



## Original Research Article

# Comparison of the efficacy and safety of bepotastine besilate 1.5% and loteprednol etabonate 0.5% ophthalmic solution in patients of vernal keratoconjunctivitis

Utsav Deep<sup>1</sup>, Ashish Chander<sup>1,\*</sup>, Priye Suman Rastogi<sup>1</sup>, Munavvar Ansari<sup>1</sup>

<sup>1</sup>Dept. of Ophthalmology, Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India



## ARTICLE INFO

## Article history:

Received 10-04-2020

Accepted 26-05-2020

Available online 30-09-2020

## Keywords:

Conjunctiva

Itching

Photophobia

Tearing

Vernal keratoconjunctivitis

## ABSTRACT

**Background:** Vernal keratoconjunctivitis is a chronic, recurrent, bilateral inflammatory disease of cornea and conjunctiva affecting young children. Various treatment modalities of VKC are topical mast cell stabilizers, anti-histaminics, corticosteroids, and immunomodulators.

**Aim and Objectives:** This study compared the efficacy of bepotastine besilate 1.5% and loteprednol etabonate 0.5% topical eye drops in subjects with allergic conjunctival disease.

**Materials and Methods:** The patients were re-examined after 1 week and 2 weeks. At each follow up visit, best corrected visual acuity, anterior segment examination using slit lamp, tear film examination (Schirmer's test and tear film breakup time) and intraocular pressure were measured. Patients were scored based on severity of signs and symptoms on day 1, 7 and 15.

**Results:** Itching, tearing, photophobia, upper tarsal papillae, limbus, keratitis and discharge score 1 and 2 for both eyes at day 1, 7 and 15 was significantly more among Bepotastine Besilate 1.5% compared to Loteprednol Etabonate. The mean IOP for both eyes at day 1, 7 and 15 was significantly more among Loteprednol Etabonate 0.5% compared to Bepotastine Besilate 1.5%.

**Conclusion:** This study demonstrated that LE was more efficacious than B.B in treating patients of VKC, but the mean IOP was found to be more in patients on LE.

© 2020 Published by Innovative Publication. This is an open access article under the CC BY-NC license (<https://creativecommons.org/licenses/by-nc/4.0/>)

## 1. Introduction

Allergic conjunctival disease (ACD) is defined as “a conjunctival inflammatory disease associated with a type I allergy accompanied by some subjective and objective symptoms.”<sup>1</sup> Types of ocular allergy include seasonal conjunctivitis, perennial conjunctivitis, atopic keratoconjunctivitis and vernal keratoconjunctivitis.<sup>2</sup>

Vernal keratoconjunctivitis (VKC) is a chronic, recurrent, bilateral inflammatory disease of cornea and conjunctiva affecting young children, mostly in their first decade.<sup>3</sup> VKC is a disease of warm climate and warm weather months.<sup>4</sup> The pathology is an immunologically mediated, hypersensitive reaction to environmental antigens., mediated by Th-2 lymphocytes (TypeIV hypersensitivity reaction).<sup>2,5</sup>

“Diagnosis of this Allergic condition is done by the presence of characteristic clinical features which consist of itching, cobblestone papillae seen over upper tarsal conjunctiva, Tranta's spots over the limbus and superficial keratitis.”<sup>6</sup> Broadly the treatment of VKC is divided into preventive, clinical and surgical options. Preventive measures include eliminating or avoiding allergens like house dust mites and pollen, while surgical options involves scraping fibrin from non-healing shield ulcers or removing upper tarsal giant papillae; however surgical options are reserved for severe cases.<sup>2</sup> Various treatment modalities of VKC are topical mast cell stabilizers, anti-histaminics, corticosteroids, and immunomodulators.<sup>7</sup>

Steroids are being used as the mainstay of treatment for VKC. Loteprednol etabonate (LE) is the 17 $\beta$ -chloromethyl ester of  $\Delta$ 1-corticenic acid with a 17 $\alpha$ -etabonate moiety.<sup>8</sup> Various trials and studies have provided a promising result of this drug. However, because steroids are associated with

\* Corresponding author.

