



ORIGINAL RESEARCH PAPER

Ophthalmology

COMPARATIVE EFFICACY OF BEPOTASTINE BESILATE 1.5% VS OLOPATADINE HYDROCHLORIDE 0.2% OPHTHALMIC SOLUTION IN THE IMMEDIATE RELIEF OF SYMPTOMS OF ALLERGIC CONJUNCTIVITIS

KEY WORDS: allergic conjunctivitis, bepotastine, olapatadine

Thangerani Raajaseharan

Professor of Ophthalmology, Govt. Stanley Medical College and Hospital, Chennai

Nazeem Farzana Ghouse*

Postgraduate Resident of Ophthalmology, Govt. Stanley Medical College and Hospital, Chennai *Corresponding Author

ABSTRACT

Ocular and nasal discomfort associated with allergic conjunctivitis is a common complaint in an ophthalmic OPD. Allergic conjunctivitis is a Type I hypersensitivity reaction triggered by repeated antigen exposure. After sensitization, contact with the allergen causes mast cell degranulation and histamine release. Targeting this are the dual action agents having anti-histaminic and mast- cell stabilizing properties – Bepotastine besilate 1.5% and Olopatadine hydrochloride 0.2% ophthalmic solution. A study population of 100 patients between 21 - 50 years with symptoms of allergic conjunctivitis after getting an informed consent were randomly instilled with one drop of the drug and assessed for immediate relief within 5min. Our study found that Bepotastine Besilate 1.5% showed a superior efficacy in the immediate relief of symptoms within 3 min. Thus proving that this non- steroidal drug can be used as an initial therapy for immediate relief of symptoms of allergic conjunctivitis.

INTRODUCTION:

Ocular discomfort associated with allergic conjunctivitis is a common patient complaint in the Ophthalmic OPD. These patients also have symptoms of nasal itching and rhinorrhea¹. All these symptoms have a negative impact on patients' daily activities and performance². This highlights the importance of proper treatment of allergic conjunctivitis.

Allergic conjunctivitis is due to a type I hypersensitivity reaction triggered by repeated antigen exposure. After sensitization, contact with the same allergen causes mast cell degranulation and histamine release³. Targeting this mechanism, are the topical FDA approved medication with both antihistaminic and mast cell-stabilizing properties - Bepotastine besilate 1.5% and Olopatadine hydrochloride 0.2% ophthalmic solution⁴. Our study aims to compare the immediate symptomatic relief of ocular itching, congestion and nasal symptoms of allergic conjunctivitis with both the drugs in a single-centre, patient preference study.

INCLUSION CRITERIA: All patients between 21- 50 years of age, who presented with symptoms of allergic conjunctivitis like ocular itching, congestion and itchy/runny nose

EXCLUSION CRITERIA: Concurrent ocular diseases, history of recent ocular surgery/infection in the last 6 months, narrow anterior chamber angles, pregnant/ lactating females, patients with known hypersensitivity to either agent used in the study, history of alcohol or drug abuse, presence of any significant illness, h/o intake of concurrent oral steroids or antihistaminics.

MATERIALS AND METHODS:

100 consecutive patients presenting during a 1 year period fulfilling the inclusion criteria participated in this study conducted at Govt. Stanley Medical College and Hospital, Chennai. An informed consent was obtained from the patients. One half of the patients were instilled with a drop of bepotastine besilate 1.5% and the other half received a drop of olopatadine hydrochloride 0.2% (each drug received by 50 patients) randomly. Patients were asked about the relief of each symptom - ocular itching, conjunctival congestion, itchy/runny nose at the end of 1, 2, 3, 5 min of instillation of one drop of the assigned topical drug (graded on a 1–5 scale, with 4-5 very satisfied, 3 – somewhat satisfied and <3 – not satisfied) as defined by the patient.

RESULTS:

Out of the 100 patients studied, 58 (58%) were males and 42 (42%) were females.

