Original Research Paper

Volume - 14 | Issue - 11 | November - 2024 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Pharma

A COMPARATIVE STUDY OF THE EFFICACY AND SAFETY OF POLYETHYLENE GLYCOL AND SODIUM HYALURONATE IN DRY EYE DISEASE

Karthick S*	Junior Resident, Department of Pharmacology, PGIMS, Rohtak, Haryana *Corresponding Author
Kaushal J	Senior Professor and Head, Department of Pharmacology, PGIMS, Rohtak, Haryana
Sachdeva S	Professor, Regional Institute of Ophthalmology, PGIMS, Rohtak, Haryana

ABSTRACT **Background:** Dry eye disease is defined as "A multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface". This study aimed to investigate the efficacy and safety of polyethylene glycol and sodium hyaluronate in treating dry eye disease. **Methods:** A prospective, randomised comparative clinical study was conducted on 50 patients. The patients were randomly divided into two groups of 25 each to receive the following treatments Group A (n=25) polyethylene glycol eye drops 0.1% and Group B (n=25) Sodium hyaluronate eye drops 0.1% both TDS for 6 weeks. Efficacy assessment was done at end of 2 and 6 weeks by Schirmer-1, Tear film breakup time (TBUT), Rose Bengal staining, Lissamine staining, Fluorescein staining and Marginal tear strip tests. Safety was assessed by monitoring adverse drug reactions and ophthalmological examination. **Results:** Improvement of Schirmer-1 test score in Group A and B was 8.56 and 7.2 mm/5 min respectively, compared to their baseline value.While the improvement of TBUT score was 7.52 and 6.44 sec respectively over 6 weeks. The reduction of Rose Bengal score in Group A and Group B was 2.8 and 3.4 respectively. Both the drugs improved the dry eye symptoms statistically significantly as compared to the baseline values. **Conclusions:** Both drugs were found to be safe and efficacious in patients suffering from dry eye disease. Polyethylene glycol was found to be more efficacious regarding improvement in tear film stability and was safer compared to sodium hyaluronate

KEYWORDS : Dry eye disease, polyethylene glycol, sodium hyaluronate

INTRODUCTION

Dry Eye Disease (DED) is a multifactorial disorder marked by a loss of the tear film and ocular surface disruption, affecting individuals across all age groups but being particularly prevalent among adults and women.[1] DED is increasingly recognised as an inflammatory condition with characteristics similar to autoimmune diseases.[2,3] The prevalence of DED varies widely, ranging from 5% to 50% in the general population, and can affect up to 75% of adults over 40 years old, with a notable gender disparity—women are affected more frequently than men.[4] This increased prevalence is especially significant in postmenopausal women, where hormonal imbalances contribute to tear film instability and ocular inflammation. Long-term contact lens wearers and individuals with high computer usage are also at elevated risk.[5]

DED is associated with a disruption in the lacrimal functional unit, The condition is characterized by tear film instability, epithelial dysfunction, and inflammation. Additional factors such as lid margin changes and nerve damage can exacerbate the condition.[6,7] Common symptoms include a gritty sensation, burning, stinging, and excessive tearing. Severe cases may lead to conjunctival scarring, corneal ulcers, and potential vision loss.[8]

Tear supplements, often known as artificial tears, are lubricating eye drops that provide symptomatic relief for DED. Anti-inflammatory drugs (NSAIDs, steroids) and Immunosuppressants (cyclosporine) are currently utilized to restore the inflamed ocular surface, as DED is now considered an inflammatory condition with many similarities to autoimmune disease. But none of these drugs keep the eye surface moist for a long time, help in affecting the disease pathology and have several side effects.[9]

The newer drugs polyethylene glycol and sodium hyaluronate keep the eye surface moist for a long time and also repair the damaged corneal epithelial cells.[10] The present study was done to evaluate and compare the efficacy and safety of polyethylene glycol and sodium hyaluronate in dry eye disease.

