



## Original Research Article

## Role of topical ophthalmic solutions (0.1%) olopatadine hydrochloride and (0.05%) epinastine hydrochloride in vernal keratoconjunctivitis

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## ABSTRACT

**Background:** VKC is of great concern to all ophthalmologists in India because it is found to be quite common in our country and the tropical countries and if untreated it can lead to sight threatening complications.

**Materials and Methods:** The present study was carried out in forty patients who attended the outpatient department ophthalmology, Darbhanga Medical College and Hospital, Laheriasarai. The study was carried out from July 2007 Dec 2008. Forty patients with symptoms of VKC (ocular itching, ropy discharge, papillary hypertrophy, gelatinous thickening and (horner-trantas spots) were selected and included in our study.

**Results:** Olopatadine treated group- Means score of itching at 0, 14, 28, 42 days in olopatadine treated eye were 3.2, 2.1, 1.2, and 0.4 respectively having value  $P < 0.01$ ,  $< 0.01$  and  $< 0.001$  respectively while means score at same stages in Placebo eye were 3.2, 3.1, 3 and 2.6 having p value  $> 0.05$ . Olopatadine Treated Group-Mean scores of ropy discharge at 0, 14, 28, and 42 days in were 2.9, 2.1, 1.3 and 0.6 respectively having P value  $< 0.01$ ,  $< 0.01$ ,  $< 0.001$  and  $< 0.001$  in between them and mean scores at same stages in placebo eye were 2.9, 2.8, 2.7 and 2.4 respectively having P value  $> 0.05$ .

**Conclusion:** It was concluded that the present study shown that both olopatadine and epinastine is effective and reducing itching and ropy discharge of VKC as compared to placebo.

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## 1. Introduction

Vernal keratoconjunctivitis (VKC) is a recurrent, bilateral, external, ocular inflammation primarily affecting young adults living in warm dry climates. It is an allergic disorder in which IgE and cell mediated immune mechanism play and important role. It is characterized by intense itching, photophobia, white ropy discharge and appearance of well defined polygonal raised areas of papillary hypertrophy on the palpebral conjunctiva and a wall of gelatinous thickening at the limbus.<sup>1</sup>

The earliest reference to vernal conjunctivitis is available in early part of 19<sup>th</sup> century. It was the limbal type which was initially described by Arlt (1846) as “Conjunctivitis

Lymphatica” and by Desmarres (1874) as “prekeratic Hypertrophy. But Von Graefe (1871) was the first to associate the gelatinous perilimbal infiltrate with pavement like proliferation of the tarsal conjunctiva. The disease was characterized as a clinical entity by Saemisch (1876) who called it spring catarrh but Hunsen – Grut (1888<sup>5</sup>) describes that the disease recurs in early summer rather than in spring. Tobgy (1935) named fine corneal epithelial disturbances as “Keratitis Epithelialis vernalis.”<sup>2</sup>

Topical steroid preparations are the mainstay of treatment of VKC earlier but their long term use is associated with increased risk for the development of glaucoma, cataract and can potentiate ocular herpetic, bacterial or fungal corneal superinfections. So their use should be strictly limited to severe cases. Recent increased understanding of the cellular and mediator mechanisms that

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are involved in VKC has greatly facilitated the development of more effective treatment options.<sup>3</sup> Of these newer drugs, olopatadine is a new topical ocular dibenzoxepin derivative. It inhibits the release of preformed and newly synthesized inflammatory mediators from mast cells upon allergen challenge and also has antihistaminic properties towards H1- receptors.

Its dual activity is an advantage and the drug may be used both as therapeutic and prophylactic agent the dual action also renders the drug superior in term of clinical effectiveness.

Epinastine hydrochloride is a topically active, direct H1-receptor antagonist and an inhibitor of release of histamine from mast cell. It is selective for histamine and has affinity for the histamine H2-receptors. IT was first approved for the treatment of rhinitis. US food and drug administration (FDA) approved IT for the treatment of allergic conjunctivitis and the drug is indicated for the prevention of itching and hyperemia associated with the disorder. It was found to have antiitching efficacy with early onset (3 minute) and duration of action consistent with twice daily dosing.

