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A Comparative Study of Olopatadine Hydrochloride and Bepotastine Besilate in the Treatment of Allergic Conjunctivitis

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ABSTRACT

Background - Ocular allergy is a commonly encountered pathology in clinical practice, which often is under diagnosed and consequently undertreated. These are rarely vision-threatening but can significantly decrease the quality of life for patients. Olopatadine and Bepotastine eyedrop have both antihistaminic and mast cell stabilization action. Their use can control acute symptoms and prevent relapses as well. We conducted this single blinded trial directly comparing the efficacy of the two topical anti allergic medications in mild forms of allergic conjunctivitis.

Materials and Methods - A single blinded randomised control clinical trial study was conducted in patients visiting OPD of Ophthalmology at the institute for duration of 6 months. All the patients above 18 years of age having mild to moderate allergic conjunctivitis were included in the study. Patients were randomly placed in one of the two groups according to computer generated random numbers and given topical anti-allergic medication for twice daily. Group A was given Topical 0.1% Olopatadine eye drops BD and Group B was given Topical 1.5% Bepotastine eye drops BD. Ophthalmological check-up was done using slit lamp on next day, after 1 week, after 21-28 days.

Results - It was seen from the study that on follow up day 1 in patients receiving Bepotastine 1.5% eyedrop, there was 50% relief of symptoms and signs seen in 80% patients while in 60% patients, only 40% relief in symptoms and sign was seen with olopatadine 0.1% eyedrop. On follow up day 7, 90% of symptoms and signs of allergic conjunctivitis were relieved in all patients receiving Bepotastine eyedrop while 80% relief was seen in those receiving olopatadine. Almost 100% relief from signs and symptoms were seen in both the groups on follow up day 21-28th.

Conclusion- We conclude from our study that, Bepotastine besilate 1.5% ophthalmic solution is a preferred drug compared to Olopatadine 0.1% in the immediate relief of symptoms and signs of allergic conjunctivitis. It can be used as an initial therapy in the symptom relief and alternative to the topical steroids used in mild-moderate allergic conjunctivitis.

Keywords: Allergic conjunctivitis, Ocular allergy, Olopatadine hydrochloride, Bepotastine besilate.

INTRODUCTION

Ocular allergy is a commonly encountered pathology in clinical practice, which often is under diagnosed and consequently undertreated. Allergic conjunctivitis can be seen as an isolated finding but is often associated with allergic rhinitis, atopic dermatitis, and/or asthma. Allergic diseases have dramatically increased in the last decades [(1-4)]. The International Study of Asthma and Allergy in Childhood spanning 52 countries reported that allergic conjunctivitis affects 1.4–39.7% of children and adolescents [(5)].

These are rarely vision-threatening but can significantly decrease the quality of

life for patients. There are three subtypes of simple allergic conjunctivitis: seasonal allergic conjunctivitis (SAC) & perennial allergic conjunctivitis (PAC); vernal keratoconjunctivitis (VKC), and atopic keratoconjunctivitis (AKC).

Seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC) are the most common forms of ocular allergies that affect at least 15–20% of the population [(6)]. The pathogenesis of allergic conjunctivitis is predominantly an IgE-mediated hypersensitivity reaction caused by an allergen-induced inflammatory response in which allergens interact with IgE bound to sensitized mast cells resulting in the clinical ocular allergic expression. Activated mast cells induce enhanced tear levels of histamine, tryptase, prostaglandins and leukotrienes. This immediate or early response lasts clinically 20–30 min [(7)]. Diagnostic features consist of itching, redness, and chemosis. Corneal involvement is rare. VKC is a chronic allergic inflammation of the ocular surface mediated mainly by Th2-lymphocyte; also, there is over-expression of mast cells, eosinophils, neutrophils, Th2-derived cytokines, chemokines, adhesion molecules, growth factors, fibroblast and lymphocytes. IL-4 and IL-13 are involved in the formation of giant papillae by inducing the production of extra-cellular matrix and the proliferation of Conjunctival fibroblasts [(8-10)]. Atopic keratoconjunctivitis (AKC) is a bilateral chronic inflammatory disease of the ocular surface and eyelid. Its pathomechanism involves both a chronic degranulation of the mast cell mediated by IgE, and immune mechanisms mediated by Th1- and Th2-lymphocyte derived cytokines. Also, eosinophils and other inflammatory cells play a role [(11)].