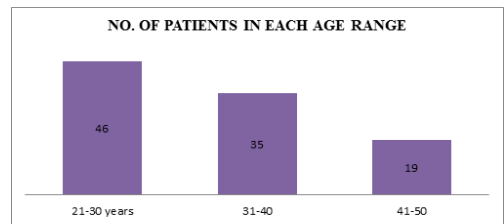


Figure 1:

Table 1: Classification based on symptomatology

	Ocular itching alone	Ocular itching + conjunctival congestion	Ocular itching + nasal symptoms
Males (total 58)	16 (28%)	34 (59%)	8 (13%)
Females (total 42)	8 (19%)	30 (71%)	4 (10%)

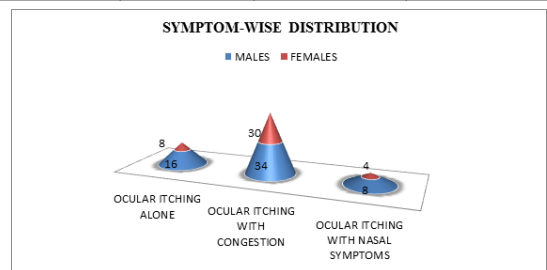


Figure 2:

According to table 1, majority of both male (59%) and female (71%) patients presented with symptoms of ocular itching with conjunctival congestion in our study. Out of 58 males and 42 females, half of them received 1.5% bepotastine besilate drop and the remaining received a drop of 0.2% olopatadine hydrochloride.

Table 2: Satisfactory level of patients according to symptom relief with each drug

	VERY SATISFIED (grade 4-5) Bepotastine vs Olopatadine	SOMEWHAT SATISFIED (grade 3) Bepotastine vs Olopatadine	NOT SATISFIED (grade < 3) Bepotastine vs Olopatadine
Males (total 58- 29 vs 29)	18 (62%) / 10 (34%)	7 (24%) / 6(21%)	4 (14%)/ 13 (45%)
Females (total 42 -21 vs 21)	14 (67%) / 8 (38%)	4 (19%) / 2 (10%)	3 (14%) / 11 (52%)

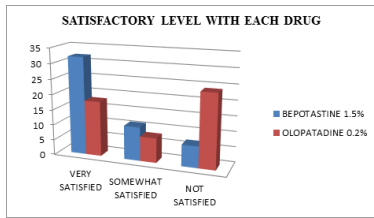
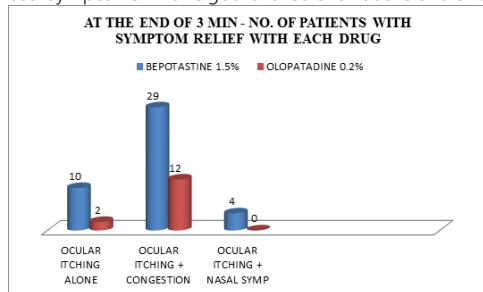


Figure 3:

TABLE 3: Comparison between time of relief of each symptom with either drug

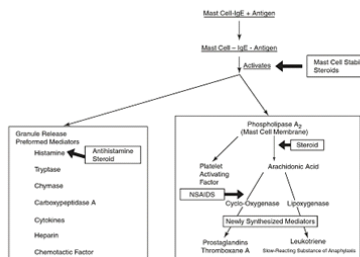
Relief of symptoms (BEPOTASTINE VS OLOPATADINE)	At the end of 1 min	2 min	3 min	5 min	Not relieved after 5 min
Ocular itching alone (24 patients – 12 vs 12)	2 (16.5%)/ 0	5 (42%)/ 2 (16.5%)	3 (25%)/ 0	0 / 1(8.5%)	2(16.5%)/ 9 (75%)
Ocular itching with conjunctival congestion (64 patients – 32 vs 32)	6 (19%)/ 1 (3%)	8 (25%)/ 4 (12.5%)	15 (47%)/ 7 (22%)	0/ 11 (34.5%)	3 (9%)/ 9 (28%)
Ocular itching with nasal symptoms (12 patients – 6 vs 6)	0/ 0	1(17%)/ 0	3 (50%)/ 0	0/ 0	2 (33%)/ 6 (100%)

As per table 3, on receiving a drop of BEPOTASTINE BESILATE 1.5% - with regards to ocular itching – 42% and 25% got relieved at the end of 2 and 3 min respectively, in case of ocular itching with congestion - 25% and 47% got relieved at the end of 2 and 3 min respectively, in case of ocular itching with nasal symptoms – 50% got relieved at the end of 3 min. On receiving a drop of OLOPATADINE HYDROCHLORIDE 0.2% - with regards to ocular itching – only 16.5% got relieved at the end of 2 min, in case of ocular itching with congestion – 12.5 %, 22% and 34.5% got relieved at the end of 2, 3 and 5 min and in case of ocular itching with nasal symptoms – none got relieved even at the end of 5 min.