The purpose of present study is to compare the therapeutic effect of two ophthalmic solutions (0.1%) olopatadine hydrochloride and (0.05%) epinastine hydrochloride on symptoms of VKC.

## 2. Materials and Methods

The present study was carried out in forty patients who attended the outpatient department ophthalmology, Darbhanga Medical College and Hospital, Laheriasarai. The study was carried out from July 2007 Dec 2008. Forty patients with symptoms of VKC (ocular itching, ropy discharge, papillary hypertrophy, gelatinous thickening and (horner-trantas spots) were selected and included in our study. Neither of the patients have a systemic or other ocular illness nor, received systemic or ocular medications during the four weeks prior to study. Presence of symptoms Eg. : Itching foreign sensation, swollen eyes, ropy discharge, photophobia were graded according to scoring system as indicated in Table 1 and patient symptoms were categorized by asking the severity of symptoms to the patient.

The patient selected for study were divided into two group:-

**Group-1** (comprised 20 patients) these patients received olopatadine drop in one eye and the placebo (artificial tear) in other eye both twice daily.

**Group-2** (comprised 20 patients)- these patients received Epinastine drop in one eye and the placebo (artificial tear) in the other eye twice daily.

Informed consent was obtained from all patients. In order to achieve better rates of compliance, patients were given two months time table indicating the control days and

drop instillation times. Patients were asked to mark each medication administration on these schedules and these lists were checked at each control visit.

### 2.1. Data processing and analysis

Clinical signs and symptoms were evaluated at base line (day0) and at day 14, 28 and day 42 of treatment. Data obtained were analyzed by using student “t” test (paired and unpaired) for comparison.

## 3. Results

Patient satisfying inclusion criteria were categorized in single group and study was carried out to evaluate the clinical efficacy of olopatadine (0.1%) ophthalmic solution and epinastine (0.05%) drops in symptoms of vernal conjunctivitis. Each patient was receiving drug in one eye while tear drop (placebo) in other eye. In the study group the age of the patients were ranging from 5 years to 27 years. Most of the patients were found to be between 6 years to 15 years.

Most of the patients were male 32 (80%) in number and female patients were 8 in number (20%). Large number of patients were school going children (85%). Majority of patients were from rural area (82.5%) and 17.5% from urban area. majority of the patients were presented in the month of April to June (72.5%) and in month of July to August (27.5%).

Majority of the patients were of bulbar variety (57.5%) followed by palpebral (25%) and mixed variety (17.5%). One out of ten (10%) case of palpebral, six out of 23 (26%) case of bulbar and three out of seven (42.86%) case of mixed form shows corneal involvement. Superficial punctate keratitis in six case and sub epithelial scarring in four case were observed. Corneal involvement was observed more among patients having bulbar and mixed type of disease.

### 3.1. Ocular itching

Olopatadine treated group- Means score of itching at 0, 14, 28, 42 days in olopatadine treated eye were 3.2, 2.1, 1.2, and 0.4 respectively having value  $P < 0.01$ ,  $< 0.01$  and  $< 0.001$  respectively while means score at same stages in Placebo eye were 3.2, 3.1, 3 and 2.6 having p value  $> 0.05$ . Thus statistically very significant reduction ( $p < 0.01$ ) of itching at day 14 and highly significant reduction at day 28 and 42 was observed in olopatadine treated group compared to placebo.

Epinastine treated group-Mean score of itching at 0, 14, 28 & 42 days in epinastine treated eye were 3.1, 2.6, 1.7, & 0.6 respectively having p value  $< 0.01$ ,  $< 0.01$  &  $< 0.001$  in between them. Thus statistically very significant reduction of itching at day 14 & 28 and highly significant reduction at day 42 was observed in epinastine treated eye.

