International Journal of Research in Medical Sciences
Ansari TH et al Int J Res Med Sci. 2020 Oct;8(10):3565-3570
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20204230

Original Research Article

Comparison of two ophthalmic solutions of olopatadine hydrochloride (0.1%) and epinastine hydrochloride (0.05%) on clinical signs of vernal keratoconjunctivitis and side effects of the two drugs

Tahir Husain Ansari[1], Yusuf Rizvi[2]*

[1]Department of Ophthalmology, Government Medical College, Badaun, Uttar Pradesh, India
[2]Department of Ophthalmology, Rohilkhand Medical College, Bareilly, Uttar Pradesh, India

Received: 19 July 2020
Revised: 19 August 2020
Accepted: 20 August 2020

***Correspondence:**
Dr. Yusuf Rizvi,
E-mail: yrizavi06@yahoo.co.in

ABSTRACT

Background: Vernal keratoconjunctivitis (VKC) is a recurrent, bilateral, external, ocular inflammation primarily affecting young adults living in warm dry climates. The objectives of the research was to compare the two ophthalmic solutions of olopatadine hydrochloride (0.1%) and epinastine hydrochloride (0.05%) on clinical signs of vernal keratoconjuntivitis and to determine side effects of both the drugs.
Methods: The study was carried out in 40 patients who attended the out-patient department (OPD) Ophthalmology, Darbhanga Medical College and Hospital, Laheriasarai from July 2007 to December 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: Mean score of palpebral hyperemia at 0, 14, 28 and 42 days in olopatadine treated eye were 2.1, 1.4, 0.8 and 0.4 respectively having p value <0.01, and <0.01 and <0.05 respectively, while mean score at same stages in placebo eye were 2.1, 2, 1.9, and 1.5 having value >0.05. Epinastine treated group mean score of palpebral hyperemia were <0.01 and <0.01 respectively in epinastine treated eye whereas in placebo treated eye, mean score were 2.1, 2.0, 1.8 and 1.6 respectively having p value >0.05 in all stages. Statistically insignificant reduction at day 14 while very significant reduction at day 28 and 42 was observed in epinastine treated eye as compared to placebo.
Conclusions: The present study had shown that both olopatadine and epinastine were effective in treating clinical signs of VKC as compared to placebo.

Keywords: Olopatadine hydrochloride, Epinastine hydrochloride, Vernal keratoconjunctivitis, Placebo, Palpebral hyperemia

INTRODUCTION

Vernal keratoconjunctivitis (VKC) is an allergic disorder in which immunoglobulin E (IgE) and cell mediated immune mechanism play an 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.[1] 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) describes that the disease recurs in early summer rather than in spring. Tobgy (1935)

named fine corneal epithelial disturbances as "keratitis epithelialis vernalis".[2]

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 (Herbert, 1903-1907) and if untreated it can lead to sight threatening complications.

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 are involved in VKC has greatly facilitated the development of more effective treatment options.[3]

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 histaminic H1-receptors.

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. United States food and drug administration (US-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 anti-itching 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 olopatadine hydrochloride (0.1%) and epinastine hydrochloride (0.05%) on the clinical signs of VKC and side effects of two drugs.[1]

METHODS

The present hospital based 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 to December 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. Purposive sampling was used. 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 e.g. itching foreign sensation, swollen eyes, ropy discharge and photophobia were graded according to scoring system as indicated in Table 1 and patients' symptoms were categorized by asking the severity of symptoms to the patients.

The patients selected for study were divided into two groups: group 1 comprised 20 patients who received olopatadine drop in one eye and the placebo (artificial tear) in other eye both twice daily; and group-2 comprised 20 patients who 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.

Clinical signs were evaluated at base line (day 0) and at day 14, 28 and 42 of treatment. Data obtained were analyzed by using student t test (paired and unpaired) for comparison.

Table 1: Scoring of signs of vernal conjunctivitis.

