly more effective than epinastine in controlling itching ,redness and chemosis associated with allergic conjunctivitis. Olopatadine became available early in 2003 and is now available in South Asia including India and is rapidly become a gold standard treatment option for allergic conjunctivitis. Olopatadine has also been shown to be more efficacious in its duration of action than epinastine and has superior comfort upon instillation in the eyes.

CONCLUSION

Vernal keratoconjunctivitis being usually a bilateral, although can be occasionally present unilaterally, at least initially with its predominant symptom of intense ocular itching,[3,15] followed by lacrimation, mucous stringy discharge, severe photophobia, blepharospasm and foreign body sensation warrants alleviation of symptoms as early as possible. It can present as purely palpebral or purely limbal disease, but a range of mixed appearances exist.[10] Our study showed that all the signs and symptoms were improved significantly in eyes receiving both olopatadine and epinastine drop as compared to placebo eyes. However the mean score of clinical features were shown to be lower in olopatadine treated group than epinastine treated group indicating better therapeutic effectiveness although difference did not reach up to statistical significance. Both olopatadine and epinastine ophthalmic solution were found to be effective in alleviating the clinical signs and symptoms of VKC as compared to placebo .However the improvement in clinical parameters particularly ocular itching, hyperaemia and limbal infiltrates were more in olopatadine treated group as compared to epinastine treated group.

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