METHODS

This was a prospective, randomised, comparative, open clinical study conducted by the Departments of Pharmacology and Regional Institute of Ophthalmology, Pt BD Sharma Post Graduate Institute of Medical Sciences, Rohtak, India on 50 patients, between January 2023 to December 2023. A simple, standard technique for random assignment with computer-generated numbers was used to allocate the treatment schedule. The enrollment of the patients for the study is shown in Figure 1. The patients in each group were found to be comparable at the time of their initial visit with regard to demographic parameters such as age, gender, weight and other parameters as shown in Table 1.

The trial was registered prospectively with CTRI (CTRI/2023/02/049510) and was undertaken after the approval of protocol from the Biomedical Research Ethics Committee (BREC/22/Th/Pharma-07) and all the principles of Good Clinical Practice were followed.

A total of 50 patients of both genders aged more than 18 years were divided into two groups of 25 patients each. The patients were randomly allocated to receive one of the treatments. Informed consent was obtained from the attendants of all patients enrolled for the study. Inclusion criteria were patients of either gender >18 years of age, patients diagnosed with moderate dry eye disease (i.e. score ranging from 9-13) according to Khurana`s scoring system[12], and those willing to give written informed consent. Exclusion criteria were any structural abnormalities (such as eyelid trichiasis, entropion and scarring), presence of pinguecula or pterygium, active allergy, infection or inflammatory disease at the ocular surface unrelated to dry eye, any inflammation or active structural change in the iris or anterior chamber, previous punctual occlusion or eye surgery, a positive history of refractive surgery or contact lens wearing, glaucoma, diabetes, hypertension or other systemic, dermatologic or neurologic diseases, use of any other topical medication other than artificial tears within the past one month, use of any systemic anti-inflammatory drugs or medication that could interfere with tear production, such as anti-anxiety, anti-depressive and antihistamine medications for the last 3 months, history of allergy to study medication. Pregnant and lactating women were excluded from the study. The eligible patients after screening were randomly allocated to the treatment groups. Each study group had 25 patients and received one of the following treatments topically for 6 weeks: Group A (n=25) polyethylene glycol eye drops 0.1% and Group B (n=25) sodium hyaluronate eye drops 0.1% , both TDS for 6 weeks. Available commercial preparations (same brand) of the drugs were used. Before the treatment was initiated, the ophthalmological examination was done to check the visual acuity, and to know the condition of the ocular surface, adnexa and retinal status with the help of direct and indirect ophthalmoscopy.

All the relevant ophthalmological tests i.e Schirmer, Tear breakup time (TBUT), Rose Bengal staining, Lissamine staining, Fluorescein staining and Marginal tear strip tests were done at baseline and then subsequently at the end of 2 and 6 weeks for efficacy assessment. Schirmer`s test quantitatively measures tear production from the lacrimal gland during fixed time intervals while TBUT measures the

time required for tear film to break up following a blink. As dry eye disease gets treated, there is an improvement in their scores. Rose Bengal and Lissamine staining detect abnormalities of the surface of the eye and there is a reduction of respective scores. Marginal tear strip test detects the tear content and as the patient improves, its status changes from absent to intact. Fluorescein staining detects abrasions and scratches on the cornea and as the patient improves status of staining changes from diffuse to absent. At each visit, patients were assessed for drug response, IOP measurement, visual acuity and any adverse drug reactions to the drugs.