Avoidance of the offending antigen is the primary behavioural modification for all types of allergic conjunctivitis; however, the eyes present a larger surface area and thus it is often impossible to avoid ocular exposure to air borne allergens. Artificial tear substitutes provide a barrier function and help to improve the first line defence at the level of conjunctival mucosa. These agents help to dilute various allergens and inflammatory mediators that may be present on the ocular surface, and they help to flush the ocular surface of these agents. When avoidance of non-pharmacologic strategies does not provide adequate symptoms relief, pharmacological treatment may be applied topically or given systemically to diminish the allergic response.

The mainstay of management of ocular allergy involves the use of anti-allergic therapeutic agents like anti histaminic, multiple action anti-allergic agents and mast cell stabilizers such as olopatadine, Bepotastine, azelastine, alcaftadine.

Amongst all, olopatadine and Bepotastine have both antihistaminic and mast cell stabilization action. Their use can control acute symptoms and prevent relapses as well. We conducted this single blinded trial directly comparing the efficacy of the two topical anti allergic medications in mild forms of allergic conjunctivitis.

Aim Of Study:

To compare Bepotastine Besilate Ophthalmic solution with Olopatadine hydrochloride ophthalmic solution in subjects suffering from allergic conjunctivitis.

MATERIALS AND METODS

A single blinded study was conducted in patients visiting OPD of Ophthalmology at the institute for duration of 6 months. All the patients above 18 years of age having mild to moderate allergic conjunctivitis were included in the study. Patients with ocular infection or concurrent ocular diseases (dry eye, blepharitis, dermatitis, meibomian gland dysfunction and severe form of allergic conjunctivitis with corneal involvement), planning to undergo ocular surgery, contact lenses users, pregnant/ lactating women, history of alcohol/drug abuse, patients on drugs like anti histaminic, steroids, lubricating agents

or any other ocular medications were excluded. The study was approved from the local Institutional Review Board/ Ethical Committee and follows declaration of Helsinki. The data was entered and analysed using IBM SPSS statistics.

A written informed consent from the patients was taken before conducting the interview and examination. Visual Acuity was measured using Snellen's charts. Both uncorrected and best corrected visual acuities were noted. Anterior segment evaluation by diffuse torch light and slit lamp examination was done to look for signs of allergic conjunctivitis. Patients were randomly placed in one of the two groups according to computer generated random numbers and given topical anti-allergic medication for twice daily

Group A) Topical 0.1% Olopatadine eye drops BD

Group B) Topical 1.5% Bepotastine eye drops BD.

Ophthalmological check-up was done using slit lamp on next day, 7th day and day 21-28th.

For uniform grading of symptoms and signs at each visit, following scoring scale was used (table no 1 and 2).

Symptoms:

Table no 1

Redness	0-absent 1-mild 2-moderate 3-severe
Itching	0-absent 1-occasional 2-frequent 3-constant
Watering	0-normal tear 1-sensation of fullness of conjunctival sac 2-infrequent spilling of tears over lid margin 3-constant spilling of tears over lid margin
Discomfort	0-absent 1-mild 2-moderate 3-severe

Signs:

