Clinical and Experimental Vision and Eye Research (2023), 6, 5–9

ORIGINAL ARTICLE

To study the role of systane hydration and sodium hyaluronate alone in managing post-operative dryness following LASIK: A single-center, two-arm, open-label, prospective, interventional study

Chitra Ramamurthy[1], Ashalyne James Joseph[2], B. Soundarya[2], Shreyas Ramamurthy[2], Ramamurthy Dandapani[1]

[1]The Eye Foundation, Coimbatore, Tamil Nadu, India, [2]Cornea, Cataract and Refractive Surgery, The Eye Foundation, Coimbatore, Tamil Nadu, India

Keywords:

Artificial tears,
Dry eyes,
LASIK,
Sodium hyaluronate,
Systane HYDRATION

Address for correspondence:
Chitra Ramamurthy, The Eye Foundation, 582, Diwan Bahadur Rd, R.S. Puram, Coimbatore, Tamil Nadu 641 002, India.
E-mail: drchitra@theeyefoundation.com

Received: 18-09-2023;
Accepted: 20-10-2023
doi: 10.15713/ins.clever.102

Abstract

Aim: The aim of the study is to evaluate the role of Systane HYDRATION versus Soha in post-operative dryness in Indian patients undergoing LASIK surgery.
Methods: 60 patients (30 patients in each group-Systane HYDRATION versus sodium hyaluronate) between the ages of 18 and 45 years undergoing flap-based bilateral LASIK procedures for any amount of refractive error are included in the study. Pre-operative, 1-week, and 4-week post-operative visits are done. Each visit includes dry eye evaluation using the DEQ-5 questionnaire, Schirmer's test, tear film breakup time (TBUT), and total ocular symptom score (TOSS) score. The results of each group are being compared to note the improvement in dry eye symptoms from week 1 to week 4 and also to look for statistically significant differences between the two groups.
Results: The mean DEQ-5 score showed an improvement from 5.23 ± 2.88 at week 1 to 3.57 ± 2.37 at week 4 and 5.45 ± 3.87 at week 1 to 4.1 ± 2.68 at week 4 in the Systane HYDRATION and Soha groups, respectively. Mean Schirmer's value improved from 23.4 ± 6.4 to 24.2 ± 6.16 and from 21.22 ± 6.69 to 24.15 ± 6.33 from week 1 to week 4 in the Systane HYDRATION and Soha groups, respectively. TBUT and TOSS scores also showed improvement in both groups. No statistically significant difference was noted between the two groups.
Conclusion: From the data analysis, we conclude that both Systane HYDRATION and Soha are effective in managing post-LASIK dry eye.

Introduction

Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film.[1] LASIK is an iatrogenic cause of dry eye. It occurs due to damage to the corneal nerves, use of topical anesthesia, and usage of benzalkonium chloride-containing eye drops. Artificial tears play an important role in the management of dry eye. They help to supplement the tear film volume and stability. Several types of artificial tears are available today. They mostly differ based on the composition of polymers, electrolytes, osmolarity, solutes, and preservatives used.[2]

In this study, we compare the outcomes of Systane HYDRATION (Alcon Laboratories) versus Soha (Sun Pharmaceutical Industries Ltd.) in the management of dry eye in post-LASIK patients. Systane HYDRATION is a sterile solution containing hydroxypropyl-guar, propylene glycol, polyethylene glycol, 0.15% sodium hyaluronate and is preserved with 0.001% polyquad. Soha contains only sodium hyaluronate (0.1%) as the polymer and is preserved with 0.01% stabilized oxychloro complex.

Polymers play an important role in stabilizing the tear film by increasing the retention time on the ocular surface.[3] Hydroxypropyl-guar is a mucomimetic agent that reduces surface friction. It possesses similar rheological properties to those of

tears.[4] Several studies have demonstrated the effectiveness of hydroxypropyl-guar in dry eye.[5,6] Hyaluronic acid is widely used in dry eye due to its viscoelastic and hygroscopic properties.[7] Several studies have demonstrated the effectiveness of hyaluronic acid in dry eye.[8,9]

Artificial tear preparations containing a combination of polymers are expected to perform better than teardrop preparations containing only a single polymer in dry eye. The purpose of this study was to compare the efficacy of Systane HYDRATION to Soha eye drops in the management of dry eye in post-LASIK patients using the DEQ-5 questionnaire, Schirmer's test, tear film breakup time (TBUT), and total ocular symptom score (TOSS).