Signs	Score 0	Score 1	Score 2	Score 3	Score 4
Palpebral conjunctival hyperemia	Absent	Minimal redness	Obvious redness but not diffuse	Diffuse redness	Very marked diffuse redness
Bulbar conjunctival hyperemia	Absent	Minimal redness	Obvious but not diffuse redness	Diffuse redness	Very marked diffuse redness
Limbal gelatinous infiltrate	Absent	Upto one quadrant	Upto two quadrant	Upto three quadrant	More than three quadrant
Horner trantas dots	Absent	Upto one quadrant	Upto two quadrant	Upto three quadrant	More than three quadrant
Chemosis of conjuctival	Absent	Minimal	Focal area of chemosis	Obvious	Marked diffuse with conjunctival prolapse
Papillae	Absent	Mosaic flat appearance	Some are elevated and some flat	Elevated with definite appearance	Cobble stone papillae
Ropy discharge	Absent	Minimal	Thin ropy	Thick ropy	Very thick profuse discharge

Data processing and analysis

Clinical signs and symptoms were evaluated at base line (day 0) and at day 14, 28 and day 42 of treatment. Data obtained were analyzed by using student "t" test (paired and unpaired) for comparison.

RESULTS

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 the 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%) cases of palpebral, six out of 23 (26%) cases of bulbar and three out of seven (42.86%) cases of mixed form shows corneal involvement. Superficial punctate keratitis in six cases and sub epithelial scaring in four cases were observed. Corneal involvement was observed more among patients having bulbar and mixed type of disease.

Palpebral hyperemia

Olopatadine treated group mean score of palpebral hyperemia at 0, 14, 28 and 42 days in olopatadine treated eye were 2.1, 1.4, 0.8 and 0.4 respectively having p value <0.01, and <0.01 and <0.05 respectively while mean score at same stages in placebo eye were 2.1, 2, 1.9, and 1.5 having value >0.05. Thus statistically significant reduction was observed at day 14, 28 and 42 with olopatadine.

Epinastine treated group mean score of palpebral hyperemia were <0.01 and <0.01 respectively in epinastine treated eye whereas in placebo treated eye mean score were 2.1, 2.0 1.8 and 1.6 respectively having p value >0.05 in all stages.

Thus statistically very significant reduction of palpebral hyperemia was observed in epinastine treated group as compared to placebo (Table 2).

Bulbar hyperemia

Olopatadine treated group-mean scores of bulbar hyperemia at 0, 14, 28 and 42 days in olopatadine treated eye were 2.5, 1.8, 1.2 and 0.4 respectively having p value <0.01, 0.01 and <0.01 in between them respectively while mean scores at same stages in placebo eye were 2.5, 2.4, 2.2 and 1.9 having p value >0.05.

Thus statistically significant reduction of bulbar hyperemia was observed in all stages of eye as compared to placebo.

Epinastine treated group-mean score of bulbar hyperemia at 0, 14, 28 and 42 days in epinastine treated eye were 2.3, 1.6, 1.0 and 0.5 respectively having p value <0.01, <0.01 and <0.01 in between them while mean score at same staged in placebo eye were 2.3, 2.2, 2.0 and 1.7 respectively having p value >0.05 in all stages.

Thus statistically significant reduction of bulbar hyperemia was observed in all stages of visit in epinastine treated eye as compared to placebo (Table 3).

Limbal infiltrate

Olopatadine treated group-mean scores of limbal infiltrate at 0, 14, 28 and 42 days in olopatadine treated eye were 2.2, 2, 1.7 and 0.7 and respectively having p value >0.05,<0.01 and <0.01 respectively in between them while mean scores at same stages in placebo eye were 2.2, 2.2, 2.1 and 1.9 respectively having p value >0.05 at all stages.

Thus statistically insignificant reduction of limbal infiltrate at day 14 and very significant reduction at day 28 and 42 were observed in olopatadine treated eye as compared to placebo.

