ORIGINAL ARTICLE

Assessmentof Adverse Effects of Lodoxamideand Sodium Cromoglycateduring the Treatment of Vernal Keratoconjunctivitis

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ABSTRACT

Aim: To assess the adverse effects of lodoxamide as compared to those of sodium cromoglycate when it is given topicallyfor treatment of vernal keratoconjunctivitis.

Place of study: Study was conducted in the Pharmacology Department and Therapeutics Chandka Medical College, ShaheedMohtarma Benazir Bhutto Medical University (SMBBMU),Larkana in collaboration with Ophthalmology Department of Chandka Medical College (CMC) Hospital,Larkana.

Period of study: From April 2013 to September 2013.

Study design: Prospective comparative clinical trial.

Methods:A total of80 untreated cases clinically diagnosedas vernal keratoconjunctivitis (VKC) of age ranging between 5-25 years, both sexes male and female were included in this study. Patients of otherthan VKC and who arepreviously on the treatmentfor VKC were excluded from the study. Follow up visits were carried out fortnightlyfor the period of three (03) months to observe adverse effects of the two drugs.

Results: Atotal of 80 diagnosed cases of VKCwere studied; 56 males (70%) and 24 females (30%). The individuals who already received some medication for VKC and those having other forms of eye allergies were not included in this study. All patients were distributed in two groups; group A and group B. Group A included 40 caseswho used lodoxamide drops topicallywhile; group B similarly covered 40 patients whoinstilled sodium cromoglycate drops. Demographicallyno significant difference was exposed in both groups ($p>0.05$). The results revealed excellent profile of adverse effects of lodoxamide in group Aas compared with group B($p<0.001$)throughout the studywhich was statistically highly significant ($P<0.001$) when evaluated statistically using SPSS version 11.5.

Conclusion: The adverse effects profile in group A (lodoxamide) was better than group B.

Keywords: Adverse effects, Lodoxamide, Sodium cromoglycate, VKC.

INTRODUCTION

Since the last decades,occurrence of allergic diseases has increased. Amongst these, the allergic eye diseases comprise of most common allergies ever reported[1].Vernal keratoconjunctivitis (VKC) is an ocular ailment that recurs repeatedly and has anorigin that is related to antigen antibody related changes that occur in the body in response to common environmental allergens; the pollens in particular.Other ocular allergies sharing some of the common symptoms and signs in this group of allergic eye diseases are perennial allergic conjunctivitis (PAC), seasonal allergic conjunctivitis (SAC), atopic keratoconjunctivitis (AKC) and Giant papillary conjunctivitis (GPC)[2,3].The individuals commonly affected by this disease, dwell in hot climatic areas[4].Pathologically, atopic inflammation in this disease involves cornea(-kerato) along with conjunctiva (-conjunctivitis)[5]. Two of immune systemmechanisms play important role in pathogenesis of VKC;one is IgE-mediated (type-I) and other the cell-mediated (type- IV)[6].Disease is more common in males than in femalesin pre-pubertal age having a ratio of almost 2:1which become equal as the puberty is attained[7]. The challenges for management of this ocular ailment still prevails during childhood as these individuals also concomitantlydevelop other types of atopies like eczema and asthma along withfamily history of other atopies[5]. Literally elaborated, VKC is a disease that occurs in spring asthe word 'Vernal' means "Occurring in spring" (this meaning comes from Greek). If it is matched to thesaurus it means

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'youthful'. Thus, collectivelyit matches with symptoms and signs &occurrence of disease in children and adolescents age groupin spring season[8,9].

Vernal keratoconjunctivitisis also called as 'Round the year eye ailment' as some of the affected individuals show symptoms & signs for whole of the year. This disease shows a remarkable seasonal variation having increase in episodes during spring and decline in fall winter[4,10]. Observational studies show demographic pattern to be present more commonly in Sub Saharan and Middle East and non-existent in areas where climate is cold.Its prevalence inPakistanis also observed[9,11,12].

Types of VKC presented in clinical practice are palpebral, limbal and mixed. VKC affected individuals mostly present with severe itching, lacrimation and photophobia along with ocular discomfort[13,14]. Ropy mucous discharge and cobblestone papillae are the characteristic signs of disease. Permanent damage to vision is to be avoided by drastic therapeutic measures[6,8].