Data was entered into MS Excel and analyzed using SPSS Version 20.0. Continuous parametric data was reported as Means and standard deviation. Categorical variables were expressed in percentages. A comparison of continuous variables between the two groups was done using an unpaired t-test. For non-normal distributions, the Mann-Whitney test was used to compare between two groups. Comparison of normal continuous variables over a single time interval was done using paired t-test and over multiple time intervals was done using repeated measures ANOVA. Comparison of non-normal continuous data over a single time interval was done using the Wilcoxon signed rank test and over multiple time intervals was done using the Friedmann test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The demographic parameters of the patients are tabulated in Table I. The difference in demographic paramteres was not statistically significant at the time of intiation of the study. Table II shows the mean Schirmer`s score and TBUT score of both treatment groups, at baseline and different periods in the study. Regarding Schirmer`s score, as shown in Table II there was a statistically significant improvement in Schirmer`s score at the end of 2 and 6 weeks compared to baseline values in both the groups. In groups A and B, there was an improvement of the score by 3.44 mm and 2.24 mm respectively at the end of 2 weeks compared to their baseline values ($p<0.05$). At the end of 6 weeks in Groups A and B there was still an improvement in score by 8.56 mm and 7.2 mm respectively compared to their baseline values ($p< 0.05$). On intergroup analysis, the difference was statistically significant at the end of the 2nd week (p-value-0.037) as well as at the end of the 6th week (p-value-0.008). Thus group A (polyethylene glycol) showed a statistically significant better response. In TBUT test, as shown in Table there was a statistically significant improvement in the Tear film break-up time (TBUT) score at the end of 2 and 6 weeks compared to baseline values in both the groups. In groups A and B, there was an improvement of a score by 2.52 and 2.2 sec respectively at the end of 2 weeks compared to their baseline values ($p<0.05$). At the end of 6 weeks in groups A and B there was still an improvement of the score by 7.52 and 6.44 sec respectively compared to their baseline values ($p<0.05$). On intergroup analysis, at the end of 2 weeks, better response was seen with group A as compared to group B which continued till the end of 6 weeks, but it was not statistically significant. (p-value of group A versus B at the end of 6 weeks was 0.338).

Regarding Rose Bengal staining score, as shown in fig-2 there was a statistically significant reduction in Rose Bengal staining score at the end of 2 and 6 weeks compared to baseline values in both the groups. In groups A and B there was a decrement of scores by 1 and 1.24 respectively at the end of 2 weeks compared to their baseline values ($p <0.05$). At the end of 6 weeks in groups A and B there was still decrement in scores by 2.8 and 3.4 respectively compared to their baseline values ($p<0.05$). On intergroup analysis, at the end of 2 weeks, better response was seen with group B compared to group A which continued till the end of 6 weeks, but it was not statistically significant. (p-value of group A versus B at the end of 6 weeks was 0.115). In Lissamine staining score, there was a statistically significant reduction in Lissamine staining score at the end of 2 and 6 weeks compared to baseline values in both the groups. In groups A and B, there was a decrease in scores by 1.48 and 1.32 respectively at the end of 2 weeks compared to their baseline values ($p<0.05$). At the end of 6 weeks in groups A and B there was still a decrease in scores by 2.76 and 2.84 respectively compared to their baseline values ($p<0.05$). On intergroup analysis, at the end of 2 weeks, a better response was seen with group A compared to group B (reduction was 1.48 vs 1.32 respectively) but it was not statistically significant (p-value 0.769). However, at the end of 6 weeks group B showed a slightly better response than group A (reduction was 2.84 vs 2.76 respectively) but it was not statistically significant (p-value 0.434).

Regarding fluorescein staining, all patients in both groups were completely cured i.e. absent fluorescein staining (Khurana scoring system 0) at the end of 6 weeks. However, on comparison of both the groups, a better response was seen at the end of 2 weeks in group B than group A and it was statistically significant i.e number of patients complelety cured i.e having absent fluorescein staining (Khurana scoring system 0) were 5 vs 0 (p-value 0.047).

Regarding marginal tear strip test there was also a statistically significant improvement in the number of patients who were completely cured i.e that showing intact marginal tear strip test (Khurana scoring system 0)in both the groups, However on comparison of both the groups, slightly better response was seen at the end of 6 weeks in group B than group A, as number of patients completley cured were 21 vs 19 respectively but the differenc was not statistically significant ($p>0.05$).