Epinastine treated group-mean score at 0, 14, and 28 and 42 days in epinastine treated eye were 2.2, 2.0, 1.6 and 0.9 respectively having p value >0.05, <0.01 and 0.01 in between them while mean score at same stages in placebo treated eye were 2.2, 2.1, 1.9 and 1.7 respectively having p value >0.05 at all stages.

Thus statistically in significant reduction at day 14 while very significant reduction at day 28 and 42 was observed in epinastine treated eye as compared to placebo (Table 4).

Papillary hypertrophy

Olopatadine treated group-mean scores of papillary hypertrophy at 0, 14, 28 and 42 days in olopatadine treated eye were 2.2, 1.9, 1.4 and 0.7 respectively having p value >0.05, <0.01 and <0.01 in between them respectively while mean scores at same stages in placebo eye were 2.2, 2.1, 1.9 and 1.7 respectively having p value >0.05 in all stages.

Thus statistically insignificant reduction of papillary hypertrophy at day 14 and 28 but significant reduction at day 42 of papillary hypertrophy was observed in olopatadine eye drop as compared to placebo.

Epinastine treated group-mean score at 0, 14, 28 and 24 day in epinastine treated eye were 2.2, 1.9, 1.3 and 0.8 respectively having p value more than 0.5, <0.01 and <0.01 in between them while mean score at same stages in

placebo eye were 2.2, 2.1, 1.8 and 1.5 respectively having p value >0.05, >0.05 and 0.05 in between them. Thus statistically insignificant reduction of papillary hypertrophy at day 14 and very significant reduction at day 28 and 42 was observed in epinastine treated eye as compared to placebo (Table 5).

Table 2: Effect of olopatadine (0.1%) and epinastine (0.05%) ophthalmic on palpebral hyperemia 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	2.1	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	1.0 p<0.01	0.5 p<0.02	76.19
Placebo	2.1	2.0 p>0.05	1.8 p>0.05	1.6 p>0.05	23.81

Table 3: Effect of olopatadine (0.1%) and epinastine (0.05%) on bulbar hyperemia 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	2.5	1.8 p>0.1	1.2 p<0.01	0.4 p<0.01	80.0
Placebo	2.5	2.4 p>0.05	2.2 p>0.05	0.4 p>0.05	24
Epinastine	2.3	1.6 p<0.01	1.0 p<0.01	0.5 p<0.01	78.26
Placebo	2.3	2.2 p>0.05	2.0 p>0.05	1.7 p>0.05	26.08

Table 4: Effect of olopatadine (0.1%) and epinastine (0.05%) on limbal infilterate in VKC.

Drug	Day 0 mean score (baseline)	Day 14 mean score	Day 28 mean score	Day 42 mean score	Percentage reduction in signs and symptoms (%)
Olopatadine	2.2	2.0 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	2.0 p>0.05	1.6 p<0.01	0.9 p<0.01	59.09
Placebo	2.2 p>0.05	2.1 p>0.05	1.9 p>0.05	1.7 p>0.05	22.73

Table 5: Effect of olopatadine (0.1%) and epinastine (0.05%) on papillary hypertrophy 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	2.2	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

DISCUSSION

The aim of this study was 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 e.g. olopatadine and epinastine eye drops.

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

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

Vernal conjunctivitis is an allergic disorder and existence of sensitivity to pollen, animal inhalant, dust and moulds have been investigated by several workers. Other researchers 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 the rural area while 7 patients (17.50%) were from urban area.[7]

Kanski and Elder described the limbal form is common in dark races and palpebral and corneal involvement in light skinned races.[8,9] In the present study the bulbar variety was found to be more common 57.5% followed by palpebral 26% and mixed 17.3%.

Lanier et al (2004) on their study on clinical efficacy of olopatadine verses epinastine ophthalmic solution in the conjuntival allergen challenge model come to the conclusion that olopatadine is significantly more effective than epinastine in controlling itching, redness and chemosis associated with allergic conjunctivitis.[7]

Olapatadine 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 the sign and symptom of allergic conjunctivitis.

