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The Effectiveness of loteprednol etabonate Ophthalmic 0.5% Suspension and Topical Ketorolac Tromethamine 0.5% Solution in the Treatment of Vernal Kerato-Conjunctivitis.

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Abstract:
Introduction: *Vernal kerato-conjunctivitis (VKC) is a recurrent bilateral chronic allergic inflammatory disease of cornea and conjunctiva affecting mainly young males in the first decade of life. Diagnosis is based on signs and symptoms including itching, photophobia, sticky mucous discharge, giant papillae on the upper tarsal conjunctiva or at the limbus, superficial keratopathy and corneal shield ulcer. Several reports indicate that topical anti-inflammatory and antiallergic eye-drops are the mainstay of treatment for vernal kerato-conjunctivitis (VKC), but a gold-standard treatment has not yet been established for this disease. In the present study we compared the effectiveness of topical corticosteroids (loteprednol etabonate 0.5%) and NSAIDs (ketorolac tromethamine 0.5%) in the treatment of VKC and to establish which therapeutic regimen is most suitable for this condition.* ***Aim of the study:*** *The aim of this study is to find out the effectiveness of loteprednol etabonate ophthalmic 0.5% suspension and topical ketorolac tromethamine 0.5% solution in the treatment of vernal kerato-conjunctivitis.* ***Material &Methods:*** *This comparative cross-sectional study was carried out in the Out Patient Department of Ophthalmology, Sylhet MAG Osmani Medical College, Sylhet during the period from July 2010 to June 2012 to find out the effectiveness of loteprednol etabonate ophthalmic 0.5% suspension and topical ketorolac tromethamine 0.5% solution in the treatment of vernal kerato-conjunctivitis. Sample size in this study was 47 in each treatment group of loteprednol etabonate and ketorolac tromethamine. Simple random sampling technique was applied to select sample. Study sample was divided randomly into group-A and group-B by considering the outdoor hospital registration number as sample frame. The patients of group A were treated with Loteprednol etabonate 0.5% ophthalmic suspension while patients of group B were treated with Ketorolac tromethamine 0.5% ophthalmic solution. Both loteprednol etabonate 0.5% and ketorolac 0.5% drops were used as 1 drop in each eye 4 times a day for 4 weeks. Quantitative data were expressed as mean and standard deviation; and comparison was performed between the two groups by 'Z' test. Qualitative data were expressed as frequency and percentages; and comparison was done by the chi-Square ($\chi 2$) test. Statistical analysis was performed by using SPSS (Statistical package for social science) for windows version 21.0. A probability (p) of <0.05 was considered statistically significant, $p<0.01$ considered highly significant and $p>0.05$ considered non- significant.* ***Results:*** *This study shows that mean (SD) age of group-A was 9.6 (SD 4.0) years and mean (SD) age of group-B was 9.4 (SD 4.7) years. Male to female ratio was 1.5: 1 in group-A and 2.1:1 in group-B. Both groups were similar in age and sex ($p<0.05$). Reduction of bulbar conjunctival injection, itching, discharge and photophobia in both loteprednol and ketorolac treated group as estimated at the end of day 7, day 14 and day 28 as compared to baseline (day 0) was significant ($p<0.01$). But no significant differences estimated between two treatment group ($p>0.05$). Adverse reaction such as initial burning and stinging on instillation of medication; foreign body sensation, chemosis, hyperaemia and change in IOP were not significantly differed between group-A and group-B.* ***Conclusions:*** *Both loteprednol etabonate 0.5% and ketorolac tromethamine 0.5% ophthalmic solution is effective and safe in reducing the signs and symptoms of vernal kerato-conjunctivitis with similar efficacy and safety profile.*

Key Words: *Vernal Kerato-Conjunctivitis, Bilateral Chronic Allergic Inflammatory Disease, Itching, Photophobia, Sticky Mucous Discharge, Giant Papillae.*