Materials and Methods

This was a two-arm, open-label, prospective, interventional study conducted in a tertiary eye care center in South India. Patients between the ages of 18 and 45 years undergoing flap-based bilateral LASIK procedures for any amount of refractive error are included in the study. In a total of 60 patients, 30 patients in each group completed the study. Both groups received artificial tear drops 6 times daily postoperatively for 4 weeks.

Table 1: The descriptive statistics of age and gender

Variable	Subcategory	Soha (*n*=30)	Systane HYDRATION (*n*=30)	Total (*n*=60)
Age	Mean±SD	25.7±4.89	24.6±3.25	25.1±4.15
Gender	Male	12 (20%)	14 (23.33%)	26 (43.33%)
	Female	18 (30%)	16 (26.67%)	34 (56.67%)

Pre-operative, 1 week, and 4-week post-operative visits are done. Each visit includes dry eye evaluation using the DEQ-5 questionnaire, Schirmer's test, tear film breakup time (TBUT), and corneal staining index. The results of each group are being compared to note the improvement in dry eye symptoms from week 1 to week 4 and also to look for statistically significant differences between the two groups.

Schirmer's, TBUT, TOSS, and DEQ-5 scores were compared between the groups using the Mann–Whitney *U*-test. The comparison of Schirmer's, TBUT, TOSS, and DEQ-5 scores across the time points was compared using the Friedman test.

The percentage change from week 1 to week 4 post-operative is calculated for Schirmer's, TBUT, TOSS, and DEQ-5 scores. This shift from week 1 is compared between Systane HYDRATION and Soha using the Mann–Whitney *U*-test. The normality of the data was assessed using the Shapiro–Wilk test. The mean and 95% CI for each variable's mean at each visit are presented graphically. All the tests were conducted with a 5% level of significance. The data analysis was conducted using SAS v9.4.

The study protocol adhered to the tenets of the Declaration of Helsinki. This study was approved by the Institutional Ethics Committee.

Results

A total of 120 eyes were included in the study. 60 eyes of 30 patients were included in each group. All patients were followed up for a minimum of 4 weeks. Overall, the average age of patients is 25.1 years with 4.15 years of standard deviation. Out of 60 patients, 34 (56.67%) are females and 26 (43.33%) are males.

Table 2: Comparison of DEQ-5 score, Schirmer's, over the groups and time points

Variables	Time points	Soha			Systane HYDRATION			*P*-value
		n	Mean±SD	Median (Min, Max)	*n*	Mean±SD	Median (Min, Max)	
DEQ-5 Score	Pre-operative	30	3.2±2.75	2 (0, 12)	30	3.6±2.54	3 (0, 9)	0.441^{MW}
	1-week post-operative	30	5.45±3.87	5 (0, 15)	30	5.23±2.88	5.5 (0, 12)	0.939^{MW}
	4-week post-operative	30	4.1±2.68	4.5 (0, 10)	30	3.57±2.37	4 (0, 10)	0.444^{MW}
P-value			0.045^{F*}			0.027^{F*}		-
Schirmer's	Pre-operative	60	26.43±7.61	30 (5, 35)	60	24.75±6.9	25 (4, 35)	0.094^{MW}
	1-week post-operative	60	21.22±6.69	20 (10, 35)	60	23.4±6.4	25 (10, 35)	0.054^{MW}
	4-week post-operative	60	24.15±6.33	25 (10, 35)	60	24.2±6.16	25 (8, 35)	0.972^{MW}
P-value			<0.001^{F*}			0.350		-
TBUT	Pre-operative	60	9.8±3.82	8 (4, 16)	60	10.85±4.1	12 (4, 17)	0.148^{MW}
	1-week post-operative	60	7.82±3.69	6 (4, 15)	60	8.75±4.06	8 (3, 15)	0.313^{MW}
	4-week post-operative	60	8.95±3.16	8 (5, 15)	60	9.73±4.03	10 (4, 25)	0.307^{MW}
P-value			0.003^{F*}			0.013^{F*}		-
TOSS	Pre-operative	60	0.17±0.38	0 (0, 1)	60	0.23±0.5	0 (0, 2)	0.587^{MW}
	1-week post-operative	60	0.27±0.48	0 (0, 2)	60	0.28±0.45	0 (0, 1)	0.727^{MW}
	4-week post-operative	60	0.23±0.5	0 (0, 2)	60	0.18±0.39	0 (0, 1)	0.756^{MW}
P-value			0.515			0.400		-