**Table 1:** Allergic ocular symptoms with scoring

Symptoms	Score 0	Score 1	Score 2	Score 3	Score 4
Itching	Absent	Intermittent Tickling Sensation	Occasionally Rubs the eye	Rubs eye regularly	Vigorous knuckle with severe itch
Ropy discharge	Absent	Occasionally discharge accumulate	Occasionally wipes eye	Wipe eye daily	Wipes eye several times a day
Foreign body sensation	Absent	Occasionally feels sand in eye	Feels sandy daily	Looks for foreign body	Sandy feeling very much distressing
Burning sensation	Absent	Feels occasionally	Daily with occasional closing	Closes eye daily	Desire to close eye all the time
Photophobia	Absent	Occasional	Occasional	Close eye regularly	Desire to close eye all the time

**Table 2:** Number of patients reported in different months of year

Month of Year	No. of cases	Percentage
January	00	0.00%
February	00	0.0%
March	00	0.0%
April	07	17.5%
may	09	22.5%
June	13	32.5%
July	05	12.5%
August	04	10.0%
September	02	05.0%
October	00	0.0%
November	00	0.0%
December	00	0.0%
Total	40	100%

**Table 3:** Effect of olopatadine (0.1%) and epinastine (0.05% eye drops on ocular itching in VKC

Drug	Day 0 mean score (base line)	Day14 mean score	Day 28 mean score	Day 42 mean score	Percentage reduction in signs and symptoms
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>0.01	2.9 P<0.01	2.5 P<0.05	19.35%

However there is significant reduction of itching score in both the group but there more reduction in symptoms of itching (87.5%) in olopatadine group as compare to epinastine group where symptom reduction is 80.65 but these value are statistically not significant.

### 3.2. Ropy discharge

Olopatadine Treated Group-Mean scores of ropy discharge at 0, 14, 28, and 42 days in were 2.9, 2.1, 1.3 and 0.6 respectively having P value <0.01, <0.01, <0.001 and <0.001 in between them and mean scores at same stages in placebo eye were 2.9, 2.8, 2.7 and 2.4 respectively having P value >0.05. Thus statistically very significant reduction (p<0.01) of ropy discharge day 14 and 28 and highly significant reduction at 42 (p<0.001) was observed in olopatadine treated eye while insignificant reduction in

placebo eye at all stages.

Epinastine Treated Group-Mean score at 0,14, 28 and 42 days in epinastine treated eye were 3.1, 2.1, 1.2 and 0.7 respectively having P value <0.01, <0.01 and <0.01 in between them and mean score at same stages in placebo eye were 3.1, 3.0, 2.9 and 2.6 respectively having P value >0.05, >0.05 and >0.05 in between them. Thus statistically significant reduction of ropy discharge at day 14, 28 and 42 was observed in epinastine group as compared to placebo.

## 4. Discussion

In the present study efficacy of olopatadine and epinastine eye drop in alleviating the signs and symptoms of vernal keratoconjunctivitis was observed by comparing these with placebo. 40 patients were selected having bilateral signs and symptoms of VKC attending upgraded department of

**Table 4:** Effect of Olopatadine (0.1%) and Epinastine (0.05%) on ropy discharge in VKC

Drug	Day 0 mean score (base line)	Day 14 mean score	Day 28 mean score	Day 42 Mean score	Percentage reduction in signs and symptoms
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	3.0 P>0.05	2.9 P>0.05	2.6 P>0.05	16.13%

ophthalmology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga. Irrespective of age and sex they were divided into two groups containing twenty patients each. In both group one eye is treated with drug (either olopatadine or epinastine) and other eye with placebo. Patients having age above than 5 years were selected in the study. Change in mean score of symptoms were compared on 14, 28 and 42 days in both eye.

Vernal conjunctivitis is a disease of young adults, occurring most frequently between ages six to twenty years. Study conducted by Secchi, A.G. et al, 9 out of 11 (82.82%) patients were between 7 and 17 years.<sup>4</sup>

Another researcher reported mean of the patient is 12.32 years. In the present study 36 patients out of 40 (90%) were between age of 6 and 20 years.<sup>5</sup> Predominance of males in vernal conjunctivitis has been observed by majority of worker. Preponderance in male in VKC is largely confined to children and after puberty the incidence in both sexes tends to be equal.<sup>6</sup>

Functional expression of steroid receptors on inflammatory cells might explain VKC Predominance in male in prepubertal children. This male dominance might be due to increase chance of exposure to exogenous allergens like pollen and dusts due to more outdoor activity.