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I. Introduction

Vernal kerato-conjunctivitis (VKC) is a bilateral, chronic, external ocular inflammatory disorder of cornea and conjunctiva, mainly affecting male patients in their first or second decade; characterized by intense ocular itching, followed by tearing, mucous sticky discharge, severe photophobia, blepharospasm and foreign body sensation.[1] Although it is a rare allergic disorder in temperate regions, in many parts of Africa, Latin America and Asia VKC represents an important cause for hospital attendance, ranging from 3% to 6% of patients of all ages, rising to 33% and 90% in children and adolescents. A population prevalence of 4% to 5% has been found among African children.[1,2] An immune-pathogenic mechanism has been proposed for this disease on the basis of personal or familial history of atopy, increased serum levels of total and specific IgE, the response to antiallergic therapy and the presence of several immune cells and mediators in the conjunctiva.[3-5]At present, the exact pathogenic mechanism has not been completely identified. It is generally benign and self-limited presentation; and therapeutic measures are required to control signs and symptoms of the disease and to avoid the longstanding permanent inflammatory sequelae that may lead to fibrovascular reaction, new collagen deposition, tissue remodeling and permanent visual damage.[3-5] Several reports indicate that topical anti-inflammatory (steroids and NSAIDS) and anti-allergic (Sodium cromoglycate, Ketotifen, etc.) eye drops are the mainstay of treatment for VKC, but a gold-standard treatment has not yet been established for this disease.[6]Loteprednoletabonate is a novel corticosteroid designed to be active at its site of application and to undergo a rapid, predictable hydrolysis to an inactive metabolite[7], and exerts immediate anti-inflammatory activity within the eye on instillation, followed by rapid hydrolysis to an inactive metabolite on entering the systemic circulation.[8]Loteprednoletabonate ophthalmic 0.5% suspension was approved by the US Food and Drug Administration in March 1998 for use in the treatment of corticosteroid responsive conditions.[9] In a large-scale clinical study, LE 0.5% was effective in prophylaxis of signs and symptoms of seasonal allergic conjunctivitis (SAC).[10]Loteprednoletabonate 0.5% has been found effective and relatively safe in double-masked, controlled studies in several indications, including prophylaxis of SAC[10], treatment of giant papillary conjunctivitis[11], uveitis[8], and postoperative inflammation[8,12]. However prolonged use of steroids may result in glaucoma, cataract, dry eye and secondary infections. Serious side effects seen with steroids and incomplete amelioration of symptoms with the use of vasoconstrictors and antihistamines necessitated the study of efficacy of other therapeutic agents.[13] Ketorolac tromethamine is a new nonsteroidalanti-inflammatory drug that blocks the cyclo-oxygenase enzyme that catalyzes the conversion of arachidonic acid to prostaglandins.[13] The efficacy and safety of ketorolac tromethamine 0.5% solution has evaluated in the treatment of VKC[13] and other ocular inflammatory conditions.[14,15] Ketorolac tromethamine has been evaluated and found effective in controlling postoperative inflammation following cataract surgery.[13] In this study, we evaluated efficacy of topical loteprednoletabonate ophthalmic 0.5% suspension and topical ketorolac tromethamine 0.5% solution in vernal kerato-conjunctivitis.

II. Methodology And Materials

This comparative cross-sectional study was carried out in the Out Patient Department of Ophthalmology, Sylhet MAG Osmani Medical College, Sylhet during the period from July 2010 to June 2012 to find out the effectiveness of **loteprednol etabonate** ophthalmic 0.5% suspension and topical ketorolac tromethamine 0.5% solution in the treatment of vernal kerato-conjunctivitis. Sample size in this study was 47 in each treatment group of **loteprednol etabonate** and ketorolac tromethamine. Simple random sampling technique was applied to select sample. Study sample was divided randomly into group-A and group-B by considering the outdoor hospital registration number as sample frame. Every odd number of patients was taken in group-A and even number of patients in group-B. Data collected by both qualitative and quantitative method using semi-structured and predesigned questionnaire designed for the study. The questionnaire was pre-tested and face validated by consulting with experts. The clinical histories of the patients were noted. Each patient was examined thoroughly. Complete ophthalmic examination including details of symptoms, visual acuity, slit lamp bio microscopy, applanation tonometry and direct ophthalmoscopy were done. Vernal kerato-conjunctivitis was diagnosed on the basis of itching, ropy discharge, presence of papillae in upper tarsal conjunctiva and limbal changes. The patients of group A were treated with **loteprednol etabonate** 0.5% ophthalmic suspension while patients of group B were treated with Ketorolac tromethamine 0.5% ophthalmic solution. Both **loteprednol etabonate** 0.5% and ketorolac 0.5% drops were used as 1 drop in each eye 4 times a day for 4 weeks. Patients were asked to return on day 7, day 14 and day 28 for evaluation, and at approximately the same time as on visit 1 to control for diurnal variations in IOP. Ocular external examination, slit-lamp examination, applanation tonometry and visual acuity

taken at the scheduled visits during the follow up study to see improvement of bulbar conjunctival injection, ocular itching, discharge and photophobia; and local adverse effects such as foreign body sensation, burning/stinging, chemosis and hyperemia and change in intraocular pressure. Efficacy such as bulbar conjunctival injection, ocular itching, discharge and photophobia were measured by using Efficacy Measurement Scale used by Shulman et al (1999) (Annex-II). Quantitative data were expressed as mean and standard deviation; and comparison was performed between the two groups by 'Z' test. Qualitative data were expressed as frequency and percentages; and comparison was done by the chi-Square ($\chi 2$) test. Statistical analysis was performed by using SPSS (Statistical package for social science) for windows version 21.0. A probability (p) of <0.05 was considered statistically significant, p <0.01 considered highly significant and p >0.05 considered non- significant.