The incidence of blurred vision, eye itching, ocular hyperemia and headache was more in group B as compared to group A, however, the difference was not statistically significant ($p>0.05$). The incidence of increased eye pain was slightly more in group A compared to group B, but the difference was not statistically significant. (Figure-3)

FIG-1

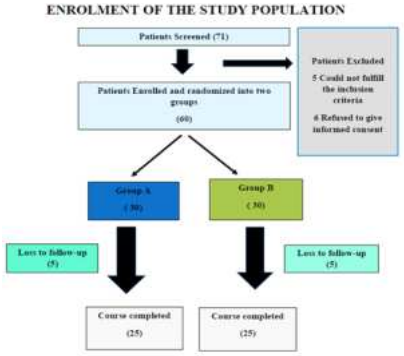

Table-1 COMPARISON OF STUDY POPULATION CHARACTERISTICS IN BOTH GROUPS

VARIBALBE	GROUP-A (n=25)	GROUP-B (n=25)
AGE	43.12±12.33	45.08±11.03
MALE	11 (44%)	14 (56%)
FEMALE	14 (56%)	11 (44%)
LITERATE	12 (48%)	12 (48%)
ILITERATE	13 (52%)	13(52%)
DRUG ALLERGY	0	0

Age is expressed as Mean±SD

TABLE-2 COMPARISON OF SCHIRMER`S I TEST SCORE AND TEAR BREAK UP TIME IN BOTH THE GROUPS

TIME INTERVAL	SCHRIMER SCORE (mm/5min)			TBUT SCORE (sec)		
	GROUP-A	GROUP-B	P-VALUE (INTER GROUP)	GROUP-A	GROUP-B	
BASELINE	4.88±1.53	4.88±1.66	1.00	5.00±2.36	5.24±2.12	0.707
2ND WEEK	8.32±2.01*	7.12±1.94*	0.037#	7.52±2.93*	7.44±2.64*	0.920
6TH WEEK	13.44±1.73*	12.08±1.75*	0.008#	12.52±3.47*	11.68±2.59*	0.338

All values are expressed as Mean±SD

Inter group comparison showing statistically significance($p<0.05$)

* Intra group comparison showing statistical significance($p<0.05$)

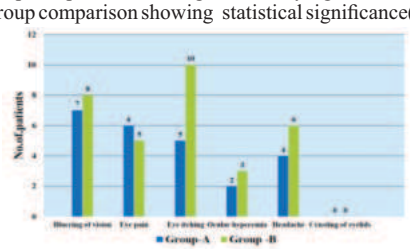

FIG- 2 COMPARISON OF LISSAMINE STAINING SCORE

DISCUSSION

Dry eye disease (DED) is a multifactorial disorder characterized by a loss of the tear film and ocular surface disruption, accompanied by both signs and symptoms.1 Keratoconjunctivitis "Dryness of the cornea and conjunctiva" is a literal translation of the Latin term sicca, and "sicca" is a portion of the English word "desiccate." Dry eye illness is now classified as an inflammatory condition with many similarities to autoimmune disease.[3]

Artificial tears are lubricating eye drops that are used to relieve the dryness and discomfort caused by DED's lack of tear production. Lubricating tear ointments can be used during the day, but due to poor vision after application, they are usually used at night. Dry eye disease (DED) is primarily treated by targeting inflammation, with anti-inflammatory strategies as a first-line approach. Medications such as NSAIDs, corticosteroids, tetracyclines, and immune suppressants like cyclosporine are commonly used. [11]

Polyethylene glycol binds to injured corneal epithelial cells & protects the eye surface for a long time. It has mucin-like action and is adsorbed on the injured corneal epithelial region to repair the damage.Sodium hyaluronate easily combines and adsorbs water molecules allowing the water layer to be stabilized and the lacrimal film breakup time to be delayed. It protects corneal epithelial cells and maintains barrier function and conjunctival cell healing.

