The Effect of Olopatadine 0.1% Ophthalmic Solution on Ocular and Nasal Symptoms in Patients with Seasonal Allergic Rhino- Conjunctivitis

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ABSTRACT

Objective: To evaluate the effect of olopatadine 0.1% ophthalmic solution twice daily on ocular and nasal symptoms in patients with seasonal allergic rhino-conjunctivitis.

Method: This study was conducted at the Ophthalmology and ear, nose and throat (ENT) clinics on patients with seasonal allergic rhino-conjunctivitis during spring and early summer seasons (March to end of June) in 2010 at Princess Haya Al Hussein hospital in the south of Jordan and in 2011 at Prince Rashid Bin Al Hassan hospital in the north of Jordan. The patients were divided randomly into 2 groups; group A (50 patients) received Olopatadine 0.1% ophthalmic solution (Patanol) twice daily, group B (51 patients) received placebo in the form of balanced salt solution. All patients attended ENT and Ophthalmology clinics weekly for 2 visits; they were reviewed regarding the improvement of ocular symptoms (itching, redness and lacrimation) and nasal symptoms (sneezing, itchy nose and runny nose).

Results: In those patients who received Olopatadine 0.1% ophthalmic solution, after two weeks 98%, 98% and 90% of them showed satisfactory improvement according to a scale of 1 to 5 marked by the patients for itching, lacrimation and redness respectively compared to 14%, 12% and 6% in group B respectively (P-value <0.05). Regarding nasal symptoms 90%, 84% and 78% of patients in group A showed satisfactory improvement regarding sneezing, running nose and nasal itching respectively compared to 8%, 16% and 10% in group B (P-value <0.05).

Conclusion: The treatment of ocular allergy positively impacts nasal symptoms. The use of ocular solution of Olopatadine 0.1% ophthalmic solution twice daily has an excellent effect on ocular symptoms and good effect on nasal symptoms, this effect was more significant at two weeks of treatment. Olopatadine 0.1% ophthalmic solution is a well-tolerated drug and may be considered as a primary treatment for patients with seasonal allergic rhino-conjunctivitis.

Key Words: Allergic rhino-conjunctivitis, Olopatadine.

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Introduction

Allergic rhino-conjunctivitis is a common disorder in the society that affects different age groups. In USA, it was found that 15% of population are affected by allergic rhinitis and there is an increase in prevalence with time,[1] also it is considered a known cause of seeking

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medical advice at the primary care clinics.[2] Although rhino-conjunctivitis may affect any age, yet it is considered a disease of childhood and adolescence. It usually shows ocular symptoms like itching, tearing and redness, nasal symptoms such as nasal itching, running nose and sneezing, and general symptoms such as fatigue and cough.[1,2] If uncontrolled allergic rhino-conjunctivitis may have adverse impacts on health- related and economic consequences; it can lead to learning problems especially in school children, [3] may worsen the symptoms of asthma,[4] and has major impact on daily life as it can lead to sleep disturbances, absence from school or work and impairment of daily activities like sports.[5] Chronic allergic rhino-conjunctivitis manifests as either seasonal allergic rhino-conjunctivitis that accounts for 50-90% of cases or perennial allergic rhino-conjunctivitis, both seasonal and perennial allergic rhino-conjunctivitis are IgE-mediated hypersensitivity reaction to specific aeroallergens but vary according to the duration of exposure.[6,7] The term allergic rhino-conjunctivitis is preferable to allergic rhinitis because most patients of allergic rhinitis have ocular symptoms of allergic conjunctivitis.[5] The mainstay for treatment of patients with allergic conjunctivitis is prevention by avoidance of exposure to aeroallergens. A lot of topical and systemic products have also been used for the management of allergic rhino-conjunctivitis.[5,6] One of these products used to control ocular symptoms of allergic rhino-conjunctivitis is topical Olopatadine ophthalmic solution. Olopatadine hydrochloride is considered the first antihistamine used once daily with both selective histamine (H 1) receptor antagonist and mast cell stabilization effects.[8] It has a dual action of inhibiting the activity of the already released histamine on its receptors and suppressing further release of histamine and inflammatory mediators from the mast cell.[7] The chemical structure for Olopatadine is 11 - [(Z) - 3- (dimethylamino) propylidene] - 6- 11 – dihydrodibenz [b,e] oxepin -2-acetic acid hydrochloride, it is a white water-soluble crystalline powder with a molecular weight of 373.88.[7,8] There are two concentrations of Olopatadine ophthalmic preparations: 0.1% used twice daily and 0.2% used once daily. The aim of this study was to evaluate the effect of ocular olopatadine 0.1% ophthalmic solution twice daily on ocular and nasal symptoms in patients with seasonal allergic rhino-conjunctivitis.