III. Results

Every odd number of patients was taken as group-A and even number of patients as group-B. The patients of group-A were treated with **loteprednol etabonate** 0.5% ophthalmic suspension while the patients of group-B were treated with ketorolac tromethamine 0.5% ophthalmic solution. It was evident from table-II that among the total VKC patients the mean age was 9.5(SD 4.3) years. The mean age of patients of loteprednol group and ketorolac group was almost identical [9.6 (SD 4.0) years vs 9.4 (SD 4.7) years; Z=0.225; p>0.05].It was also evident from this table that among the total VKC patients 59 (62.8%) patients were in the age group of 5 to 10 years, 28 (29.8%) patients in the age group 11 to 15 years and 7 (7.4%) patients were in the age group of 15 to 20 years. Age distribution was similar in both loteprednol and ketorolac groups when classified in different categories (χ^2=2.724; p>0.05). Table-II showed that among the total VKC patients 60 (63.8%) were male and 34 (36.2%) were female with a ratio of male to female 1.8:1. There were 28 (59.6%) male and 19 (40.4%) female in the loteprednol group; while 32 (68.1%) male and 15 (31.9%) female in ketorolac group. The sex difference between the groups wasnot statistically significant (χ^2=0.737; p>0.05). Table-III showed distribution of the patients according to clinical presentation. All patients of both groups had conjunctival injection, conjunctival itching, conjunctival discharge and photophobia. On slit lamp examination kearatitis [6(12.8%) VAS 4 (8.5%); χ^2=0.448; p>0.05)], limbal change [11 (23.4%) VAS 7 (14.9%); χ^2=1.099; p>0.05)] and upper tarsal conjuctival papillae [8 (17.0%) VAS 6(12.8%); χ^2=0.336; p>0.05)] did not differ significantly between group-A and group-B. Table- IV and Figure-I showed the bulbar conjunctival injection at different interval of time after treatment. In the loteprednol group, the mean bulbar conjunctival injection was 2.66 (SD 0.48) before the initiation of treatment which decreased steeply to 1.83 (SD 0.60) at day 7, 1.02 (SD 0.64) at day 14 and 0.28 (SD 0.45) at day 28; while In the ketorolac group, mean bulbar conjunctival injection was 2.49 (SD 0.51) before the initiation of treatment which decreased steeply to 2.00 (SD 0.66) at day 7, 1.13 (SD 0.54) at day 14 and 0.40 (SD 0.50) at day 28. Reduction of bulbar conjunctival injection in both loteprednol group and ketorolac group treated group as estimated at the end of day 7, day 14 and day 28 as compared to baseline was significant (F=334.606; p<0.01). But when the in bulbar conjunctival injection of the two treatments groups were compared, there were no significant differences in bulbar conjunctival injection estimated at baseline, at day 7, day 14 and day 28 (Z=1.676, p>0.05; Z=-1.308, p>0.05; Z=-0.872, p>0.05; Z=-1.304; p>0.05; respectively). Table-V and Figure-II showed the itching at different interval of time after treatment. In the loteprednol group, the mean itching was 3.49 (SD 0.69) before the initiation of treatment which decreased steeply to 2.32 (SD 0.63) at day 7, 1.40 (SD 0.96) at day 14 and 0.30 (SD 0.46) at day 28; while In the ketorolac group, mean itching was 3.70 (SD 0.46) before the initiation of treatment which decreased steeply to 2.53 (SD 0.69) at day 7, 1.34 (SD 0.76) at day 14 and 0.20 (SD 0.41) at day 28. Reduction of itching in both loteprednol group and ketorolac group treated group as estimated at the end of day 7, day 14 and day 28 as compared to baseline was significant (F=710.578; p<0.01). But when itching of the two treatments groups were compared, there were no significant differences in itching estimated at baseline, at day 7, day 14 and day 28 (Z=-1.761, p>0.05; Z=-1.566, p>0.05; Z=0.360, p>0.05; Z=0.941; p>0.05; respectively). Table-VI and Figure-III showed the discharge at different interval of time after treatment. In the loteprednol group, the mean discharge was 2.70 (SD 0.46) before the initiation of treatment which decreased steeply to 1.85 (SD 0.59) at day 7, 1.02 (SD 0.77) at day 14 and 0.40 (SD 0.68) at day 28; while In the ketorolac group, mean discharge was 2.79 (SD 0.41) before the initiation of treatment which decreased steeply to 2.00 (SD 0.47) at day 7, 0.83 (SD 0.76) at day 14 and 0.30 (SD 0.46) at day 28. Reduction of discharge in both loteprednol group and ketorolac group treated group as estimated at the end of day 7, day 14 and day 28 as compared to baseline was significant (F=480.983; p<0.01). But when discharge of the two treatments groups were compared, there were no significant differences estimated at baseline, at day 7, day 14 and day 28 (Z=-0.941, p>0.05; Z=-1.359, p>0.05; Z=1.216, p>0.05; Z=0.886; p>0.05; respectively). Table-VII showed the photophobia at different interval of time after treatment. In the loteprednol group, the mean photophobia was 2.87 (SD 0.34) before the initiation of treatment which decreased steeply to 1.77 (SD 0.60) at day 7, 0.79 (SD 0.75) at day 14 and 0.21 (SD 0.41) at day 28; while In the ketorolac group, mean photophobia was 2.74 (SD 0.44) before the initiation of treatment which decreased steeply to 1.96 (SD 0.51) at day 7, 1.00 (SD 0.63) at day 14 and 0.32 (SD 0.47) at day 28. Reduction of photophobia in both loteprednol group and ketorolac group treated group as estimated at the end of day 7, day 14