Vernal conjunctivitis is allergic disorder and existence of sensitivity to pollen, animal inhalant, dust and moulds have been investigated by several workers. Other researcher have reported that the great majority of cases were pollen sensitive. Animal epithelia, and moulds to be responsible. In the present study, 33 patients (82.5%) belong to rural area while 7 patients (17.50) were from urban area.<sup>7</sup> Darbhanga is rich in pollen, dusts, domestication of animal in rural population in our study.

In the present study, majority of the patients were student (85%), Large percentage of students in our study were from rural areas, where allergen exposure was more common and most of them were in age group of VKC. So, no specific correlation can be quoted between the disease and occupation.

The seasonal incidence of VKC obviously points to the important of heat, humidity and blossoming of flowers of certain plants

In present study, 55% of total number of patients reported in month of May and June which is considered the hot months in Bihar, 27.5% patients turned in hot and humid month of July, August whereas 17.5% in spring season (April) and none of the patient come in month of autumn

and winter season.

Kanski and Duke elder described the limbal form is common in dark races and palpebral and corneal involvement in light skinned races.<sup>7,8</sup> In the present study the bulbar variety was found to be more common 57.5% followed by palpebral 26% and mixed 17.3%.

Corneal involvement is common in whites' races as described by Kanski Duke elder.<sup>7,8</sup> In the present study 1 out 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 shows corneal involvement. Superficial punctate keratitis is seen in 6 cases and subepithelial caring in 4 cases was observed.

The aim of this study is to review the effectiveness of currently available treatment options mainly newer topical medication that have multiple actions such as an antihistaminic effect coupled with mast cells stabilizers. Eg.-olopatadine and epinastine eye drops.

Our study has some limitations; firstly this is an environmental study and thus differs from conjunctival allergen challenge (CAC) model. The CAC model was reported to provide standardized, reproducible results there by avoiding the possibility of variability symptoms inherent in naturally occurring conditions, implying that they might have been exposed to varying amounts of allergen during the study. In order to minimize a large fluctuation of pollen, subjects of each season are selected in single group and evaluated within the same season. Moreover the patients included in the patients included in the study came from difference parts of our region both rural and urban and taking pollen counts and many difference areas would not have been feasible It might be argued that the observed results in this study were due to decreased allergen exposure during the study that the reduction in placebo scores serves as evidence of this purpose. The dual acting gents are those that have both antihistamine and mast cell stabilizing effect giving us two for the price of one. Primary drugs are azelastine, ketotifen, significantly better than placebo in relieving different symptoms clustures associated with allergic eye diseases. There were differences found, however in comparison studies.

Olopatadine became available early in 2003 and now currently available in South Asian country including India and has rapidly become the gold standard treatment option for allergic eye disease. Olopatadine has been shown to be more efficacious at duration of action than epinastine and have superior comfort upon instillation in the eye. It has

been approved for all symptom of allergic conjunctivitis.

In the present study olopatadine reduce itching by (87.5%), ropy discharge (79.3%). Epinastine reduce itching by (80.64%), ropy discharge (77.4%).

Reduction symptom were also observed in placebo eye of each group which was significant at day 42 when compared to baseline score which may be due to flushing and diluting effect of artificial tear on allergic antigen and chemical mediators.

## 5. Conclusion

It was concluded that the present study shown that both olopatadine and epinastine is effective and reducing symptoms of VKC as compared to placedo. However olopatadine is more effective than epinastine in alleviating the clnical feaure of VKC mainly itching.

## 6. Conflict of Interest

None.

## 7. Source of Funding

None.

## 8. Ethical Approval

Permission for the study was obtained from the College authorities prior to commencement

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