The present study was done to evaluate and compare the efficacy and safety of polyethylene glycol and sodium hyaluronate in dry eye disease by assessment of parameters Schirmer-1 test, Tear break-up time, RoseBengal staining score, Fluorescein staining, Lissamine green staining and Marginal strip test.

Regarding the Schrimer-1 test, there was a statistically significant improvement in the Schrimer score over 6 weeks compared to the baseline value in both the treatment groups. However, a statistically significant better response was seen with polyethylene glycol than sodium hyaluronate at the end of 2 weeks (p-0.037) as well as 6 weeks (p-0.008). Although exact similar studies were not available in which similar treatment groups were compared for observing the effects on the Schirmer score. However, after a literature search, we could get the study done by Park et al comparing 0.1%, 0.15%, and 0.3% sodium hyaluronate with 0.05% cyclosporine. One hundred seventy-six patients were divided into 4 groups and given sodium hyaluronate of different concentrations for 12 weeks. The mean change from baseline to week 12 in the Schirmer test result were1.31±6.04 for the 0.1% sodium hyaluronate group, 2.54±6.46 for the 0.15% sodium hyaluronate group, 0.70±6.39 for 0.3% sodium hyaluronate and 1.07±6.57 for 0.05% cyclosporine group. However, the score in the 0.15% sodium hyaluronate showed a significant tendency for better improvement at week 12 compared with other groups. There was no statistically significant difference in improvement in the Schrimer1 test score between the groups and the p-value ($p>0.05$).[9]

The findings of our study are similar to the above-mentioned study in the context that there was an improvement in the Schirmer score with 0.1% sodium hyaluronate at the end of the study. However, the exact comparison was not possible from the above-mentioned study, as in our study similar drugs with the same formulations were not compared. Moreover, the drugs were given for 84 days (12 weeks) in the above-mentioned study whereas in our study the drugs were given for 42 days (6 weeks). After a literature search, we were not able to find any study in which the Schirmer-1 test was evaluated in patients with dry eye disease with polyethylene glycol.

Regarding TBUT, there was a statistically significant improvement in TBUT score over 6 weeks compared to baseline value in both groups. Polyethylene glycol showed a better response but it was not statistically significant at the end of 2 weeks (p-0.920) as well as 6 weeks (p-0.338).

Although exact similar studies were not available in which similar treatment groups were compared for observing the effects on TBUT. However, after a literature search, we found a study in which polyethylene glycol lubricant eye drops were used in reducing squamous metaplasia in patients with dry eye disease. In a study done by Aguilar et al., a total of 50 patients with dry eye disease were given polyethylene glycol 1 drop for three times a day for 90 days. Patients had follow-up visits of 30,60 and 90 days. At baseline, the mean Tear film break-up time (TBUT) was 4.8±1.0 sec and increased to 5.8±1.0 sec at 30 days and 6.3±0.9 sec at day 60, ending at 6.8±0.9 sec at 90 days. Almost 61% patients reached a TBUT of >7 sec. There was a significant improvement in tear break-up time compared to the baseline and the improvement was statistically significant ($p<0.001$).[10]

The findings of our study are similar to the above-mentioned study as there was an improvement in TBUT with polyethylene glycol when it was given for 6 weeks and the improvement was statistically significant ($p<0.05$) as in above mentioned study. However, the exact comparison was not possible from the above-mentioned study, as in our study similar groups were not compared. Moreover, the drugs were given for 90 days in above mentioned study whereas in our study the drugs were given for 42 days (6 weeks).

In a study done by Park et al, one hundred seventy-six patients were divided into 4 groups. In Group A 43 patients were treated with (0.1% sodium hyaluronate)), Group B 41 patients were treated with (0.15% sodium hyaluronate), Group C 47 patients were treated with (0.3% (sodium hyaluronate), and in Group D 45 patients were treated with (0.05% cyclosporine) for 12 weeks. TBUT showed significant improvement in all groups. The findings of our studies are similar in the context that there was an improvement with 0.1% sodium hyaluronate at the end of the study. However, the exact comparison was not possible from the above-mentioned study, as in our study similar drugs with the same formulations were not compared.