and day 28 as compared to baseline was significant (F=555.509; p<0.01). But when photophobia of the two treatments groups were compared, there were no significant differences estimated at baseline, at day 7, day 14 and day 28 (Z=1.577, p>0.05; Z=-1.673, p>0.05; Z=1.494, p>0.05; Z=1.163; p>0.05; respectively). Distribution of patients by adverse effects was shown in table-VIII. There was no significant difference of occurrence of adverse effects between the groups such as burning/stinging on instillation [3 (6.4%) Vs 5 (10.6%); χ^2=0.547; p>0.05]; foreign body sensation [1 (2.1%) Vs 2 (4.3%); χ^2=0.344; p>0.05]; chemosis and hyperemia [2 (4.3%) Vs 3 (6.4%); χ^2=0.211; p>0.05]. None of the patients of both groups developed epiphora and sticky eyes. Distribution of patients by intraocular pressure change was shown in Table-IX. Intraocular pressure (IOP) at day 0 was 13.63 (SD 1.89) mm of Hg and 13.70 (SD 1.91) mm of Hg at day 28 in group-A; while intraocular pressure (IOP) at day 0 was 14.32 (SD 2.12) mm of Hg and 14.25 (SD 2.19) mm of Hg at day 28 in group-B. Intraocular pressure change from day 0 (baseline) today 28 (at the end of treatment) in both group did not differ significantly (Z=-1.771; p>0.05 and Z=0.476; p>0.05 respectively). When intraocular pressure was compared between two treatment groups at day 0 (baseline) and day 28 (at the end of treatment), no significant difference were observed at day 0 (baseline) (Z=-1.643; p>0.05) and at day 28 (at the end of treatment) (Z=-1.305; p>0.05). Distribution of patients by acceptability was shown in Table-X. Patient's assessment was poorly acceptable in 2 (4.3%), moderately acceptable in 10 (21.3%) and highly acceptable in 35 (74.3%) patients in group-A; while poorly acceptable in 2 (4.3%), moderately acceptable in 10 (21.3%) and highly acceptable in 35 (74.3%) patients in group-B (χ^2=1.762; p>0.05).

Table-I: Distribution of the patients by age

Age	Study group			*P*
	Group-A (n=47)	Group-B (n=47)	Total (n=94)	
5-10 years	28 (59.6)	31 (66.0)	59 (62.8)	* p>0.05
11-15 years	17 (36.2)	11 (23.4)	28 (29.8)	
16-20 years	2 (4.3)	5 (10.6)	7 (7.4)	
Mean	9.6 (SD 4.0)	9.4 (SD 4.7)	9.5 (SD 4.3)	† p>0.05

***χ^2=2.724; df=2** **†Z=0.225**

SD= Standard deviation. Figure in the parenthesis indicates corresponding percentage.

Table-II: Distribution of patients according to sex

Sex	Study group			*P*
	Group-A (n=47)	Group-B (n=47)	Total (n=94)	
Male	28 (59.6)	32 (68.1)	60 (63.8)	p>0.05
Female	19 (40.4)	15 (31.9)	34 (36.2)	
Total	47 (100.0)	47 (100.0)	94 (100.0)	

χ^2=0.737; df=1

Table-III: Distribution of the patients according to clinical presentation

Clinical Presentation	Study group		*P*
	Group-A (n=47)	Group-B (n=47)	
Conjunctival itching	47 (100.0)	47 (100.0)	
Conjunctival discharge	47 (100.0)	47 (100.0)	
Photophobia	47 (100.0)	47 (100.0)	
Conjunctival injection	47 (100.0)	47 (100.0)	
Slit lamp findings			
Keratitis(Noninfective)	6 (12.8)	4 (8.5)	p=0.503
Limbal change	11 (23.4)	7 (14.9)	p=0.294
Upper tarsal papillae	8 (17.0)	6 (12.8)	p=0.562

Table-IV: Change in bulbar conjunctival injection at different interval of time

Study group	Evaluation at				†*P*
	Baseline	Day 7	Day 14	Day 28	
Group-A	2.66 (SD 0.48)	1.83 (SD 0.60)	1.02 (SD 0.64)	0.28 (SD 0.45)	p<0.01
Group-B	2.49 (SD 0.51)	2.00 (SD 0.66)	1.13 (SD 0.54)	0.40 (SD 0.50)	
***P**	p>0.05	p>0.05	p>0.05	p>0.05	

*** "Z" test and †Repeated measure ANOVA were applied to analyze the data. Data were presented as mean (SD)**

Figure-I: Change in bulbar conjunctival injection at different interval of time

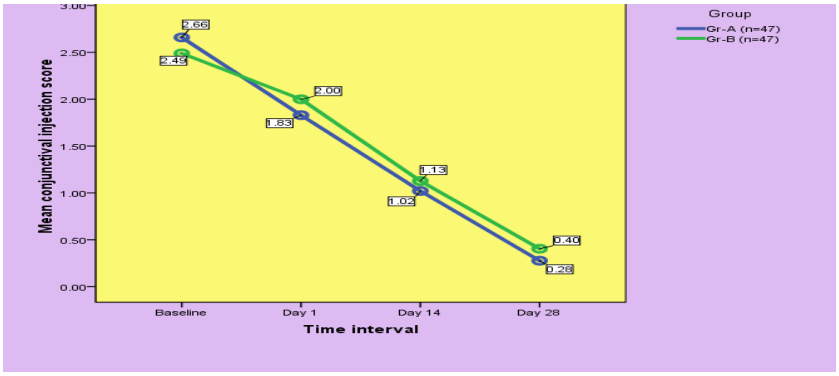

Table-V: Change in conjunctival itching at different interval of time

Study group	Evaluation at				†*P*
	Baseline	**Day 7**	**Day 14**	**Day 28**	
Group-A	3.49 (SD 0.69)	2.32 (SD 0.63)	1.40 (SD 0.96)	0.30 (SD 0.46)	p<0.01
Group-B	3.70 (SD 0.46)	2.53 (SD 0.69)	1.34 (SD 0.76)	0.21 (SD 0.41)	
**P* value	p>0.05	p>0.05	p>0.05	p>0.05	

