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ORIGINAL ARTICLE

Effectiveness and safety assessment of polyethylene glycol/propylene glycol with hydroxypropyl guar lubricating eye drops in dry eye due to computer vision syndrome: A prospective, single-center, single-arm, interventional study

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Abstract

Purpose: The objective of this prospective real-world evidence-based study was to investigate the clinical effectiveness and safety of polyethylene glycol and propylene glycol/hydroxypropyl-guar (PEG/PG with HPG) for treating computer vision syndrome (CVS)-related dry eye.

Participants and Methods: In this prospective, single-arm, single-center, interventional study, adult participants from India with dry eye disease were instilled with PEG/PG with HPG in each eye twice a day for 30 days. Change in ocular surface disease index (OSDI) from baseline to end of the study (Day 30) was the primary endpoint of the study. The secondary endpoints included mean changes in tear film break-up time (TFBUT) and CVS questionnaire (CVS-Q). Safety was assessed during the study.

Results: Sixty-six patients in total received treatment. The study demonstrated a significant reduction of the mean (SD) OSDI ($P < 0.0001$) on Day 15 and Day 30 from baseline (−3.8 on Day 15 and −9.6 on Day 30). The magnitude of change in TFBUT from the baseline (intragroup) to subsequent visits was significant (Day 15: Mean [SD] – 1.2 [3.15], $P = 0.0081$; Day 30: 1.3 [2.35], $P < 0.0001$). The mean (SD) CVS-Q scores also reduced significantly from baseline to both time points (mean [SD], baseline: 10 [1.89], day 15: −2.5 [2.01], day 30: −5.7 [2.29], and all $P < 0.0001$). There were no adverse events (AEs) reported during the study.

Conclusion: The study suggested that short-term treatment with PEG/PG with HPG was effective for treating dry eye symptoms associated with CVS. No new safety findings emerged from this study.

Introduction

Computer vision syndrome (CVS) can be characterized by a group of visual, ocular, and muscular symptoms that develop because of prolonged exposure to digital display devices, such as computers, tablets, and smartphones.[1,2] The prevalence of CVS varies worldwide based on the type of work with higher prevalence reported among office workers and college students.[2,3] Around 60 million people worldwide suffer from CVS, and among computer users, CVS prevalence was found to range from 64% to 90%. Moreover, every year there are about a million new cases of CVS.[4] CVS usually develops due to >3 h/day or >30 h/week use of a computer.[2] Extended use of visual display terminals reduces blink frequency, blink amplitude, and blink quality, which results in the instability of the tear film.[5] Headaches, dry eyes, blurred vision, eyestrain, and soreness in the shoulders and neck are among the typical symptoms of CVS.[6] The development of dry eye disease (DED) is the primary symptom seen in CVS.[2] DED is one of the most frequent eye disorders that affect millions of individuals worldwide and has a global prevalence of 5% and 50% depending on the region and population lifestyle.[7]

Artificial tear supplements are the mainstay treatment for dry eyes due to CVS, regardless of the severity of the dry eye.[5] Artificial tears are known to lubricate the ocular surface and increase tear volume, thereby reducing CVS symptoms.[8] Polyethylene glycol/propylene glycol with hydroxypropyl guar (PEG/PG with HPG) lubricating eye drops has been made available commercially since 2008. Hydrophilic demulcents PEG/PG - the active components in PEG/PG-HPG eye drops have a lower viscosity than cellulose derivatives. Borate and sorbitol are used to buffer HPG, a natural polysaccharide gelling agent. Due to its high molecular weight (1000–5000 kDa), PEG/PG with HPG lubricating drops increase the viscosity of the eye drop.[9] A clinical study has shown improvement in patients with a reduction in DED symptoms, lower frequencies of foreign-body sensation, and effective moisture retention providing proper lubrication to the corneal epithelium. This demonstrated that PEG/PG with HPG lubricating drops successfully reduced dry eye symptoms.[10]

It has been reported that the daily use of PEG/PG-HPG for 4 weeks or more in patients with DED resulted in a substantial rise in tear film break-up time (TFBUT) and a reduction in dry eye symptoms. Clinical efficacy and safety evaluation indicated that PEG/PG-HPG is effective in improving DED symptoms and is well-tolerated by patients.[11] The objective of this prospective real-world evidence-based study was to investigate the clinical effectiveness and safety of PEG/PG-HPG for treating CVS-related dry eye.