Table no 2

Palpebral conjunctival hyperaemia	3 – impossible to distinguish individual blood vessel 2- dilatation of many vessels 1-Dilatation f several vessels 0-none
Oedema	3- diffuse oedema with opacity 2- thinner diffuse oedema 1-slight oedema 0-none
Follicles	3- 20 or more 2- 10 to 19 to 9 0-none
Papillae	3- papilla size 0.6mm or more 2- 0.3 – 0.5mm 1-0.1-0.2 mm 0-none
Giant papillae (size ≥1mm)	3-Elevated papillae in half or more of upper palpebral conjunctiva 2- Elevated papillae in less than half of upper palpebral conjunctiva 1-flat papillae 0-none
Bulbar conjunctival hyperaemia	3-diffuse dilated blood vessels over entire bulbar conjunctiva 2-- dilatation of many vessels 1-Dilatation f several vessels 0-none
Oedema	3-bullousodema 2-thinner diffuse oedema 1-localised oedema 0-none
Swelling	3-≥2/3rd found in limbal 2-1/3rd to ≤2/3rd 1-≤13rd 0-none
Limbus Tranta's spot	3-≥9 2-5 to 8 to 4 0-none

Table no 2	
Corneal epithelial signs	3-sheild ulcer/erosions 2-exfoliation SPK 1-SPK 0-none

RESULTS

A total of 200 patients with mild to moderate allergic conjunctivitis were included in the study. They were randomly divided into 2 groups each of 100. One group received Bepotastine 1.5% eyedrop while the other group received Olopatadine 0.1% eyedrop and the results were based on relief of symptoms according to the scale and signs seen on torch and slit lamp examination. Out of the total patients included in the study, 80 were females and 120 were males. Maximum patients had symptoms up to grade 2 and signs co related to symptoms.

In group A, the number of females were 30 and males were 70; while in group B females were 50 and males were 50. It was seen from the study on follow up day 1 that in patients receiving Bepotastine 1.5% eyedrop, there was 50% relief of symptoms and signs in 80 patients while in 60 patients, 25-50% relief in symptoms and sign was seen with olopatadine 0.1% eyedrop.

On follow up day 7, about 90% of symptoms and signs of allergic conjunctivitis were relieved in all patients receiving Bepotastine eyedrop while about 75% relief was seen in those receiving olopatadine. Out of 2 patients from Group A, 1 patient showed worsening of signs and symptoms and was shifted to steroid eyedrop; while the other patient was not satisfied regarding symptoms and signs showed no change. So he was shifted on Bepotastine eyedrop. Almost 100% relief from signs and symptoms were seen in both the groups on follow up day 21-28th.