*** "Z" test and †Repeated measure ANOVA were applied to analyze the data. Data were presented as mean (SD).**

Figure-II: Change in conjunctival itching at different interval of time

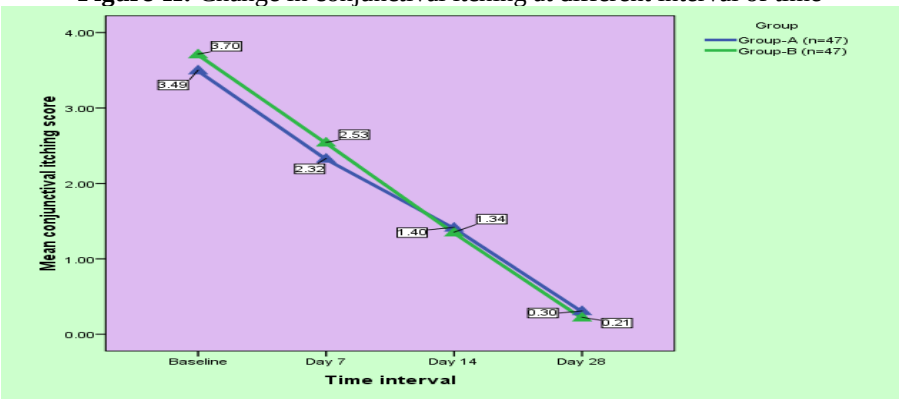

Table-VI: Change in conjunctival discharge at different interval of time

Study group	Evaluation at				†*P*
	Baseline	**Day 7**	**Day 14**	**Day 28**	
Group-A	2.70 (SD 0.46)	1.85 (SD 0.59)	1.02 (SD 0.77)	0.40 (SD 0.68)	p<0.01
Group-B	2.79 (SD 0.41)	2.00 (SD 0.47)	0.83 (SD 0.76)	0.30 (SD 0.46)	
**P*	p>0.05	p>0.05	p>0.05	p>0.05	

*** "Z" test and †Repeted measure ANOVA were applied to analyze the data. Data were presented as mean (SD).**

Figure-III Change in conjunctival discharge at different interval of time

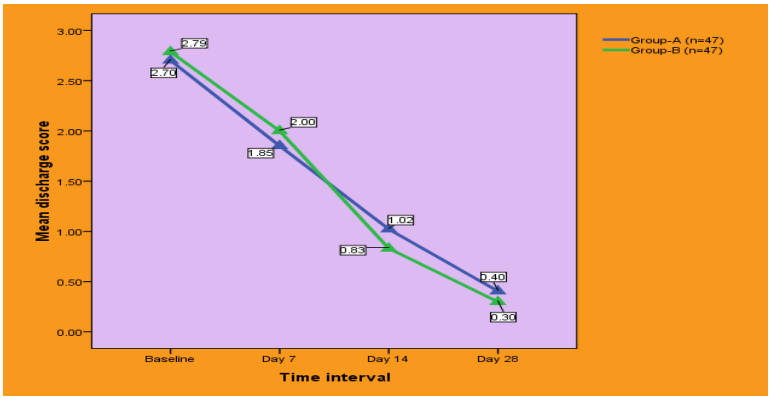

Table-VII: Change in photophobia at different interval of time

Study group	Evaluation at				†P
	Baseline	**Day 7**	**Day 14**	**Day 28**	
Group-A	2.87 (SD 0.34)	1.77 (SD 0.60)	0.79 (SD 0.75)	0.21 (SD 0.41)	p<0.01
Group-B	2.74 (SD 0.44)	1.96 (SD 0.51)	1.00 (SD 0.63)	0.32 (SD 0.47)	
*P	p>0.05	p>0.05	p>0.05	p>0.05	

*** "Z" test and †Repeated measure ANOVA were applied to analyze the data. Data were presented as mean (SD)**

Table-VIII: Distribution of patients by adverse effects

Adverse effects		Study group		P
		Group-A	Group-B	
Burning/stinging on instillation		3 (6.4)	5 (10.6)	p>0.05
	Mild	2	3	
	Moderate	1	2	
	Severe	0	0	
Foreign body sensation		1 (2.1)	2 (4.3)	p>0.05
	Mild	1	1	
	Moderate	0	1	
	Severe	0	0	
Chemosis and hyperaemia		2 (4.3)	3 (6.4)	p>0.05
	Mild	1	1	
	Moderate	1	2	
	Severe	0	0	
*Total		4 (8.5)	7 (14.9)	

***Total adverse effects were less than that of individual adverse effect due to multiple adverse effect in some of the patients.**

Table–IX: Distribution of patients by intraocular pressure change

Study group	Intraocular pressure		p
	At day 0 (mm of Hg)	**At day 28 (mm of Hg)**	
Group-A (n=47)	13.63 (SD 1.89)	13.70 (SD 1.91)	*p>0.05
Group-B (n=47)	14.32 (SD 2.12)	14.25 (SD 2.19)	*p>0.05
†p	p>0.05	p>0.05	

Data were presented as mean (SD). SD: standard deviation * Paired t test and †Z were applied to analyze the data.

