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Original Research Article

Assessing Efficacy and Safety of Olopatadine 0.1% Ophthalmic Solution and Bepotastine 1.5% Ophthalmic Solution in Patients with Vernal Keratoconjunctivitis

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Abstract

Aim: The purpose of the present study was intended to compare the effectiveness and safety of olopatadine 0.1% ophthalmic drops and bepotastine besilate 1.5% ophthalmic drops with BD administration to relieve the symptoms of VKC in a tertiary care hospital in Bihar region.

Methods: The study was done in the Department of Pharmacology, DMCH, Laheriasarai, Darbhanga, Bihar, India for duration of 10 months. By simple randomization (odd/even number) method, registered patients were grouped into A and B. Group A and Group B were given olopatadine 0.1% ophthalmic drops and bepotastine besilate 1.5% ophthalmic drops, respectively, administered one drop in the affected eye twice daily for 6 weeks.

Results: The itching scores among the treatment groups with all follow-ups compared with baseline are not statistically significant. The mean ocular discomfort scores during each visit. At the 1st, 2nd, and 3rd follow-up, there is statistical significance in ocular discomfort scores with Group B. In Group B, during the 2nd, 3rd, and 4th follow-ups, there is statistical significance in watering scores ($P < 0.05$).

Conclusion: In this study, based on the evaluation of therapeutic performance, bepotastine eye drops proved quicker relief of symptoms and signs compared to olopatadine eye drops but was not statistically significant which would prove beneficial for the patients.

Keywords: Bepotastine, Efficacy, Olopatadine, Vernal keratoconjunctivitis

Introduction

Ocular allergic diseases are common worldwide and mainly consist of conjunctivitis with or without involvement of cornea. Allergic Conjunctivitis (AC) is the most common type of ocular allergy and affects 6-30 % of the general population and up to 30% of children and adolescents. [1] Eye allergies can be seasonal, perennial, or chronic; and, are a part of generalised allergic syndromes like seasonal or perennial keratoconjunctivitis which are directly related to allergic diseases like rhinitis, asthma, or other atopic conditions. [2] Ocular surface diseases are classified into Seasonal Allergic Conjunctivitis (SAC), Perennial Allergic Conjunctivitis (PAC), Vernal Keratoconjunctivitis (VKC), Atopic Keratoconjunctivitis (AKC), contact blepharoconjunctivitis; and non allergic hypersensitivity ailments like Giant Papillary Conjunctivitis (GPC). [3]

The VKC is a chronic, recurrent, bilateral inflammation of the conjunctiva mainly occurring in kids and adolescents with a male predominance. It is a seasonal allergic disease, but in severe cases, it may turn into a perennial one. It includes a wide spectrum of manifestations like intense itching, tearing, red eye, foreign body sensation, mucus discharge, photophobia, lid oedema, chemosis, papillae hypertrophy in tarsal and/or limbal areas, giant papillae, Horner-Trantas dots, and corneal epitheliopathy. [4,5] Vernal Keratoconjunctivitis has a worldwide occurrence, usually affects young males in dry and hot climatic regions. In western Europe in a survey, the prevalence of the disease ranged from 1.16 to 10.55 per 10,000 population. The disease is common in temperate zones of Mediterranean areas, Central and West Africa, the Middle East, Japan, the Indian subcontinent and South America. In regions of Cameroon, Turkey, India, and Israel, prevalence ranges from 3% to 10%

in younger population. [6] Two studies from northern and southern parts of India also reported the prevalence of VKC to be 5.1% and 18% in school going children. [7,8]

In VKC, avoidance of allergens/triggers along with basic eye hygienic practices should be advocated in all patients. Topical agents having dual antihistaminic and mast cell stabilising activity are first line measures in in mild to moderate cases; in refractory, complicated and severe cases, additional treatment options are corticosteroids and immunomodulators. Surgical treatment may be required in complications like shield ulcers, corneal opacities, refractory giant papillae. [6,9] Olopatadine was the first dual-action topical agent approved for the treatment of AC, with the convenience of once or twice daily preparations, and was more effective than second-generation oral or topical antihistamines. In addition, when compared to ketotifen, epinastine, and azelastine, it had a better efficacy and was more comforting for patients. [10] Bepotastine is the last to be approved among dual-action topical agents; and has demonstrated superior efficacy in controlling the allergic symptoms in AC when compared with other drugs having similar properties. [11]