E-mail address: [utsavthemanchala@gmail.com](mailto:utsavthemanchala@gmail.com) (A. Chander).

treatment related adverse effect, such as cataract, glaucoma and keratitis, they should be reserved for the management of acute allergic crises and for no more than 2 to 4 weeks.<sup>2</sup>

The newest type of topical anti- allergy medications for allergic conjunctivitis is the dual action agent, namely bepotastine which combines strong antihistaminic activity with mast cell stabilizing properties to provide both rapid and long lasting relief. “Bepotastine besilate is a dual-action agent, a highly selective histamine H<sub>1</sub>-receptor antagonist<sup>9,10</sup> with potent mast cell-stabilizing effects.<sup>11–16</sup>”

In the past, various studies have been done to compare the efficacy of bepotastine and loteprednol with other anti-allergic drugs. However, there are no study available comparing bepotastine and loteprednol in vernal keratoconjunctivitis. On the basis of that, this study compared the efficacy of bepotastine besilate 1.5% and loteprednol etabonate 0.5% topical eye drops in subjects with allergic conjunctival disease.

## 2. Materials and Methods

This prospective randomized clinical study was conducted after clearance from Board of Studies and Ethical committee in the Department of Ophthalmology, TMMC & RC, Moradabad (UP).

### 2.1. Sample size

The study population has been calculated by using G-power with 80% of the power and 5% of the significance level. The total sample size was determined to be 100, randomly divided into 2 groups of 50 each.

### 2.2. Randomization

Patients were randomized into two groups, group A and group B based on alternate sequencing of patients, even numbers were Group A and odd numbers were Group B. Group A patients (n=50) were started on topical bepotastine 1.5% twice a day and Group B patients (n=50) were started on topical loteprednol 0.5% four times a day.

### 2.3. Inclusion and Exclusion criteria

The study subjects were chosen as per the inclusion and exclusion criteria:

#### 2.4. Inclusion criteria

1. Patients diagnosed with allergic conjunctivitis on slit lamp examination.
2. Age more than 5 years.

#### 2.5. Exclusion criteria

1. Patients having known hypersensitivity to either agent.

2. Patients already on medication(s for seasonal allergic conjunctivitis.
3. Patients having any active ocular disease or other significant illness, which hampers the examination as per the protocol.
4. Patients who had undergone refractive surgery within 6 months.
5. Patients using contact lenses.

### 2.6. Study procedure

After obtaining a written informed consent, each patient were asked a detailed ocular and systemic history, using a pre-formed proforma. The characteristic symptoms, duration of symptoms, occurrence of symptoms, whether seasonal or perennial, family and personal history of allergy and past treatment.

Patients were re-examined after 1 week and 2 weeks. At each follow up visit, best corrected visual acuity, anterior segment examination using slit lamp, tear film examination (Schirmer's test and tear film breakup time) and intraocular pressure were measured.

### 2.7. Evaluation

After the initial approach and group assignment, we applied a grading score for the objective assessment of signs and symptoms. The Symptoms and signs were assessed and graded by severity from 0 to 3, with higher scores indicating greater severity. Patients were also assessed regarding changes in IOP, tear film status, slit lamp examination. Patients were also assessed for any adverse effects on day 1, 7 and 15. Patients were scored based on severity of signs and symptoms on day 1, 7 and 15.

## 3. Results

The distribution of age groups and gender had no significant difference in distribution of age groups between Bepotastine Besilate 1.5% and Loteprednol Etabonate 0.5%. (Table 1)(Figure 1)

Itching and tearing score 1 and 2 for both eyes at day 1, 7 and 15 was significantly more among Bepotastine Besilate 1.5% compared to Loteprednol Etabonate 0.5%. (Table 2) Foreign body Sensation score 1 and 2 for both eyes at day 1 and 7 was significantly more among Loteprednol Etabonate 0.5% compared to Bepotastine Besilate 1.5%. (Table 3)

Photophobia score 1 and 2 for both eyes at day 1, 7 and 15 was significantly more among Bepotastine Besilate 1.5% compared to Loteprednol Etabonate 0.5%. Conjunctival hyperemia score 1 and 2 for both eyes at day 1, 7 and 15 was significantly more among Bepotastine Besilate 1.5% compared to Loteprednol Etabonate 0.5%.

Upper tarsal papillae score 1 and 2 for right eye at day 7 and 15 was significantly more among Bepotastine Besilate 1.5% compared to Loteprednol Etabonate 0.5%.

Upper tarsal papillae score 1 and 2 for left eye at day 1, 7 and 15 was significantly more among Bepotastine Besilate 1.5% compared to Loteprednol Etabonate 0.5%.