Table-X: Distribution of patients by acceptability

Acceptability	Study group		P
	Group-A	**Group-B**	
Not acceptable	0 (0.0)	0 (0.0)	
Poorly acceptable	2 (4.3)	3 (31.9)	p>0.05
Moderately acceptable	10 (21.3)	15 (31.9)	
Highly acceptable	35 (74.3)	30 (61.7	
Total	47 (100.0)	47 (100.0)	

χ^2=1.762 **df=2**

IV. Discussion

Symptoms of vernal kerato-conjunctivitis (VKC) usually persist despite treatment. Topical vasoconstrictors alone or in combination with antihistamines, sodium cromoglycate, topical corticosteroids and systemic antihistamines have been advocated for the treatment of vernal kerato-conjunctivitis (VKC). Vasoconstrictors alone or in combination with antihistamines provide short term and inadequate symptomatic relief. Topical corticosteroids remain the mainstay of therapy. However prolonged use of steroids may result in glaucoma, cataract, dry eye and secondary infections. Serious side effects seen with steroids and incomplete amelioration of symptoms with the use of vasoconstrictors and antihistamines necessitated the study of efficacy of other therapeutic agents.[13]Loteprednoletabonate is a novel corticosteroid designed to be active at its site of application and to undergo a rapid, predictable hydrolysis to an inactive metabolite. At the 0.5% concentration, **loteprednol etabonate** was found effective and relatively safe in double-masked, controlled studies in several indications, including prophylaxis of seasonal allergic conjunctivitis, treatment of giant papillary conjunctivitis, uveitis, and postoperative inflammation.[7] Ketorolac tromethamine is a new nonsteroidal anti-inflammatory drug that blocks the cyclo-oxygenase enzyme that catalyzes the conversion of arachidonic acid to prostaglandins. The efficacy and safety of ketorolac tromethamine 0.5% solution has not been widely evaluated in the treatment of VKC though this drug has been used in other ocular inflammatory conditions. Ketorolac tromethamine has been evaluated and found effective in controlling postoperative inflammation following cataract surgery.[13]This prospective comparative study was conducted in the Department of Ophthalmology during the study period from 1st July 2010 to 30th June 2012. Ninety-four patients with VKC were selected according to inclusion and exclusion criteria and were divided randomly into group-A and group-B each consisting 47 patients. The patients of group-A were treated with **loteprednol etabonate** 0.5% ophthalmic suspension while the patients of group-B were treated with ketorolac tromethamine 0.5% ophthalmic suspension. The outcome of the study was discussed below: It was evident from the study that among the total VKC patients the mean age was 9.5 (SD 4.3) years. The mean age of patients of loteprednol group and ketorolac group was almost identical [9.6 (SD 4.0) years vs 9.4 (SD 4.7) years; $p>0.05$]. This result was in agreement with the study of Deharet al.[16] that the mean age of the patients was 10.26 ± 3.86 years (range 4-18 years). This result was nearly by Sharma et al.[13] that the mean age of the patients was 14.7 years (range 5 to 38 years). The difference was may be due to inclusion of VKC patients of 5 to 38 years but in this study, we included VKC patients 5 to 20 years. This study showed that among the total VKC patients 60 (63.8%) were male and 34 (36.2%) were female. There were 28 (59.6%) male and 17 (40.4%) female in the loteprednol group; while 32 (68.1%) male and 15 (31.9%) female in ketorolac group. The sex difference between the groups was not statistically significant ($p>0.05$). Definite male predominant of VKC patients was reported in several studies.[13,16] Sharma et al.[13] reported 76.2% male and 23.8% female; while Dehar et al.[16] reported 70.0% male and 30.0% female of their enrolled patients. In the present study the mean bulbar conjunctival injection was 2.66 (SD 0.48) before the initiation of treatment which decreased steeply to 1.83 (SD 0.60) at day 7, 1.02 (SD 0.64) at day 14 and 0.28 (SD 0.45) at day 28 in the loteprednol group; while In the ketorolac group, mean bulbar conjunctival injection was 2.49 (SD 0.51) before the initiation of treatment which decreased steeply to 2.00 (SD 0.66) at day 7, 1.13 (SD 0.54) at day 14 and 0.40 (SD 0.50) at day 28. Reduction of bulbar conjunctival injection in both loteprednol group and ketorolac group treated group as estimated at the end of day 7, day 14 and day 28 as compared to baseline was significant ($p<0.01$). But when the in bulbar conjunctival injection of the two treatments groups were compared, there were no significant differences in bulbar conjunctival injection estimated at baseline, at day 7, day 14 and day 28 ($p>0.05$ at all point). Shulman et al.[8] reported that reduction of bulbar conjunctival injection in loteprednol group estimated at the end of day 42 days as compared to baseline was significant ($p<0.01$). Dell et al., (1998) also found similar results in loteprednol group. Sharma et al.[13] reported that bulbar conjunctival injection in ketorolac group estimated at the end of day 14 days as compared to baseline was significant ($p<0.01$). Deharet al.[16] also found similar results in ketorolac group. Both these studies compared their effectiveness with placebo. In the current study the mean itching was 3.49 (SD 0.69) before the initiation of treatment which decreased steeply to 2.32 (SD 0.63) at day 7, 1.40 (SD 0.96) at day 14 and 0.30 (SD 0.46) at day 28 in the loteprednol group; while In the ketorolac group, mean itching was 3.70 (SD 0.46) before the initiation of treatment which decreased steeply to 2.53 (SD 0.69) at day 7, 1.34 (SD 0.76) at day 14 and 0.20 (SD 0.41) at day 28. Reduction of itching in both loteprednol group and ketorolac group treated group as estimated at the end of day 7, day 14 and day 28 as compared to baseline was significant ($p<0.01$). But when itching of the two treatments groups were compared, there were no significant differences in itching estimated at baseline, at day 7, day 14 and day 28 ($p>0.05$ at all point). Shulman et al.[8] reported that reduction of itching in loteprednol group estimated at the end of day 42 days as compared to baseline was significant ($p<0.01$). Dell et al.[7] also found similar results in loteprednol group. Sharma et al.[13] reported that itching in ketorolac group estimated at the end of day 14 days as compared to baseline was significant ($p<0.01$). Deharet al.[16] also found similar results in ketorolac group. Both these studies compared their effectiveness with placebo. The preset study showed that the mean discharge was 2.70 (SD 0.46) before the initiation of treatment which decreased steeply to 1.85 (SD 0.59) at day 7, 1.02 (SD 0.77) at day 14 and 0.40 (SD 0.68) at day 28 in the loteprednol group; while In the ketorolac group, mean discharge was 2.79 (SD 0.41) before the initiation of treatment which decreased steeply to 2.00 (SD 0.47)