The variables DEQ-5 score, Schirmer's, TBUT, and TOSS are compared between the groups and across the different time points. The normality of the data was assessed using the Shapiro–Wilk test.

The mean score for each variable was compared at each time point between Systane HYDRATION and Soha groups using the Mann–Whitney *U*-test. From the result, between Systane HYDRATION and Soha groups, there is no significant difference in any of the variables (DEQ-5 score, Schirmer's, TBUT, and TOSS) at any time point.

Similarly, the variables are compared over the time period in each group (separately for Soha and Systane HYDRATION) using the Friedman test. In the Systane HYDRATION group, there is a significant difference in the DEQ-5 score and TBUT over time. In the Soha group, for the following variables DEQ-5 score, Schirmer's, and TBUT, there is a significant difference over time.

The TOSS variable is found to be highly varying around the average value, for both groups. In the Systane HYDRATION group, the TOSS score at 4 weeks shows an improvement when compared to the pre-operative and 1-week post-operative values. However, in the Soha group, TOSS score at 4 weeks is better than the 1-week post-operative value but worse than the pre-operative value. Furthermore, when comparing the TOSS score at 4 weeks, the Systane HYDRATION group shows a better score than the Soha group.

Mann–Whitney *U*-test was conducted for the *post hoc* analysis. It is found that the average DEQ-5 score at pre-operative time point is significantly different from 1-week post-operative ($P = 0.02$). In the Systane HYDRATION group, the average value of DEQ-5 score between pre-operative versus 1-week post-operative ($P = 0.02$) and the 1-week post-operative versus 4-week post-operative ($P = 0.02$) is statistically significant. Both the groups showed significant improvement in DEQ-5 scores when comparing 1-week post-operative scores to 4-week post-operative scores. Systane HYDRATION group had a better DEQ-5 score than the Soha group.

At the pre-operative time point, the average Schirmer's is significantly different from the average value at other time points. When comparing the pre-operative, 1-week, and 4-week Schirmer's scores, in the Systane HYDRATION group, the scores are steadily maintained whereas the Soha group shows a decline through the study duration. For TBUT, the comparison between pre-operative versus 1-week post-operative ($P = 0.002$) and the 1-week post-operative versus 4-week post-operative is statistically significant ($P = 0.02$). All the findings are graphically represented in Figure 1.