Methods

This study was conducted at the Ophthalmology and ENT clinics on patients with seasonal allergic rhino-conjunctivitis during spring and early summer seasons (March to end of June) in 2010 at Princess Haya Al Hussein Hospital in the south of Jordan and in 2011 at Prince Rashid Bin Al Hassan Hospital in the north of Jordan. All patients above 14- year of age diagnosed with allergic rhino-conjunctivitis were recruited. The following patients were excluded: age below 14 years, other external eye or nasal disease, recent eye surgery, as well as patients who were receiving anti-allergic therapy during the last month. All patients enrolled in the study were given numbers starting from 1 according to the time of their attendance to the clinic, patients with odd numbers were considered as a control group patient and received balanced salt solution (BSS) eye drop twice daily, and those with even numbers received olopatadine 0.1% ophthalmic solution twice daily, the drops trade name was not exposed to the patient. A total number of 101 patients were enrolled in this study, patients who received Olopatadine (50 patients) were group A and the remaining 51 patients were group B. All patients were examined and evaluated by ENT and ophthalmology specialists to establish the diagnosis of allergic rhino-conjunctivitis before starting the treatment and the assessment was repeated after one and two weeks of treatment. During follow up visits (after one and two weeks of treatment) the improvement of ocular symptoms (itching, redness and lacrimation) and nasal symptoms (sneezing, itchy nose and runny nose) were evaluated based on a scale marked by the patient from 0 to 5, where 0 stands for no improvement of the symptom and 5 stand for complete relieve of the symptom. We stressed on the patient's compliance before and during the follow-up period and patient were instructed not to take any medications and inform us before using any agents that may interfere with the results.

Table I: Patients' demography and distribution of prominent ocular and nasal symptoms among patients

group		A (50 patients)	B (51 patients)	Total (101 patients)
Mean age(yrs)		35.3	34.0	34.7
Gender	males	20	22	42
	females	30	29	59
Eye itching		(50)100%	(51)100%	(101)100%
Lacrimation		(46)92%	(45)88%	(91)90%
Eye redness		(35)70%	(37)73%	(72)72%
Sneezing		(40)80%	(37)73%	(77)77%
Running nose		(34)68%	(33)65%	(67)67%
Nose itching		(31)62%	(30)58%	(61)60%

Table II: The improvement scale of ocular and nasal symptoms after one weeks of treatment

	Scale 0		Scale 1		Scale 2		Scale 3		Scale 4		Scale 5	
	A	B	A	B	A	B	A	B	A	B	A	B
Eye itching	2%	57%	6%	21%	6%	8%	10%	8%	12%	2%	64%	4%
Lacrimation	4%	45%	8%	20%	10%	21%	10%	10%	22%	4%	46%	0%
Eye redness	8%	47%	10%	21%	12%	20%	12%	12%	16%	0%	42%	0%
Sneezing	6%	55%	8%	23%	12%	10%	12%	10%	14%	2%	48%	0%
Running nose	8%	43%	8%	18%	10%	21%	10%	10%	16%	8%	48%	0%
Nose itching	10%	57%	12%	21%	16%	14%	24%	4%	28%	2%	20%	2%

Table III: The improvement scale of ocular and nasal symptoms after two weeks of treatment