Methodology

Study design

This was a prospective, single-arm, single-center, interventional study conducted in an eye hospital in Chennai, India.

Before participation in the study, each patient provided written informed consent. The study was approved by the independent ethics committee, and it was conducted in accordance with the Declaration of Helsinki, the International Conference on Harmonization, and Good Clinical Practice guidelines.

Eligibility criteria

Adult patients (of age ≥18 years, both men and women, and non-smokers), with a TFBUT of ≤10 s in at least one eye, and best-corrected visual acuity of ≥20/80 (or ≥55 letters score or ≥0.6 early treatment diabetic retinopathy study log of the minimum angle of resolution value) in both eyes at screening had eligibility for inclusion. In addition, the patients who met at least one of the three following criteria in at least one eye at screening (randomization stratified based on the criteria below): (a) unanesthetized Schirmer I test score of ≤9 mm for a 5-min test duration (aqueous deficient dry eye stratum); (b) meibum quality score of ≥1 (on a 0–3 scale) or meibum expressibility score of >1 (on a 0–3 scale) in either eyelid (evaporative dry eye stratum); and (c) met both entry criteria (a) and (b) (mixed dry eye stratum) were also included. In addition, all eligible patients had daily computer/visual display unit (VDU) use >3 h/day/15 h/week, with a minimum of 3 months of exposure to any VDU and with CVS questionnaire (CVS-Q) score ≥6, and Ocular Surface Disease Index (OSDI) Score 23–32 (both inclusive) with dry eye symptoms.

The key exclusion criteria were (a) history of hypersensitivity to the study drug or any of its excipients; (b) use of any topical ocular medication preserved with benzalkonium chloride or other products known to be toxic to the tear film lipid layer, or lid hygiene therapy or punctal plug insertion within 1 month prior to the screening visit; (c) use of contact lens for the last 6 months before screening visit; (d) initiation of any topical ocular medication (with the exception of artificial tears/gels/lubricants) ≤2 weeks before the screening visit, or taking steroids, isotretinoin, or immunosuppressive drugs; (e) history of systemic disease or other ocular pathologies, history of intra- or extra-ocular surgery, or planning to undergo ocular or eyelid surgery or any other clinically significant illness. Artificial tears/lubricants were not allowed from the baseline visit till the discontinuation of the patient from the study.

The use of concomitant non-study medications during the study was based on the investigator's discretion.

Study treatment

Eligible patients received the first dose of PEG/PG with HPG (Systane Ultra®, Alcon, Fort Worth, TX, USA) on Day 1 and were needed to self-administer 4 times daily dosing (QID) for 30 days with scheduled visits on Day 15 and Day 30. In case the patients experienced any dry eye symptoms, additional doses could be administered as required.

Study endpoints

The primary endpoint of the study was the mean reduction in OSDI scores (assessed on a scale of 1–100; higher scores represent greater disability) from baseline to the end of the study (Day 30). In addition, the percentage of patients with a reduction of >4.5 in OSDI score during the study was also assessed (exploratory endpoint).

The secondary endpoints included mean changes in TFBUT and CVS-Q scores from the baseline to the end of the study.

Monitoring of treatment-emergent adverse events (AEs) and treatment-emergent serious AEs was a part of the safety assessment, during the study.

Statistical analysis

Overall, 60 patients were planned to be enrolled in the study to have 80% power. Considering 10% dropouts/withdrawals during the study, 66 patients were enrolled in this single-arm, interventional study.

Statistical software SPSS version 20.0 (Armonk, NY: IBM Corp.) was used to perform statistical analysis. Reduction in OSDI scores, TFBUT, and CVS-Q scores from baseline was

summarized descriptively. The percentage of patients who had a reduction of >4.5 in OSDI score from baseline was also summarized descriptively. To evaluate the reduction, the mean changes from baseline to day 30 were compared by calculating mean differences and 95% confidence intervals. Paired *t*-test was used for the significance in the magnitude of change from baseline (Day 0) for normal data, whereas the Wilcoxon signed-rank test was used for the non-normal data.