Vernal Keratoconjunctivitis has a worldwide occurrence, usually affects young males in dry and hot climatic regions. In western Europe in a survey, the prevalence of the disease ranged from 1.16 to 10.55 per 10,000 population. The disease is common in temperate zones of Mediterranean areas, Central and West Africa, the Middle East, Japan, the Indian subcontinent and South America. In regions of Cameroon, Turkey, India, and Israel, prevalence ranges from 3% to 10% in younger population. [12] Two studies from northern and southern parts of India also reported the prevalence of VKC to be 5.1% and 18% in school going children. [13,14]

A new generation of drugs such as bepotastine, olopatadine, epinastine, ketotifen and azelastine has shown dual activity of mast-cell stability and H1 receptor antagonism makes them suitable for twice-daily dosing. [15] Besides these action they also exert anti-inflammatory effects through several different mechanisms. These classes of drugs comprise the first line of pharmacological treatment. [16]

The purpose of the present study was intended to compare the effectiveness and safety of olopatadine 0.1% ophthalmic drops and bepotastine besilate 1.5% ophthalmic drops with BD administration to relieve the symptoms of VKC in a tertiary care hospital in Bihar region.

Materials and Methods

The study was done in the Department of Pharmacology, DMCH, Laheriasarai, Darbhanga, Bihar, India for duration of 10 months. By simple randomization (odd/even number) method, registered patients were grouped into A and B. Group A and Group B were given olopatadine 0.1% ophthalmic drops and bepotastine besilate 1.5% ophthalmic drops, respectively, administered one drop in the affected eye twice daily for 6 weeks.

For participants above 18 years of age, written informed consent was taken in an authorized format in local language after describing all study procedures and course of action. For participants less than 18 years of age, their parents or guardians were explained the procedures, and written informed consent was attained. For illiterate people, left thumb mark was taken. After acquiring informed consent from all participants, the analytical details of 85 patients including past and present history and clinical and slit-lamp examination of eyes performed were entered. Diagnosis for VKC was made by an ophthalmologist. Following the screening of 85 patients, 60 patients were enlisted in the study who fit into inclusion and exclusion criteria.

Inclusion criteria

- Clinically diagnosed with VKC by an ophthalmologist
- Patients with the age group of 5–25 years.
- Patients who can adherent to follow-up schedule.

Exclusion criteria

- Age less than 5 years
- Contact lens wearer during the period of study
- Patients with active ocular infections and pathological conditions
- Patients with ocular disorders such as pterygium, dry eyes, and ophthalmic conditions such as uveitis or glaucoma
- History of ocular surgery in 3 months.

By simple randomization (odd/even number) method, registered patients were grouped into A and B. Group A and Group B were given olopatadine 0.1% ophthalmic drops and bepotastine besilate 1.5% ophthalmic drops, respectively, administered one drop in the affected eye twice daily for 7 weeks.

The ocular signs such as conjunctival hyperemia and papillary hypertrophy were evaluated. The gradings were given according to the severity of signs (absence of signs as grade 0, mild signs as grade 1, moderate signs as grade 2, and severe signs as grade 3). Ocular symptoms such as itching, discomfort, and watering were estimated by discussing with the patients, and grading was given depending on severity (absence of signs as grade 0, mild signs as grade 1, moderate signs as grade 2, and severe signs as grade 3). During the study, none of the patients were lost to follow-up.

Statistical analysis

The observations and results were tabulated accordingly and data were analyzed using the SPSS Version 16. The unpaired t-test is used as the test of significance in between two groups. P value is statistically significant when it is less than 0.05.

Results

Table 1: Mean itching scores during each visit

Itching scores	Group A Olopatadine		Group B Bepotastine		Unpaired t-test significance level
	Mean	SD	Mean	SD	
Preintervention	2.55	0.320	2.50	0.325	1.000
1st week (1st visit)	2.60	0.330	2.56	0.328	1.000
3rd week (2nd visit)	2.10	0.4	2.05	0.296	0.430
5th week (3rd visit)	1.56	0.374	1.50	0.270	0.380
7th week (4th visit)	0.50	0.650	0.40	0.320	0.225

The itching scores among the treatment groups with all follow-ups compared with baseline are not statistically significant ($P > 0.05$).

Table 2: Mean ocular discomfort scores during each visit

Ocular discomfort scores	Group A Olopatadine		Group B Bepotastine		Unpaired t-test significance level
	Mean	SD	Mean	SD	
Preintervention	2.77	0.330	2.85	0.310	0.646
1st week (1st visit)	2.65	0.435	2.10	0.255	0.000
3rd week (2nd visit)	2.00	0.408	1.25	0.410	0.000
5th week (3rd visit)	1.25	0.415	0.80	0.480	0.000
7th week (4th visit)	0.40	0.476	0.16	0.332	0.095

At the 1st, 2nd, and 3rd follow-up, there is statistical significance in ocular discomfort scores with Group B ($P < 0.05$).