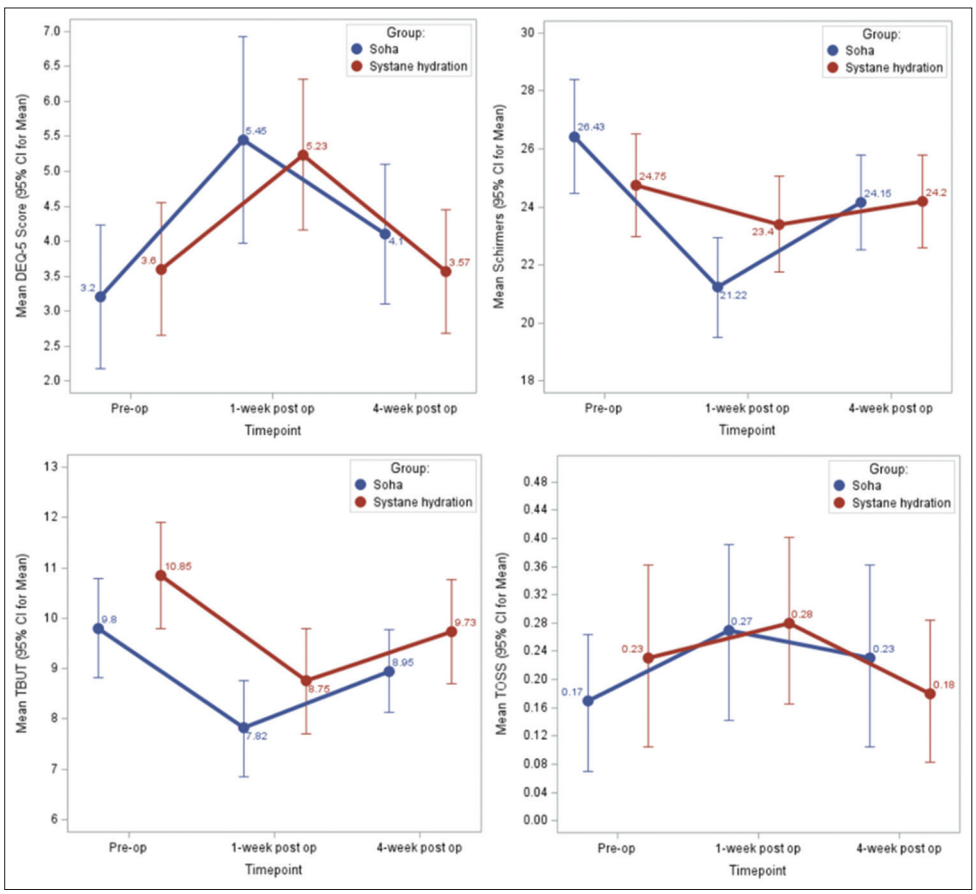

Figure 1: Graphical representation of mean DEQ-5 score, mean Schirmer's score, mean T-BUT's score, and mean TOSS in Systane HYDRATION and Soha group at pre-operative, 1-week post-operative, and 4-week post-operative visit

Thus, both Systane HYDRATION and Soha are equally effective in managing post-LASIK dry eye. There were no adverse events at any point in time.

Discussion

LASIK is an iatrogenic cause of dry eye. This study was aimed at comparing the efficacy of Systane HYDRATION and Soha in the management of post-LASIK dry eye. Our study demonstrated that both Systane HYDRATION and Soha are equally effective in managing post-LASIK dry eye. These eye drops are recommended to moisten and lubricate the eye in case of dry eye.

Hydroxypropyl-guar forms a thin cross-linked gel-like matrix when exposed to tear film which in turn allows prolonged retention of demulcents and helps in tear film stabilization.[10] Hyaluronic acid has extensive water retention capacity and provides sustained HYDRATION. Systane HYDRATION contains both hydroxypropyl-guar and hyaluronic acid. Using a combination of different polymers in a single formulation has synergizing effects. Thus, it would provide prolonged HYDRATION and help to reduce the frequency of medications. The higher efficacy of hydroxypropyl-guar and hyaluronic acid combination over hyaluronic acid alone or with other combinations has been proven in various animal models and human corneal epithelium models.[11,12]

In our prospective study, we analyzed the data for dry eye in post-LASIK patients. The artificial tear drops were administered in both groups from the 1st day postoperatively to 4 weeks postoperatively. The pre-operative data were compared to 1-week and 4-week data.

Regarding the ocular symptoms of dry eye, we found statistically significant improvement when comparing the DEQ-5 score from 1-week post-operative to 4-week post-operative. However, there was no statistically significant difference between the two groups.

Tests including T-BUT and Schirmer's showed improvement from 1-week post-operative to 4-week post-operative, with no statistically significant difference between the two groups. The TOSS score also showed improvement from 1-week post-operative to 4-week post-operative, but it was not statistically significant. Furthermore, there was no statistically significant difference between the two groups.

In our patients, T-BUT and Schirmer's were inversely correlated with the DEQ-5 score, indicating a good correspondence between signs and symptoms.

The results of our study are in line with other previous studies which had also demonstrated comparable outcomes in dry eye when using artificial tear drops containing hydroxypropyl-guar and hyaluronic acid combination to hyaluronic acid containing eye drops.[13,14]

Hence, our study proves that both Systane HYDRATION and Soha are useful in treating post-LASIK dry eye. No adverse effects were noted and it was found that both the drops are well tolerated. Moreover, using a combination formulation like Systane HYDRATION can be advantageous due to the potentially enhancing beneficial effects.