	Scale 0		Scale 1		Scale 2		Scale 3		Scale 4		Scale 5	
	A	B	A	B	A	B	A	B	A	B	A	B
Eye itching	0%	55%	0%	23%	2%	8%	2%	8%	6%	4%	90%	2%
Lacrimation	0%	51%	0%	23%	2%	14%	4%	12%	10%	0%	84%	0%
Eye redness	2%	51%	4%	23%	4%	20%	8%	6%	12%	0%	70%	0%
Sneezing	4%	57%	2%	23%	4%	12%	10%	4%	10%	4%	70%	0%
Running nose	4%	43%	6%	21%	6%	20%	12%	8%	16%	8%	56%	0%
Nose itching	4%	55%	8%	23%	10%	12%	12%	6%	24%	4%	42%	0%

Results

The mean age for group A was 35.3 years (range between15 to 54 years) and for group B was 34 years (range between 14 and 52 years), and the female to male ratio in both groups were 1.5:1 and 1.3:1 respectively; there was no significant statistical difference between the two groups regarding age and gender nor the distribution of prominent ocular and nasal symptoms, Table I summarizes patients' demography and the distribution of the prominent ocular and nasal symptoms among the patients. The most prominent ocular symptom in our study was eye itching which was seen in all patients, while sneezing was the most prominent nasal symptom, it was seen in 77% of patients.

The improvement scale of ocular and nasal symptoms after one and two weeks of treatment is summarized in Table II and III respectively. Assuming that scales below three (0, 1, 2) have no satisfactory improvement and scales 3 or more[3,4,5] have satisfactory improvement. In group A (Olopatadine group); one week treatment yielded satisfactory improvement in 86%, 78%, and 70% of patients in regard to eye itching, lacrimation, and redness respectively compared to 14%, 14%, and 12% in group B (P-value <0.05). Regarding nasal symptoms 74%, 74%, and 72% of patients in group A showed satisfactory improvement regarding sneezing, running nose, and nasal itching respectively compared to 12%, 18%, and 8% in group B (P-value <0.05). The improvement was more significant after two weeks in those who received olopatadine 0.1% ophthalmic solution; 98%, 98% and 90% of them showed satisfactory improvement in eye itching, lacrimation, and redness respectively compared to 14%, 12%, and 6% in group B respectively (P-value <0.05). Also 90%, 84%, and 78% of patients in group A showed satisfactory improvement regarding sneezing, running nose, and nasal itching respectively compared to 8%, 16%, and 10% in group B (P-value <0.05).

Discussion

The term allergic rhino-conjunctivitis is preferable to allergic rhinitis because most patients of allergic rhinitis have ocular symptoms of allergic conjunctivitis,[5] that is because of the strong anatomical and physiological relationship between the conjunctival and the nasal mucosa through the connection made by the naso-lacrimal duct.[9,10] These structures share blood vessel network, lymphatic tissue and system, and nerve networks,[11,12] this explains the usual co-existence of the allergic process in both the conjunctiva and nose. For example Pelikan reported the causal role of nasal allergy in cases of allergic conjunctivitis,[9] as well as allergic kerato-conjunctivitis.[13] Gomes *et al*,[14] concluded that there is a central role of the eye in initiating and propagating the allergic reaction to involve the nose. There was no significant statistical difference between the two groups regarding age and gender nor the distribution of prominent ocular and nasal symptoms. Although allergic rhino-conjunctivitis is more prevalent in children (40%) than adults (10-30%),[6] we decided to include only patients above 14 years of age as younger children were found much less cooperative in understanding the grading scale utilized in this study. Patients with any nasal pathology were also excluded because they may have symptoms that mimic those symptoms of allergic rhino-conjunctivitis.