Table 3: Mean watering scores during each visit

Ocular discomfort scores	Group A Olopatadine		Group B Bepotastine		Unpaired t-test significance level
	Mean	SD	Mean	SD	
Preintervention	2.92	0.275	2.90	0.270	1.000
1st week (1st visit)	2.85	0.410	2.10	0.000	0.000
3rd week (2nd visit)	2.00	0.000	1.06	0.210	0.000
5th week (3rd visit)	1.10	0.277	0.30	0.460	0.000
7th week (4th visit)	0.38	0.488	0.10	0.277	0.018

In Group B, during the 2nd, 3rd, and 4th follow-ups, there is statistical significance in watering scores ($P < 0.05$).

Table 4: Mean conjunctival hyperaemia scores during each visit

Conjunctival hyperaemia scores	Group A Olopatadine		Group B Bepotastine		Unpaired t-test significance level
	Mean	SD	Mean	SD	
Preintervention	2.90	0.215	2.90	0.205	1.000
1st week (1st visit)	2.78	0.440	1.98	0.200	0.000
3rd week (2nd visit)	2.20	0.510	1.08	0.277	0.000
5th week (3rd visit)	1.08	0.542	0.32	0.545	0.000
7th week (4th visit)	0.28	0.432	0.20	0.374	0.460

During 1st, 2nd, and 3rd follow-ups, there is statistical significance in conjunctival hyperemia scores with Group B ($P < 0.05$).

Discussion

The VKC is a relatively uncommon, chronic, allergic disease of the conjunctiva, characterised by severe itching, sticky ropy mucous discharge, conjunctival hyperaemia, and large papillae in the upper tarsal and/or limbus with corneal involvement in some. [17,18] Basic eye care, avoidance of allergens or provocative stimuli, and dual-acting topical drugs with antihistamine and mast cell stabilising properties are corner stones of

management of mild to moderate cases of VKC. [12,16,18]

Olopatadine is one such topical agent and is shown to be efficacious in reducing symptoms of AC; scores better than antihistamines. [19] It is a low-cost, effective, widely available therapy in India and without significant adverse effects. [20-22] Bepotastine, is also a similar drug, however it is less freely available and relatively costlier. It has been compared with olopatadine and other dual-action topical agents like alcaftadine in AC and was found to be more effective in controlling allergic symptoms, reducing ocular discomfort, and was preferred by patients in a few studies. [20,21,11]

The itching scores among the treatment groups with all follow-ups compared with baseline are not statistically significant. At the 1st, 2nd, and 3rd follow-up, there is statistical significance in ocular discomfort scores with Group B. In Group B, during the 2nd, 3rd, and 4th follow-ups, there is statistical significance in watering scores ($P < 0.05$). In a study done by McCabe and McCabe, bepotastine when compared to olopatadine showed a significant reduction in ocular itching and no significance between the comfort ratings. [11] A study between 0.1% olopatadine, 1.5% bepotastine, and 0.25% alcaftadine worked similarly in relief of mild-to-moderate allergic conjunctivitis symptoms, after 1 week of treatment. For allergic conjunctivitis, 0.2% olopatadine and 1.5% bepotastine eye drops are safe and well-tolerated topical medications. [23,24] In a study done by Hida et al., a comparison between 0.1% olopatadine hydrochloride and 0.025% ketotifen fumarate in VKC between the baseline and the 2nd visit, olopatadine treatment resulted in decreased burning, but ketotifen was slightly better after 4th visit. Papillae and Horner-trans dots in both classes were not significantly different.

In our study, during initial follow-ups on days 7, 21, and 35, bepotastine showed significant reduction in symptoms such as ocular discomfort, watering, and capillary hyperemia, suggesting the faster onset of action. Olopatadine showed marked reduction in papillary hypertrophy. After 7 weeks of treatment, both drugs were uniformly efficacious in reducing signs and symptoms of VKC. Studies with different attributes such as larger sample size, double masking, and patient preference and studies at different geographical locations and during different seasons of the year are needed for better definition of therapy in VKC.

Conclusion

In this study, although bepotastine altered the natural course with quicker onset of action at the end of the 8th week, both drugs are equally effective in reducing the signs and symptoms. Bepotastine proved quicker to relieve watering, ocular discomfort, and conjunctival hyperemia. Olopatadine provided faster improvement in papillary hypertrophy. Laboratory findings had no statistical significance between 0.1% olopatadine and 1.5% bepotastine in improving the AEC of the VKC patients. Being more commonly prescribed of the two drugs, olopatadine is readily available at the pharmacy store. Bepotastine, on the other hand, was available at a few selected retail outlets and was costlier. Researches with above-mentioned attributes can be done in the future.

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