Conclusion

Hyaluronic acid and hydroxypropyl-guar are effective in protecting the ocular surface and reducing post-LASIK dry eye. Thus, both Systane HYDRATION and Soha are effective in managing post-LASIK dry eye.

Acknowledgments

The study was supported by an IIT research grant from Alcon Vision LLC.

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;15:276-83.
2. Al-Saedi Z, Zimmerman A, Bachu RD, Dey S, Shah Z, Baugh R, *et al*. Dry eye disease: Present challenges in the management and future trends. Curr Pharm Des 2016;22:4470-90.
3. Torkildsen G. The effects of lubricant eye drops on visual function as measured by the inter-blink interval visual acuity decay test. Clin Ophthalmol 2009;3:501-6.
4. Benelli U. Systane lubricant eye drops in the management of ocular dryness. Clin Ophthalmol 2011;5:783-90.
5. Labetoulle M, Messmer EM, Pisella PJ, Ogundele A, Baudouin C. Safety and efficacy of a hydroxypropyl guar/polyethylene glycol/propylene glycol-based lubricant eye-drop in patients with dry eye. Br J Ophthalmol 2017;101:487-92.
6. Jacobi C, Kruse FE, Cursiefen C. Prospective, randomized, controlled comparison of SYSTANE UD eye drops versus VISINE INTENSIV 1% EDO eye drops for the treatment of moderate dry eye. J Ocul Pharmacol Ther 2012;28:598-603.
7. Dogru M, Nakamura M, Shimazaki J, Tsubota K. Changing trends in the treatment of dry-eye disease. Expert Opin Investig Drugs 2013;22:1581-601.
8. Aragona P, Papa V, Micali A, Santocono M, Milazzo G. Long term treatment with sodium hyaluronate-containing artificial tears reduces ocular surface damage in patients with dry eye. Br J Ophthalmol 2002;86:181-4.
9. Prabhasawat P, Tesavibul N, Kasetsuwan N. Performance profile of sodium hyaluronate in patients with lipid tear deficiency: Randomized, double-blind, controlled, exploratory study. Br J Ophthalmol 2007;91:47-50.
10. Ubels JL, Clousing DP, van Haitsma TA, Hong BS, Stauffer P, Asgharian B, *et al*. Pre-clinical investigation of the efficacy of an artificial tear solution containing hydroxypropyl-guar as a gelling agent. Curr Eye Res 2004;28:437-44.
11. Rangarajan R, Kraybill B, Ogundele A, Ketelson HA. Effects of a hyaluronic acid/hydroxypropyl guar artificial tear solution on protection, recovery, and lubricity in models of corneal epithelium. J Ocul Pharmacol Ther 2015;31:491-7.
12. Carlson E, Kao WW, Ogundele A. Evaluating the Effect of Hyaluronic Acid-containing Artificial Tear Products on Corneal Wound Reepithelialization in an *in vivo* study. In: ARVO 2017

Annual Meeting Abstract.
13. Labetoulle M, Schmickler S, Galarreta D, Böhringer D, Ogundele A, Guillon M, *et al*. Efficacy and safety of dual-polymer hydroxypropyl guar-and hyaluronic acid-containing lubricant eyedrops for the management of dry-eye disease: A randomized double-masked clinical study. Clin Ophthalmol 2018;12:2499-508.
14. Labiris G, Ntonti P, Sideroudi H, Kozobolis V. Impact of polyethylene glycol 400/propylene glycol/hydroxypropyl-guar and 0.1% sodium hyaluronate on postoperative discomfort following cataract extraction surgery: A comparative study. Eye Vis (Lond) 2017;4:13.

How to cite this article: Ramamurthy C, Joseph AJ, Soundarya B, Ramamurthy S, Dandapani R. To study the role of systane hydration and sodium hyaluronate alone in managing post-operative dryness following LASIK: A single-center, two-arm, open-label, prospective, interventional study. Cli Exp Vis Eye Res J 2023;6(2):5-9.