DISCUSSION:

Allergic conjunctivitis is the most common allergic disorder affecting our community. The hallmarks of the condition are ocular itching, conjunctival hyperemia with rhinorrhoea, nasal itching etc⁵.



Allergic conjunctivitis is classified as a type 1, Ig E – mediated hypersensitivity reaction. The most common inciting antigens are pollen, dust mites and molds. The allergic reaction occurs in 2 phases: early and late phase. The early phase occurs within minutes of allergen exposure leading to antigen-evoked mast cell degranulation and histamine release. This is followed by a late phase that occurs hours to days after exposure characterised by release of pro-inflammatory mediators and recruitment of eosinophils and neutrophils⁵. The symptoms and signs of this condition are caused by the mast – cell derived histamine which acts on H1 and H2 receptors in the ocular tissues. Hence topical drugs that stabilize mast cells and reduce degranulation and antagonize the action of histamine at its receptors should be the first line therapy. Among the various topical anti-allergy medications we have taken two of them in our study for

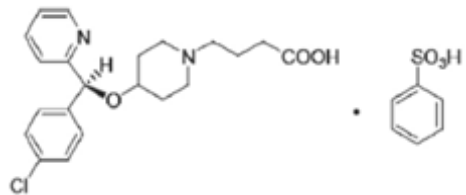
comparison with regards to immediate symptomatic relief – 1) BEPOTASTINE BESILATE 1.5% and 2) OLOPATADINE HYDROCHLORIDE 0.2%.

According to table 2, 62% of males and 67% of females were very satisfied with a drop of BEPOTASTINE BESILATE 1.5% and only 34% of males and 38% females were very satisfied with a drop of OLOPATADINE HYDROCHLORIDE 0.2%, in the immediate relief of symptoms at the end of 5 min of instillation. Only 14% of males and females receiving a drop of BEPOTASTINE BESILATE 1.5% when compared to 45% of males and 52% females receiving a drop of OLOPATADINE HYDROCHLORIDE 0.2%, were not satisfied, when graded on a scale of 1-5 in the immediate relief of symptoms at the end of 5 min of instillation.

BEPOTASTINE BESILATE

ACTIONS: dual action - selective H1 receptor antagonist with potent mast-cell stabilizing effects. It inhibits leukotriene B418, CD54, eosinophil chemotaxis and activation, suppresses pro-inflammatory cytokine production and reduces vascular hyper-permeability⁶.

STRUCTURE: (+)-4-[[[S]-p-chloro-alpha-2pyridylbenzyl]oxy]-1-piperidine butyric acid monobenzenesulfonate. Structural formula – C₁₂H₂₅ClN₂O₃·C₆H₆O₃S.



COMPOSITION: white crystalline powder with molecular weight 547.06 daltons. Each ml contains 15mg of Bepotastine besilate, with 0.005% benzalkonium chloride as preservative. It is a sterile, aqueous 1.5% solution with pH 6.8, osmolality 290mOsm/kg.

DOSAGE: one drop instilled into affected eye twice daily

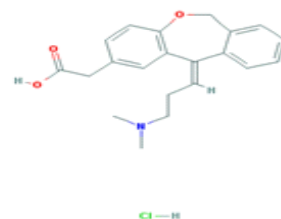
INDICATIONS: Ocular itching, allergic conjunctivitis in > 2 years of age

SIDE EFFECTS: generally well tolerated, ocular irritation, headache, taste perversion may occur.

OLOPATADINE HYDROCHLORIDE

ACTIONS: second generation topical anti-histaminic, selective for H1 receptor, with inhibition of mast cell and basophil degranulation. It inhibits production of inflammatory cytokines^{6,7}.