In the present study olopatadine reduced itching by 87.5%, ropy discharge (79.3%), palpebral conjuntival hyperemia (80.95%), bulbar conjunctival hyperemia (80%), limbal infiltrate (68.18%), and papillary hypertrophy (65.21%).

Epinastine reduce itching by 80.64%, ropy discharge (77.4%) palpebral conjunctival hyperemia (76.19%), bulbar conjunctival hyperemia (78.28%), limbal infiltrate (59.09%), and papillary hypertrophy (63.64%).

Reduction of sign 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.

The present study shown that both olopatadine and epinastine is effective and reducing the signs and symptoms of VKC as compared to placedo. However olopatadine is more effective than epinastine in alleviating the clnical feaure of VKC mainly itching, hyperemia and limbal infiltrate score.

The present study shows that both in olopatadine treated group and epinastine treated group adverse effects were seen in 2 (10%) patients in each group. The adverse effects in olopatadine treated group were headache, dry eye and asthenia and in epinastine treated group were red eye, headache, burning sensation and dry mouth.

CONCLUSION

It was concluded that the present study shown that both olopatadine and epinastine is effective and reducing signs of VKC as compared to placebo. However olopatadine is more effective than epinastine in alleviating the clinical feature of VKC mainly itching.

Limitation

This research was a hospital based study and sample size was small. The result of the study cannot be implemented to the large population of India.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

ACKNOWLEDGEMENTS

The authors would like to express their profound gratitude to all the participants.

REFERENCES

1. Aguilar J. Comparative study of clinical and tolerance in seasonal allergic conjunctivitis management with 0.1% olopatadine versus 0.05% ketotifen. Acta Ophthalmol Scand. 2000;230:52-5.
2. Kamei C, Akagi M, Mio M, Kitazumi K, Izushi K, Masaki S, et al. Anti-allergic effect of epinastine on immediate hypersensitivity reactions; elucidation of the mechanism for histamine release inhabitation. Immunopharmacol Immunotoxicol. 1992;14:191-205.

3. Spangler DL, Bensch G. Evaluation of the efficacy of 0.1% olopatadine hydrochloride ophthalmic solution and 0.05% azelastine hydrochloride ophthalmic solution in CAC model. Clin Ther. 2001;2(8):1272-80.
4. Secchi AG, Tognon S, Leonardi A. Topical use of cyclosporine in the treatment of vernal keratoconjunctivitis. Am J Ophthalmol. 1990;110(6):641-5.
5. Yani JM, Weiner LK, Sharif NA. Inhibition of histamine induced human conjunctival epithelial cells by ocular allergy drugs. Arch Ophthalmol. 1999;117(5):643-7.
6. Leonardi A, Secchо AG. Vernal keratoconjunctivitis thorough review. Int Ophthalmol Clin. 2003;43(1):41-58.
7. Lanier BQ, Finegoild I, D'Arienzo P, Granet D, Epstein AB, Ledgerwood GL. Clinical efficacy of olopatadine vs epinastine ophthalmic solution in the conkunctival llergen challenge model. Curr Med Res Opin. 2004;20(8):1227-33.
8. Kanski J, Bowling B. Kanski's Clinical Ophthalmology. 8th Edition. A Systematic Approach. 2015. Elsevier.
9. Duke-Elder S. Duke elder's system of Ophthalmology. 1958. Mosby, St. Louis.
10. Lanier BQ, Finegoild I, D'Arienzo P, Granet D, Epstein AB, Ledgerwood GL. Clinical efficacy of olopatadine vs epinastine ophthalmic solution in the conkunctival llergen challenge model. Curr Med Res Opin. 2004 Aug. 20(8) 1227-33.

Cite this article as: Ansari TH, Rizvi Y. Comparison of two ophthalmic solutions of olopatadine hydrochloride (0.1%) and epinastine hydrochloride (0.05%) on clinical signs of vernal keratoconjunctivitis and side effects of the two drugs. Int J Res Med Sci 2020;8:3565-70.