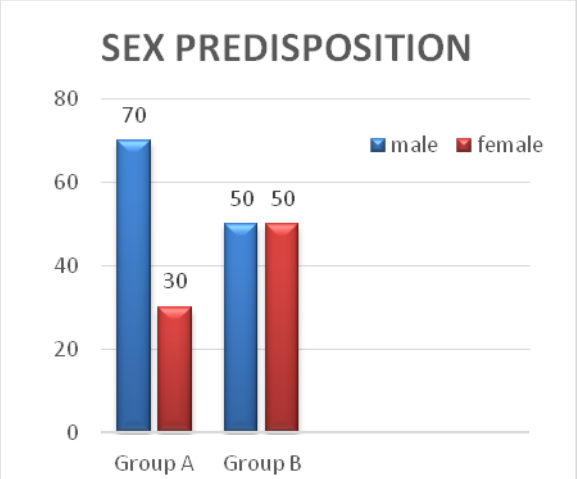


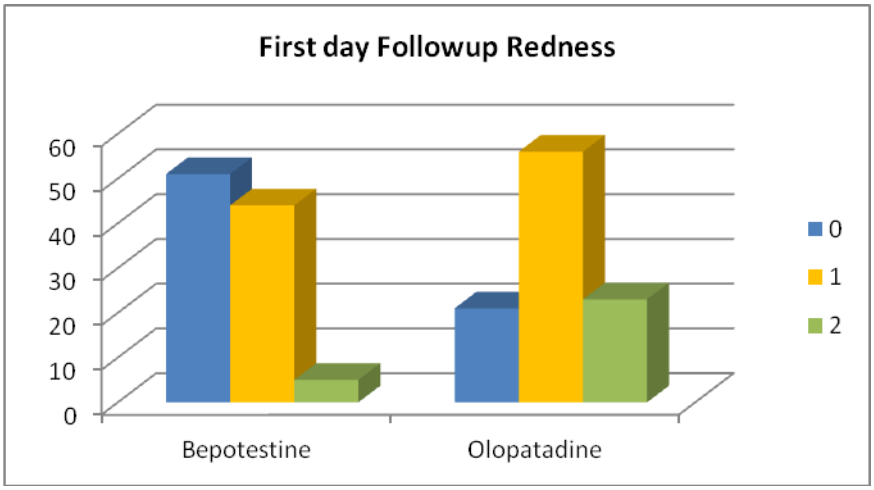
Figure 1: gender predisposition

Table no 3: COMPARISON OF SIGNS AND SYMPTOMS ON FOLLOW UP

PARAMETERS	FOLLOW UP DAY 1		FOLLOW UP DAY 7		FOLLOW UP DAY 24-28	
SYMPTOMS	GROUP A	GROUP B	GROUP A	GROUP B	GROUP A	GROUP B
Itching	Grade 2	Grade 1	Grade 1	Grade 0	Grade 0	Grade 0
Redness	Grade 2	Grade 1	Grade 1	Grade 1	Grade 0	Grade 0
Watering	Grade 1	Grade 1	Grade 0	Grade 0	-	-
Foreign body sensation	Grade 1	Grade 0	Grade 0	Grade 0	-	-
SIGNS						
Conjunctival congestion	Grade 2	Grade 1	Grade 1	Grade 0	-	-
Papillae	-	-	-	-	-	-
Limbal thickening and opacification	-	-	-	-	-	-
Limbal papillae	-	-	-	-	-	-
Horner's trantas dots	-	-	-	-	-	-

Table no 4: COMPARISON OF REDNESS ON FOLLOW UP DAY 1

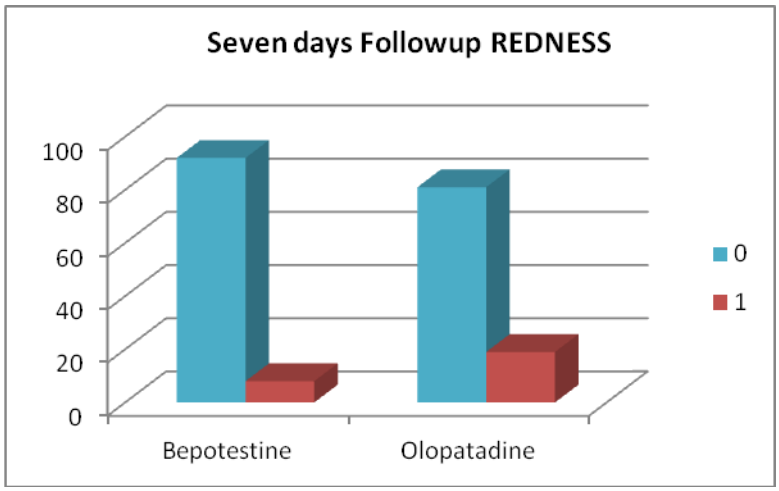
	First day Follow up Redness			
Redness gradings	**Bepotastine**	**Olopatadine**	**Total**	**p- value**
0	51	21	72	<0.001 [s]
1	44	56	100	0.089 [NS]
2	5	23	28	0.002 [S]
Total	100	100	200	



The relief of redness on follow-up day 1 was found to be significant between the two groups. Maximum patients in group B still had redness on follow-up day 1.

Table no 5: COMPARISON OF REDNESS ON FOLLOW-UP DAY 7

	Seven days Follow up REDNESS			
Redness grading	**Bepotastine**	**Olopatadine**	**Total**	**p- value**
0	92	81	173	<0.0001 [s]
1	8	19	27	0.02 [S]
Total	100	100	200	



On comparing the relief of redness on follow-up day 7, significance between the two groups was seen.

Similarly, significant difference in relief of watering (p=0.003) and foreign body sensation (p=0.007) was seen on follow-up day 7 between the two groups.