The Limbus score 1 and 2 for both eyes at day 1, 7 and 15 was significantly more among Bepotastine Besilate 1.5% compared to Loteprednol Etabonate 0.5%.

Keratitis score 1 and 2 for right eye at day 1, 7 and 15 was significantly more among Bepotastine Besilate 1.5% compared to Loteprednol Etabonate 0.5%. Keratitis score 1 and 2 for left eye at day 1 and score 1 at day 7 was significantly more among Bepotastine Besilate 1.5% compared to Loteprednol Etabonate 0.5%.

Discharge score 1 and 2 of right eye at day 1, 7 and 15 was significantly more among Bepotastine Besilate 1.5% compared to Loteprednol Etabonate 0.5%. Discharge score 1 and 2 of left eye at day 1, 7 and 15 was significantly more among Bepotastine Besilate 1.5% compared to Loteprednol Etabonate 0.5%.

The mean IOP for both eyes at day 1, 7 and 15 was significantly more among Loteprednol Etabonate 0.5% compared to Bepotastine Besilate 1.5%. (Figures 2 and 3)

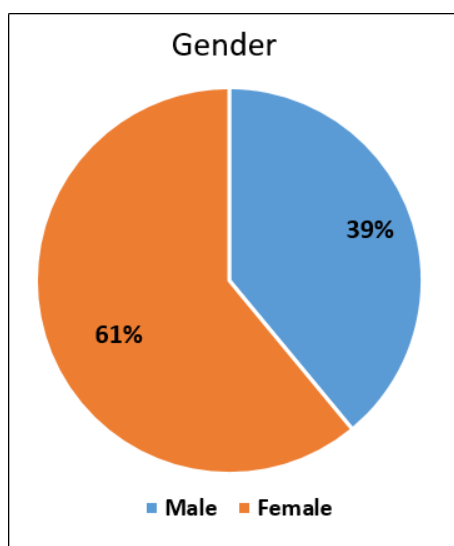


Fig. 1: Distribution of study population according to gender

#### 4. Discussion

Management strategies are changing rapidly; many new treatments are being developed and established agents are being applied differently. Eye care practitioners, primary care providers, and allergists have a growing selection of topical agents from which to choose, with the principal goal of relieving and controlling the symptoms and signs of allergic conjunctivitis.<sup>17</sup>

Corticosteroids are very effective, particularly in quieting disease exacerbations. Prednisolone, fluorometholone, and dexamethasone have been selected for this purpose.

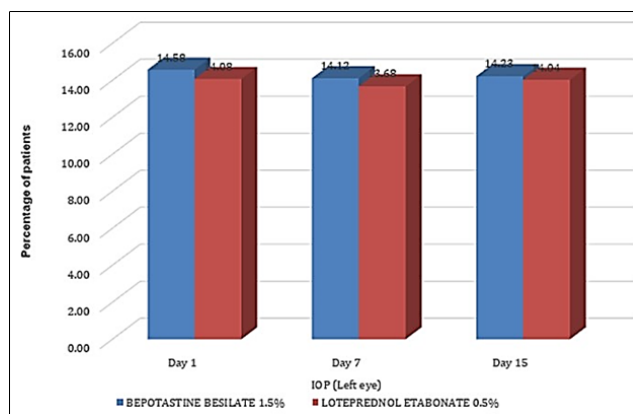


Fig. 2: Comparison of mean IOP (Left eye) at day 1, 7 and 15 between Bepotastine Besilate 1.5% and Loteprednol Etabonate 0.5%

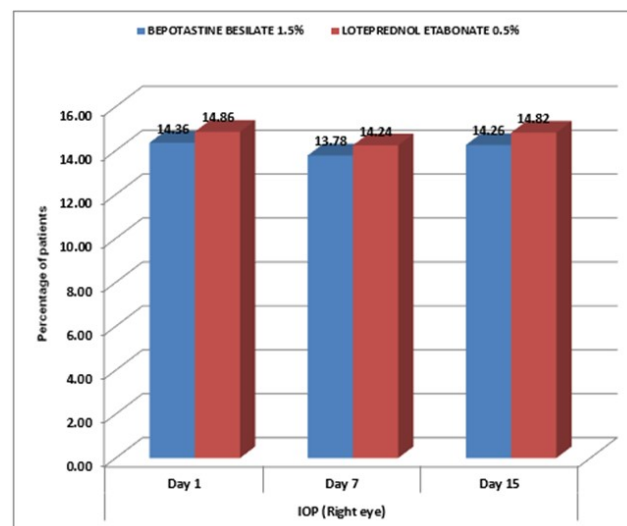


Fig. 3: Comparison of mean IOP (Right eye) at day 1, 7 and 15 between Bepotastine Besilate 1.5% and Loteprednol Etabonate 0.5%