In the present study, Lissamine green staining showed significant improvement compared with baseline in both groups and at all time points. Similar results were observed with sodium hyaluronate regarding improvement in lissamine green staining a study done by Park et al,[9] However, the exact comparison was not possible from the above-mentioned study, as in our study similar drugs with similar formulations were not compared.

In the present study, fluorescein staining showed significant improvement compared with baseline in both groups. Similar results were observed with sodium hyaluronate regarding the improvement of fluorescein staining in a study done by Park et al,[9] However, the exact comparison was not possible from the above-mentioned study, as the treatment groups were not exactly similar.

After a literature search, we were not able to get any study in which Rose Bengal staining score or Marginal strip was evaluated in patients of dry eye disease with our study drugs.

CONCLUSION

Both the treatment groups i.e. Polyethylene Glycol and Sodium Hyaluronate were found to be safe and efficacious in patients suffering from dry eye disease (led to improvement in tear film stability and reduction in severity of disease).On comparing the above-mentioned treatment groups, polyethylene glycol was found to be more efficacious regarding improvement in tear film stability and was safer compared to sodium hyaluronate. Hence, in our study polyethylene glycol was found to be the better treatment option for moderate dry eye disease patients.

ACKNOWLEDGEMENTS-

DECLARATIONS
Funding: NIL
Conflict of interest: There are no conflicts of interest
Ethical approval: Approved

REFERENCES

1. Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK, et al. TFOS DEWS II definition and classification report. Ocul Surf. 2017; 15(3):276-83.
2. Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, et al. Tfos dews ii epidemiology report. Ocul Surf. 2017; 15(3):334-65.
3. Lemp MA, Baudouin C, Baum J, Dogru M, Foulks GN, Kinoshita S, et al. The definition and classification of dry eye disease: report of the definition and classification subcommittee of the International Dry Eye. Ocular Surf. 2007; 5:75–92.
4. Rouen PA, White ML. Dry eye disease: prevalence, assessment, and management. Home healthcare now. 2018;36(2):74-83.
5. Messmer EM. The pathophysiology, diagnosis, and treatment of dry eye disease. Deutsches Ärzteblatt International. 2015;112(5):71.
6. Yu J, Asche CV, Fairchild CJ. The economic burden of dry eye disease in the United States: a decision tree analysis. Cornea. 2011;30(4):379-87.
7. Kaercher T, Bron AJ. Classification and diagnosis of dry eye. Surgery for the Dry Eye. 2008;41:36-53.
8. Pflugfelder SC, Geerling G, Kinoshita S, Lemp MA, McCulley JP, Nelson D, et al. Management and therapy of dry eye disease: report of the Management and Therapy Subcommittee of the International Dry Eye WorkShop. Ocul. Surf. 2007;5(2):163-78.
9. Park Y, Song JS, Choi CY, Yoon KC, Lee HK, Kim HS. A randomized multicenter study

comparing 0.1%, 0.15%, and 0.3% sodium hyaluronate with 0.05% cyclosporine in the treatment of dry eye. J Ocul Pharmacol Ther. 2017 ;33(2):66-72.
10. Mackor AJ, Bijsterveld OPV. Tear function parameters in Keratoconjunctivitis sicca with and without the association of Sjogren's syndrome. Ophthalmologica. 1988;196(4):169-74.
11. Javadi MA, Feizi S. Dry eye syndrome. J Ophthal Vis Res. 2011;6(3):192–8.
12. Khurana AK, Chaudhary R, Ahluwalia BK, Gupta S. Tear film profile in dry eye. Acta ophthalmologica. 1991 Feb;69(1):79-86