For management of VKC Lodoxamide and sodium cromoglycate are both clinically essential mast cell stabilizers. Inflammatory mediators are prevented from being released by both of the drugs by arresting degranulation of mast cells. This is brought about by cutting offcalcium influx across mast cell membrane[7,14,16]. Though complicated and resistant patients can becured with topical steroids on other hand these may cause raise in intra-ocular pressure[17].

MATERIAL AND METHODS

The clinical trial was done on sample size ofeighty (80) patients, at Pharmacology Departmentand Therapeutics Chandka Medical College, ShaheedMohtarma Benazir Bhutto Medical University (SMBBMU), Larkana in cooperation with Department of Ophthalmology,Chandka Medical CollegeHospital,Larkana from April 2013 to September 2013.Patients were divided in treatment group A [(Lodoxamide) 40 patients] and group B [(Sodium cromoglycate)40 patients]. For the treatment of both groups (Group A and Group B) two drops were instilled four times on daily basis separately. Adverse effects were assessed fortnightly at 15^{th}, 30^{th}, 45^{th}, 60^{th}, 75^{th} and 90^{th} day.

Statistical analysis: A comparative study of adverse effects (Lodoxamide with Sodium cromoglycate) was conducted and samples of 80 identified patients (40 in each group) with vernal keratoconjunctivitis were enrolled in this clinical trial after receivinga written approval (consent form) from respondents to join the study.For the analysis of data, SPSS version 11.5 was utilized. The outcomes were given in numbers and percentages for qualitative variables and quantitative variable (age)mean and standard deviation were calculated. For comparison of two treatment groups Chi-square test was applied. P-value of < 0.05 was considered as significant.

RESULTS

As shown in Table.1, the baselineand demographicfeatures revealed that all respondents ranged in ages between 5-25years of age. Male respondents were 56(70%) patients and female respondents were 24(30%)patients. Mean value in group A was14.7±0.96 whereas; in group B it was14.4±0.91. Regardinggender and age distribution ($p>0.05$) there was no significant differencein both treatment groups.From group A one case (2.5%) and from group B two cases (5%) left the study $p>0.05$).

Tables 2 and 3 show the adverse effects detected n both treatment groups during this clinical trial period from day $15^{th}$to day 90^{th}.At first follow-up visit60% of cases in group A (24 cases) did not detect any adverse effects. Whereas, other mild drug side effects were discomfort upon instillation /transient burning of drops (25%), dryness of eyes (5%), pain in the eyes (2.5%), blurred vision (2.5%), and edema of lids (2.5%). In group B burning (50%), dry eyes (12%), puffy eyes (15%), conjunctival injection (7.5%) and watery eyes (5%), while 12.5% had no adverse effect.

Throughout the study period the adverse effects observed in both treatment groups which were mild and transient and were subsided with continued use of the drugs. In group A (Lodoxamide) adverse effects were subsided earlier (day 60) than in group B (Sodium cromoglycate) which subsided at day 90 of the study and small proportion of patients (5%) persisted with some adverse effects in this group during entire study period.

The results in Table 4 showing the comparison of adverse effects observed during day 15^{th}today 90^{th} in both treatment groups. The outcomes exposed that in group a number of 24(60%) patients did not notice any side effects throughout the study period while in group B a number of 35(87.5%) patients experienced some adverse effects at day 15^{th}($P<0.001$).On the day30^{th}only 4 (10%) patients persisted with adverse effects ($P<0.001$). In group A, at day 60^{th}all respondents (Lodoxamide) were remained free of adverse effects, while in group B (Sodium cromoglycate), 95% patients were free of adverse effects at the completion of study. Hereafter, drug in group A (Lodoxamide) indicated less adverse effects as compared to B group (sodium cromoglycate) drug ($P<0.05$).