With adequate monitoring, this is acceptable. However, loteprednol – an agent with less of an effect on intraocular pressure – has been found to be just as effective as prednisolone in VKC.<sup>18</sup>

BBOS 1.5% has previously been shown to rapidly relieve conjunctival allergen challenge (CAC)-induced ocular pruritus 8 hours following dosing, as well as reduce secondary signs of inflammation, such as eyelid swelling, ocular tearing, and ciliary hyperemia.<sup>19</sup>

Allergic diseases are on the rise. While several practitioners may see patients with allergy as the initial point of contact, a multidisciplinary approach is needed to maximize the treatment outcomes for patients with allergic conjunctivitis and other ocular allergic diseases.

**Table 1:** Distribution of study population according to age groups

		<b>Bepotastine besilate 1.5%</b>	<b>Loteprednol etabonate 0.5%</b>	<b>Total</b>
<b>Age groups</b>	5-10 years	30 60.0%	29 58.0%	59 59.0%
	11-15 years	20 40.0%	21 42.0%	41 41.0%
<b>Gender</b>	Male	31 62.0%	30 60.0%	61 61.0%
	Female	19 38.0%	20 40.0%	39 39.0%

**Table 2:** Comparison of Itching score at day 1, 7 and 15 between Bepotastine Besilate 1.5% and Loteprednol Etabonate 0.5%

<b>Itching - Left eye</b>		<b>Bepotastine Besilate 1.5%</b>	<b>Loteprednol Etabonate 0.5%</b>	<b>Chi-square value</b>	<b>p-value</b>
<b>day 1</b>	1	26 52.0%	28 56.0%	4.169	0.124
	2	20 40.0%	22 44.0%		
	3	4 8.0%	0 0.0%		
<b>day 7</b>	0	6 12.0%	12 24.0%	7.534	0.023*
	1	32 64.0%	35 70.0%		
	2	12 24.0%	3 6.0%		
<b>day 15</b>	0	22 44.0%	33 66.0%	10.443	0.005*
	1	20 40.0%	17 34.0%		
	2	8 16.0%	0 0.0%		

**Table 3:** Comparison of Foreign body Sensation at day 1, 7 and 15 between Bepotastine Besilate 1.5% and Loteprednol Etabonate 0.5%

<b>Foreign body Sensation - Left eye day</b>		<b>Bepotastine Besilate 1.5%</b>	<b>Loteprednol Etabonate 0.5%</b>	<b>Chi-square value</b>	<b>p-value</b>
<b>Day 1</b>	0	16 32.0%	3 6.0%	16.635	< 0.001*
	1	24 48.0%	44 88.0%		
	2	10 20.0%	3 6.0%		
<b>Day 7</b>	0	10 20.0%	6 12.0%	6.167	< 0.001*
	1	36 72.0%	44 88.0%		
	2	4 8.0%	0 0.0%		
<b>Day 15</b>	0	36 72.0%	21 42.0%	9.180	0.002*
	1	14 28.0%	29 58.0%		

## 5. Conclusion

Allergen avoidance is important to prevent allergic conjunctivitis; however, when avoidance fails and patients present with isolated symptoms, such as ocular itching, dual-activity agents should be prescribed first. This study demonstrated that LE was more efficacious than BB in treating patients of VKC, but the mean IOP was found to be more in patients on LE.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