DISCUSSION

Ocular allergy is a commonly pathology in clinical practice, with an increasing number of patients noticed in the last decade with a prevalence of approximately 40% of the population globally. Avoidance of allergens plays a key role in the prevention of allergic conjunctivitis. Addition of anti-histamine reduces inflammation, whereas mast cell stabilizers prevent mast cell de-granulation on an exposure to allergens. Topical corticosteroids are the most potent agents to control inflammatory symptoms of allergic conjunctivitis but there is a risk of many side-effects.

Olopatadine is a dual action selective histamine H1 receptor antagonist and mast cell stabilizer with anti-allergic activity. Olopatadine stabilizes mast cells and prevents histamine release from mast cells. In addition, this agent also

blocks histamine H1 receptors, thereby preventing histamine from binding to these receptors. The drug also prevents histamine-induced pain and itching of mucous membranes. Olopatadine hydrochloride suppressed TNF-α release in vitro from human conjunctival mast cells as well as that of interleukin 6 (IL-6) and IL-8 from conjunctival epithelial cells (Yanni et al 1999).

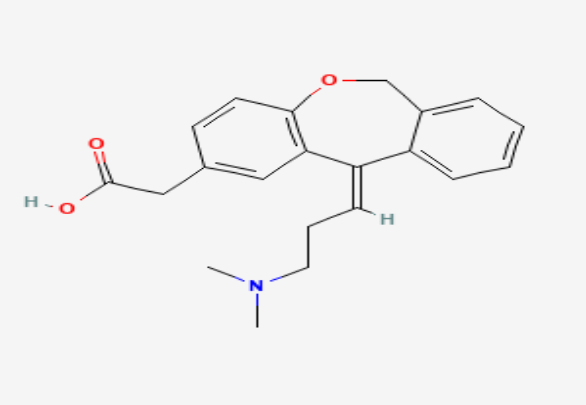


Figure 2

Bepotastine besilate (BB) is a second-generation, dual-mechanism drug possessing highly selective direct histamine H_1-receptor-antagonistic action and inhibitory effects on histamine release from mast cells. BB also acts to suppress eosinophilic migration into inflammatory sites, and at a molecular level can potentially inhibit the activation of eosinophils and maturation of eosinophil precursors in allergic inflammation [(12)]. Bepotastine besilate also inhibits leukotrienes, platelet-activating factor and interleukin-5 production [(13-15)]. Bepotastine besilate ophthalmic solution 1.5%* was approved by the FDA on September 8, 2009, for the treatment of itching associated with the signs and symptoms of allergic conjunctivitis [(16)]. A duration of action of ophthalmic solutions of ≥8 hours is considered adequate for an ophthalmic medication intended for twice-daily dosing [(17)].

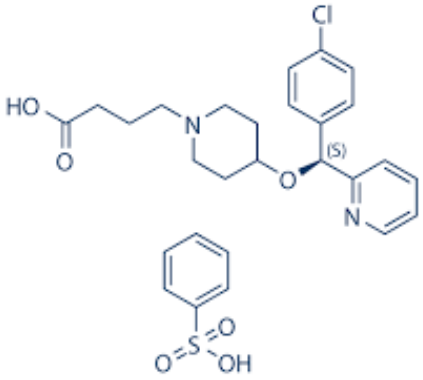


Figure 3

Craig McCabe et al, in his study found that Bepotastine was superior to Olopatadine in treating ocular itch [(18)]. In our study we found that symptoms and signs of maximum patients were relief on day 1 follow up after use of Bepotastine 1.5 % eyedrop as compared to Olopatadine 0.1% eyedrop.

CONCLUSION

Thus, we conclude from our study that, bepotastine besilate 1.5% ophthalmic solution is a preferred drug compared to olopatadine 0.1% in the immediate relief of symptoms and signs of allergic conjunctivitis. It can be used as an initial therapy in the symptom relief and alternative to the topical steroids used in mild-moderate allergic conjunctivitis.

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Conflict of Interest: None

Source of Funding: None

Ethical Approval: Approved

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