Table 1: Demographic and baseline characteristics of patients enrolled in study (n=40)

Characteristics	**Group A**	**Group B**
Remained in study	39 (97.5%)	38 (95%)
Left out	01 (2.5%)	02 (5%)
Cured	38 (97.4%)	35 (92.1%)
Gender		
Male	28 (70%)	28 (70%)
Female	12 (30%)	12 (30%)
Age		
Mean	14.7±0.96	14.4±0.91
Range	5-25 years	5-25 years

No significant difference in treatment groups (p >0.05)

Table 2: Adverse effects in the treatment group a (lodoxamide) from day 15 to day 90

Adverse effects	**Day 15th**	**Day 30th**	**Day 60th**	**Day 90th**
None	24 (60%)	35 (87.5%)	39 (100%)	39 (100%)
Transient burning/discomfort	10 (25%)	-	-	-
Dry eyes	2 (5.0%)	1 (2.5%)	-	-
Blurred vision	1 (2.5%)	-	-	-
Foreign body sensation	1 (2.5%)	1 (2.5%)	-	-
Eye pain	1 (2.5%)	1 (2.5%)	-	-
Edema	1 (2.5%)	1 (2.5%)	-	-

Table 3: Adverse effects in the treatment group b (sodium cromoglycate) from day 15 to day 90

Adverse effects	**Day 15th**	**Day 30th**	**Day 60th**	**Day 90th**
None	5 (12.5%)	7 (17.5%)	23 (60.5%)	36 (94.7%)
Burning	20 (50%)	19 (47.5%)	9 (23.7%)	1 (2.6%)
Conjunctival injection	3 (7.5%)	3 (7.5%)	2 (5.3%)	-
Watery eyes	2 (5.0%)	2 (5.0%)	2 (5.3%)	-
Puffy eyes	6 (15%)	6 (15%)	1 (2.6%)	1 (2.6%)
Dry eyes	4 (12%)	3 (7.5%)	1 (2.6%)	-

Table 4: Comparison of adverse effect in two treatment groups (Lodoxamide and Sodium Chromoglycate)

Adverse effects	**Lodoxamide**	**Sod. Cromoglycate**	**P-value**
None	24 (60%)	5 (12.5%)	0.001
Present			
Day 15	16 (40%)	35 (87.5%)	0.001
Day 30	4 (10%)	33 (82.5%)	0.001
Day 60	-	15 (37.5%)	-
Day 90	-	2 (5.0%)	-

DISCUSSION

Amongst all allergies encountered in our society, ocular type poses a great health hazard. Vernal keratoconjunctivitishas common prevalence due to atmospheric allergens i.e. pollens, animal dander & dust mites. Hot weather intensifies the disease and renders vision and quality of life to lower levels[10,12]. Topical steroids are injudiciouslyused for controlling the severe and distressing symptoms and signs (intense itching, photophobia and lacrimation). But theirprolongedcarries a high threat of steroid-induced glaucoma,cataracts and corneal ulcer with superadded viral, fungaland bacterial infections[12]. Keeping in view all these aspects and to limit use of topical ophthalmic steroids, this study was done to assess clinically detected adverse effects of the two topical mast cell stabilizerswhich are commonly used; sodium cromoglycate and lodoxamide. It is found thatsince late 1990s Lodoxamide has been used topically as ophthalmic solution [16,18].

The study was conducted in 2009 “to evaluate the safety and efficacy of lodoxamide in vernal keratoconjunctivitis”by the principal author and study also exposedencouraging outcomes in improving symptoms and signs of VKC with a smaller number of adverse effects[19]. Again in 2010 the principal author compared efficacy of lodoxamide to sodium cromoglycate and results showed fast clinical symptoms & signs improvement with lodoxamide[20].

By the FDA(Food and Drug Administration) America in 1973 approved drug named Sodium Cromoglycate also known as Cromolyn Sodium[21,22,23] the proportionalprofile of adverse effects was better

as compared with lodoxamide. The frequency of adverse effects in early days of study was significantly fewer with lodoxamideas compared to sodium cromoglycate (P<0.001). This is in agreement with the study conducted by Fahy et al (1992) who observed in their study that lodoxamide has overall lower incidence of side effects as compared to sodium cromoglycate when both the drugs were used in management of allergic eye disease[24]. Lodoxamide when used for controlling the symptoms and signs of VKC showed a fewer adverse effects and sodium cromoglycate demonstrated more adverse effects in early days of study but with its continued use those side effects also subsided at end of the study. However, at the end of this study most of the patients in both treatment groups were devoid of side effects.

CONCLUSION

This Clinical Trial exposed that between the two mast cell stabilizers which were used throughout the study, the profile of clinical adverse effects of A group (lodoxamide) was much better as compared to B group (sodium cromoglycate).

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