## References

1. Takamura E, Uchio E, Ebihara N, Ohno S, Ohashi Y, Okamoto S, et al. Japanese Guideline for Allergic Conjunctival Diseases. *Allergol Int*. 2011;60(2):191–203.
2. Müller EG, dos Santos MS, Freitas D, Gomes JAP, Belfort R. Tacrolimus eye drops as monotherapy for vernal keratoconjunctivitis: a randomized controlled trial. *Arq Bras Oftalmol*. 2017;80(3):154–8.
3. Keklikci U, Dursun B, Cingu A. Topical Cyclosporine A 0.05% Eyedrops in the Treatment of Vernal Keratoconjunctivitis–Randomized Placebo-Controlled Trial. *Adv Clin Exp Med*. 2014;23(3):455–61.
4. Jun J, Bielory L, Raizman MB. Vernal Conjunctivitis. *Immunol Allergy Clin North Am*. 2008;28(1):59–82.
5. Kumar S. Vernal keratoconjunctivitis: a major Review. *Acta Ophthalmol*. 2009;87:133–47.
6. Rajappa S, F F, S A. A Clinical Study of Vernal Keratoconjunctivitis. *Int J Biomed Res*. 2014;5(4):284–7.
7. Gupta P, Goyal E, Devendra J. Comparative Study of 0.1% Olopatadine vs 0.05% Cyclosporine in Patients of Recalcitrant Vernal Keratoconjunctivitis. *Int J Adv Integr Med Sci*. 2016;1(4):139–42.
8. Comstock TL, DeCory HH. Advances in Corticosteroid Therapy for Ocular Inflammation: Loteprednol Etabonate. *Int J Inflamm*. 2012;2012. doi:10.1155/2012/789623.
9. Narita H, Kikuchi M, Asahi T. General pharmacology of betotastine besilate (TAU-284), a novel antiallergic agent. *Jpn Pharmacol Ther*. 1997;25:907–924.
10. Tashiro M, Duan X, Kato M. Brain histamine H1 receptor occupancy of orally administered antihistamines, bepotastine and diphenhydramine, measured by PET with 11C-doxepin. *Br J Clin Pharmacol*. 2008;65:811–21.
11. Yato N, Murata T, Saito N, Sakai A, Kikuchi M, Tsuzurahara K. Anti-allergic activity of betotastine besilate (TAU-284), a new anti-allergic drug. *Nihon Yakurigaku Zasshi*. 1997;110(1):19–29.
12. Sakai A, Kikuchi M, Yato N, Kikkawa S, Saito N, Narita H. Inhibitory effect of betotastine besilate on antigen-induced airway eosinophil infiltration and peripheral blood eosinophilia in mice. *Arzneimittelforschung*. 1997;47(8):954–8.
13. Ukai K, Takeuchi M, Masuda S. Clinical pharmacological study of anti-allergic agent TAU-184 (bepotastine besilate) - the effect on counting of eosinophils in nasal discharge, and the patency improvement of nasal cavity. *J Clin Ther Med*. 1997;13:1401–12.
14. Ueno M, Inagaki N, Nagai H, Koda A. Antiallergic Action of Betotastine Besilate (TAU-284) in Animal Models: A Comparison with Ketotifen. *Pharmacol*. 1998;57(4):206–14.
15. Honda H, Murata K, Hamazaki A. Inhibitory effect on anaphylactic reaction and histamine antagonizing action. *Jpn Pharmacol Ther*. 1997;25:879–88.
16. Sakamoto O, Okanari E, Ueno H. Suppression effects of the novel drug bepotastine besilate (TAU-284) on experimental asthmatic reactions in guinea pigs. *Jpn Pharmacol Ther*. 1997;25:889–94.
17. Naggalakshmi VS, Mishra P, Manavalan S, Sridevi V, Dineshababu G, Ramya M, et al. Vernal Keratoconjunctivitis: A Review. *J Evol Med Dent Sci*. 2014;3(54):12477–86.
18. Öner V, Türkcü FM, Taş M, Alakuş MF, Işcan Y. Topical loteprednol etabonate 0.5 % for treatment of vernal keratoconjunctivitis: efficacy and safety. *Jpn J Ophthalmol*. 2012;56(4):312–8.
19. McLaughlin J, Bergmann M, Williams J, Gomes P. Treatment of allergic conjunctivitis with bepotastine besilate ophthalmic solution 1.5%. *Clin Ophthalmol*. 2014;8:1495–1505.

## Author biography

**Utsav Deep** Resident

**Ashish Chander** Professor

**Priye Suman Rastogi** Associate Professor

**Munavvar Ansari** Assistant Professor

**Cite this article:** Deep U, Chander A, Rastogi PS, Ansari M. Comparison of the efficacy and safety of bepotastine besilate 1.5% and loteprednol etabonate 0.5% ophthalmic solution in patients of vernal keratoconjunctivitis. *Indian J Clin Exp Ophthalmol* 2020;6(3):440-444.