at day 7, 0.83 (SD 0.76) at day 14 and 0.30 (SD 0.46) at day 28. Reduction of discharge in both loteprednol and ketorolac treated groups as estimated at the end of day 7, day 14 and day 28 as compared to baseline was significant ($p<0.01$). But when discharge of the two treatments groups were compared, there were no significant differences estimated at baseline, at day 7, day 14 and day 28 ($p>0.05$ at all point). Shulman et al.[8] reported that reduction of discharge in loteprednol group estimated at the end of day 42 days as compared to baseline was significant ($p<0.01$). Sharma et al.[13] reported that discharge in ketorolac group estimated at the end of day 14 days as compared to baseline was significant ($p<0.01$). In this study the mean photophobia was 2.87 (SD 0.34) before the initiation of treatment which decreased steeply to 1.77 (SD 0.60) at day 7, 0.79 (SD 0.75) at day 14 and 0.21 (SD 0.41) at day 28 in the loteprednol group; while In the ketorolac group, mean photophobia was 2.74 (SD 0.44) before the initiation of treatment which decreased steeply to 1.96 (SD 0.51) at day 7, 1.00 (SD 0.63) at day 14 and 0.32 (SD 0.47) at day 28. Reduction of photophobia in both loteprednol and ketorolac treated groups as estimated at the end of day 7, day 14 and day 28 as compared to baseline was significant ($p<0.01$). But when photophobia of the two treatments groups were compared, there were no significant differences estimated at baseline, at day 7, day 14 and day 28 ($p>0.05$ at all point). Shulman et al.[8] reported that reduction of photophobia in loteprednol group estimated at the end of day 42 days as compared to baseline was significant ($p<0.01$). Sharma et al.[13] reported that photophobia in ketorolac group estimated at the end of day 14 days as compared to baseline was significant ($p<0.01$). There was no significant difference of occurrence of adverse effects between the groups such as burning/stinging on instillation [3 (6.4%) Vs 5 (10.6%); $p>0.05$]; foreign body sensation [1 (2.1%) Vs 2 (4.3%); $p>0.05$]; chemosis and hyperemia [2 (4.3%) Vs 3 (6.4%); $p>0.05$]. None of the patients of both groups developed epiphora, sticky eyes and increased in IOP more than 10 mm of Hg. In this regards Dell et al.,[7] reported no patients in loteprednol treatment group had an intraocular pressure elevation of 10 mm Hg or greater; while Shulman et al.[8] found one (1.5%) patients in loteprednol treatment group had an intraocular pressure elevation of 10 mm Hg or greater. Sharma et al.[13] Transient stinging sensation was observed by 3 patients (14.3%) in the ketorolac treated group. Deharet al.[16] reported no serious adverse events were reported during the study. Minor adverse reaction included initial burning and stinging on instillation of medication (10%). However, this did not indicate the discontinuation of the therapy.

LIMITATIONS OF THE STUDY

The present study was conducted at a very short period of time. This was a comparative cross-sectional type of study in a single community with comparatively small number of sample size. So, the study result may not reflect the exact scenarios of the whole country.

V. Conclusion And Recommendations

Reduction of bulbar conjunctival injection, itching, discharge and photophobia in both loteprednol and ketorolac treated group as estimated at the end of day 7, day 14 and day 28 as compared to baseline (day 0) was significant ($p<0.01$). But no significant differences estimated at baseline (day 0), at day 7, day 14 and day 28 between two treatment group ($p>0.05$ at all point). No serious adverse events were reported during the study. Minor adverse reaction included initial burning and stinging on instillation of medication, foreign body sensation, chemosis and hyperaemia which did not significantly difference between the groups. In conclusion **loteprednol etabonate** 0.5% is effective and safe as ketorolac tromethamine 0.5% ophthalmic solution in reducing the signs and symptoms of vernal kerato-conjunctivitis. As **loteprednol etabonate** 0.5% and ketorolac tromethamine 0.5% ophthalmic solution is effective in reducing the signs and symptoms of vernal kerato-conjunctivitis with similar efficacy and safety profile, the present study recommends ketorolac tromethamine 0.5% ophthalmic solution in the treatment of vernal kerato-conjunctivitis as chance of increased intraocular pressure in **loteprednol etabonate**.