STRUCTURE: 2-[(11Z)-11-[3-(dimethylamino)propylidene]-6H-benzo[c][1]benzoxepin-2-yl]acetic acid; hydrochloride. Structural formula – C₁₂H₂₄ClNO₃.



COMPOSITION: Hydrochloride salt form of Olopatadine, white crystalline, water-soluble powder with molecular weight 373.88 daltons. Each ml contains 2.22mg of Olopatadine hydrochloride, with 0.01% benzalkonium chloride as preservative. It is supplied as a sterile, aqueous 0.2% solution with pH 7, osmolality 300mOsm/kg.

DOSAGE: one drop instilled into affected eye once daily

INDICATIONS: Ocular itching, allergic conjunctivitis in > 3 years of age

SIDE EFFECTS: generally well tolerated, ocular s/e - burning, stinging, discomfort, systemic s/e - headache, rhinitis, taste perversion may occur According to the patient response, 62% of males and 67% of females were very satisfied with a drop of BEPOTASTINE 1.5% and only half the percentage - 34% of males and 38% females were very satisfied with a drop of OLOPATADINE 0.2%, in the immediate relief of symptoms at the end of 5 min.

With regards to ocular itching, 42% got relieved with BEPOTASTINE 1.5% vs 16.5% with OLOPATADINE 0.2% at the end of 2 min and 25% got relieved with BEPOTASTINE 1.5% vs 0% with OLOPATADINE 0.2% at the end of 3 min, With regards to ocular itching with congestion- 19% got relieved with BEPOTASTINE 1.5% vs 3% with OLOPATADINE 0.2% at the end of 1 min, 25% got relieved with BEPOTASTINE 1.5% vs 12.5% with OLOPATADINE 0.2% at the end of 2 min, 47% got relieved with BEPOTASTINE 1.5% vs 22% with OLOPATADINE 0.2% at the end of 3 min.

With regards to ocular itching with nasal symptoms - 17% and 50% got relieved with BEPOTASTINE 1.5% got relieved at the end of 2 and 3 min vs none being relieved in the OLOPATADINE 0.2% group.

Thus it was found in our study that **at the end of 3 min**, with a drop of BEPOTASTINE 1.5% - 83% got relieved from ocular itching, 91% got relieved from ocular itching with conjunctival congestion and 67% got relieved from ocular itching and nasal symptoms.

With a drop of OLOPATADINE 0.2% - only 17% got relieved from ocular itching, 38% got relieved from ocular itching with conjunctival congestion and none got relieved from ocular itching and nasal symptoms.

CONCLUSION:

Thus our study showed that BEPOTASTINE BESILATE 1.5% ophthalmic solution is a preferred drug compared to OLOPATADINE 0.2% in the immediate relief of symptoms of allergic conjunctivitis, according to patients. And also it can be used as an initial therapy in the symptom relief, alternative to the topical steroids used in allergic conjunctivitis. By using this drug, we can improve drug compliance thereby improving the quality of life in these patients.

DISCLOSURE: No author has a financial/ proprietary interest in any material or method mentioned in the study.

REFERENCES:

1. Withrich B, Brignoli R, Canevascini M, Gerber M., 1998., Epidemiological survey in hay fever patients: symptom prevalence and severity and influence on patient management., German., Schweiz Med Wochenschr. 128:139-143
2. Blaiss MS., 2007., Allergic rhinoconjunctivitis: burden of disease., Allergy Asthma Proc., 28:393-397
3. Niederhorn JY., 2008., Immune regulatory mechanisms in allergic conjunctivitis; insights from mouse models., Curr Opin Allergy Clin Immunol., 8:472-476
4. ISTA pharmaceuticals Inc., Bepreve (package insert), Irvine, CA., 2009
5. Edward J Holland, Mark J Mannis, W. Barry Lee., 2010., Ocular surface disease: Cornea, Conjunctiva, Tear film: Acta Ophthalmol., 88:245-50
6. Jimmy D Bartlett., 2013., Clinical Ocular Pharmacology 5th edition., 27:549-559
7. Daniel C. Adelman, Thomas B. Casale., Manual of Allergy and Immunology: 85-88.