It was clear that ocular symptoms were more prevalent than nasal symptoms in patients with allergic rhino-conjunctivitis, probably because ocular surface is more exposed to environmental allergens. This finding was shared by other investigators.[9,13,14] Assuming that scales below three (0, 1, 2) have no satisfactory improvement and scales 3 or more [3,4,5] have satisfactory improvement. In group A (Olopatadine group); one week follow-up yielded satisfactory improvement in 86% of patients with complete relieve of eye itching in 64% of patients. In addition to that 78% and 70 % of patients had satisfactory improvement regarding lacrimation and eye redness respectively. The improvement was more significant after two weeks and improvement in eye itching, lacrimation, and redness was seen in 98%, 98%, and 90% of patients respectively. This proves that Olopatadine 0.1% ophthalmic solution has more significant good response after two weeks use. Other studies also focused on the effect of Olopatadine on ocular symptoms and found that Olopatadine was clinically superior to the other anti-allergic agents because of its strong dual action of antihistaminic and mast cell stabilizing properties.[15] Regarding nasal symptoms, our study showed that Olopatadine 0.1% ophthalmic solution has also an effect on nasal symptoms; after one week 74% of patients showed satisfactory improvement in sneezing and running nose and 72% of patients showed satisfactory improvement in nasal itching. While after two weeks 90%, 84%, and 78% of patients showed satisfactory improvement in sneezing, running nose, and nasal itching respectively. This also support the idea that hypersensitivity reactions of allergic rhino-conjunctivitis start primarily in the conjunctival mucosa that resulting in activation of inflammatory cells mainly mast cells and their migration through the blood stream into the nasal mucosa making benefit of the vicinity and sharing of blood vessels network, in addition to inflammatory mediators released from conjunctival mast cells pass with tears [16] via the naso-lacrimal duct and contribute to the nasal mucosa reaction. Activation of mast cells in conjunctiva and nasal mucosa will cause the release of inflammatory mediators like cytokines, chemokines and other chemotactic factors that will be responsible for the allergic reaction. The improvement of the nasal symptoms after installation of olopatadine 0.1% ophthalmic solution can be explained by two mechanisms; first is inhibition of conjunctival mast cells that is thought to be the initiating factor of the allergic reaction and second is due to ante grade migration of olopatadine 0.1% Ophthalmic solution through the naso-lacrimal duct to the nasal mucosa. Figure 1, graphically shows the satisfactory improvement in the Olopatadine group compared to the control group at one and two weeks. The above results showed that the use of ocular solution of Olopatadine 0.1% twice daily has an excellent effect on ocular symptoms and good effect on nasal symptoms. This study supported the results obtained by other studies in which they studied the efficacy of Olopatadine on ocular and nasal symptoms, for example Abelson *et al*,[17] studied the efficacy and safety of

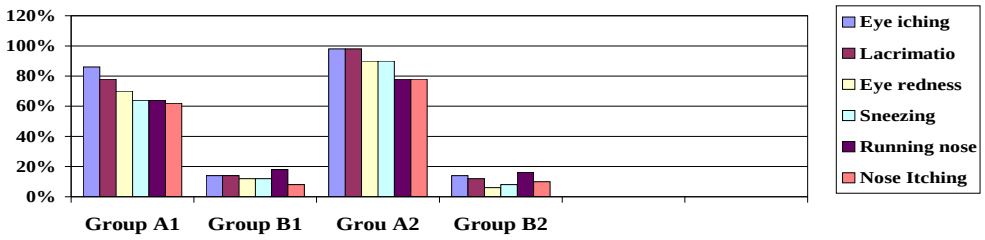

Fig.1: The percentage of patients who showed satisfactory improvement in the Olopatadine group at one week (Group A1) and two weeks (Group A2) compared to the control group for the same period (Group B1 and Group B2 respectively)

ophthalmic solution of olopatadine on nasal symptoms in subjects with history of seasonal allergic conjunctivitis or rhino-conjunctivitis in spring and fall seasons, he showed that Olopatadine significantly reduced the frequency of pollen effects on nasal symptoms. Some studies compared the effect of the two concentrations of Olopatadine and showed that there was no significant difference in their effect.[18] It is worth to mention that only 2 patients (4%) in group A and none in group B showed eye discomfort and dryness, this emphasizes that Olopatadine is well tolerated drug, this was also concluded by Mah *et al*.[19] The only limitation in this study was its dependence on subjective judgments of the patients which may vary from person to another, however this study showed clearly the effectiveness of Olopatadine ophthalmic solution on ocular and nasal symptoms in patients with allergic rhino-conjunctivitis.

Conclusion

The treatment of ocular allergy positively impacts nasal symptoms. The use of ocular solution of Olopatadine 0.1% ophthalmic solution twice daily has an excellent effect on ocular symptoms and good effect on nasal symptoms, this effect was more significant at two weeks of treatment. Olopatadine is a well tolerated drug and may be considered as a primary treatment for patients with seasonal allergic rhino-conjunctivitis.

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