References

[1]. De Smedt, S., Wildner, G., Kestelyn, P., 2013. Vernal keratoconjunctivitis: an update. Br J Ophthalmol, 97(1), 9-14.
[2]. De Smedt, S., Nkurikiye, J., Fonteyne, Y., Hogewoning, A., Esbroeck, M.V, Bacquer, D.D., et al., 2011. Vernal keratoconjunctivitis in school children in Rwanda and its association with socio-economic status: a population-based survey. Am J Trop Med Hyg, 85,711–7.
[3]. Bonini, S., Bonini, S., Lambiase, A., Marchi, S., Pasqualetti, P., Zuccaro, O., et al., 2000. Vernal keratoconjunctivitis revisited. A case series of 195 patients with long-term follow up. Ophthalmology 107: 1157–63.
[4]. Leonardi, A., 2002., Vernal keratoconjunctivitis: pathogenesis and treatment. ProgRetin Eye Res, 21, 319–39.
[5]. Leonardi, A., Secchi, A.G., 2003. Vernal keratoconjunctivitis. IntOphthalmolClin, 43, 41–58.
[6]. Mantelli, F., Santos, M.S., Petitti, T., Sgrulletta, R., Cortes, M., Lambiase, A., et al. 2007. Systematic review and meta-analysis of randomised clinical trials on topical treatments for vernal keratoconjunctivitis. Br J Ophthalmol, 91, 1656–61.
[7]. Dell, S.J., Lowry, G.M., Northcutt, J.A., Howes, J., Novack, G.D., Hart, K., 1998. A randomized, double-masked, placebo-controlled parallel study of 0.2% loteprednoletabonate in patients with seasonal allergic conjunctivitis. J Allergy ClinImmunol, 102(2), 251-5.
[8]. Shulman, D.G., Lothringer, L.L., Rubin, J.M., Briggs, R.B., Howes, J., Novack, G.D., et al., 1999. A randomized, double-masked, placebo-controlled parallel study of loteprednoletabonate 0.2% in patients with seasonal allergic conjunctivitis. Ophthalmology, 106(2), 362-9.

[9]. Pflugfelder, S.C., Maskin, S.L., Anderson, B., Chodosh, J., Holland, E.J., De Paiva, C.S., et al., 2004. A randomized, double-masked, placebo-controlled, multicenter comparison of loteprednoletabonate ophthalmic suspension, 0.5%, and placebo for treatment of keratoconjunctivitissicca in patients with delayed tear clearance. Am J Ophthalmol, 138(3), 444-57.
[10]. Dell, S.J., Shulman, D.G., Lowry, G.M., Howes, J., 1997. A controlled evaluation of the efficacy and safety of loteprednoletabonate in the prophylactic treatment of seasonal allergic conjunctivitis. Loteprednol Allergic Conjunctivitis Study Group. Am J Ophthalmol, 123, 791–7.
[11]. Friedlaender, M.H., Howes, J., 1997. A double-masked, placebo-controlled evaluation of the efficacy and safety of loteprednoletabonate in the treatment of giant papillary conjunctivitis. The LoteprednolEtabonate Giant Papillary Conjunctivitis Study Group 1. Am J Ophthalmol, 123, 455–64.
[12]. Stewart, R.H., Horwitz, B., Howes, J., Novack, G.D., Hart, K., LoteprednolEtabonate Post-operative Inflammation Study Group 1., 1998. A double-masked, placebo-controlled evaluation of 0.5% loteprednoletabonate in the treatment of post-operative inflammation. J Cataract Refract Surg, 24, 1480–9.
[13]. Sharma, A., Gupta, R., Ram, J., Gupta, A., 1997. Topical ketorolac 0.5% solution for the treatment of vernal keratoconjunctivitis. Indian J Ophthalmol, 45, 177-80.
[14]. Tinkelman, D.G., Rupp, G., Kaufman, H., 1993. Double-masked, paired comparison clinical study of 0.5% ketorolac tromethamine ophthalmic solution compared with placebo eye drops in the treatment of seasonal allergic conjunctivitis. SurvOphthalmol, 38(Suppl), 133-40.
[15]. Ballas, Z., Blumenthal, M., Tinkelman, D.G., 1993. Clinical evaluation of ketorolac tromethamine 0.5% ophthalmic solution for the treatment of seasonal allergic conjunctivitis. SurvOphthalmol, 38(Suppl), 141-48.
[16]. Dehar, N., Gupta, A., Singh, G., 2012. Comparative study of the ocular efficacy and safety of diclofenac sodium (0.1%) ophthalmic solution with that of ketorolac tromethamine (0.5%) ophthalmic solution in patients with acute seasonal allergic conjunctivitis. Int J App Basic Med Res, 2, 25-30.

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