Results

Baseline characteristics and demographics

Sixty-six patients in total diagnosed with CVS (dry eye) were included in the study from January 07, 2023 to February 17, 2023. The median (range) age of these patients was 23 (20.00, 42.00) years, 33.3% of the patients were men and all patients were Asian.

Visual acuity, Slit lamp, and retinal fundus examination

Reduction in the mean score of visual acuity in both right and left eyes was observed on Days 15 and 30; however, the magnitude of change from baseline was not statistically significant ($P > 0.05$). In addition, no statistically significant difference ($P > 0.05$) in the change between the left versus right eye was observed in the visual acuity test. The results of the slit-lamp examination (conjunctiva, cornea, eyelids, iris, and lens), anterior chamber examination (cells, flare, and vitreous cells), and retinal fundus examination (choroid, macula, optic nerve, and retina) were normal for all patients throughout the study period.

Mean reduction of OSDI

The mean (SD) OSDI scores significantly reduced from baseline to both Days 15 and 30 (end-of-study) [Figure 1]. The absolute mean change value from baseline was −3.8 on Day 15, $P < 0.0001$, and −9.6 on Day 30, $P < 0.000$ [Table 1].

About one-third of patients (n = 24; 36.36%) reported a reduction of >4.5 in OSDI scores following 2 weeks of PEG/PG with HPG treatment. By the end of the study, the majority of patients (86.36%) had a reduction of >4.5 in OSDI scores [Figure 2].

TFBUT score

An improvement in mean TFBUT score was observed for the left and right eye, at Day 15 and Day 30. The magnitude of change from the baseline (intragroup) to subsequent visits was significant (Day 15: mean [SD] – 1.2 [3.15], $P = 0.0081$; Day 30: 1.3 [2.35], $P < 0.0001$) [Figure 3]. However, the TFBUT scores of the left *vs.* right eye at both time points were not significantly different ($P > 0.05$) between the [Table 2].

Change in CVS-Q score

The mean (SD) CVS-Q scores also reduced significantly from baseline to both follow-up time points (mean [SD], baseline – 10 [1.89], Day 15: −2.5 [2.01], Day 30: −5.7 [2.29], all $P < 0.0001$) [Figure 4].

A numerical reduction in the mean score of CVS-Q was observed with an absolute mean change in values of −4.1 and −10.6 for Days 15 and 30, respectively, and the reduction in mean total CVS-Q score was statistically significant (all $P < 0.0001$) from baseline (intragroup) to visits 2 and 3 [Table 3].

Safety analysis

No AEs were reported in this study.

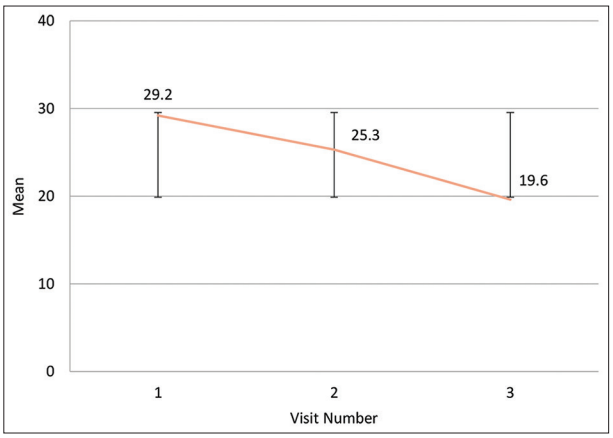

Figure 1: Reduction of ocular surface disease index score from baseline to day 30. $P<0.0001$(s), $P<0.0001$(t)

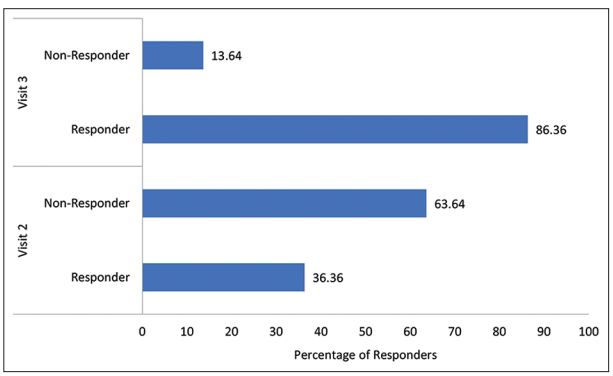

Figure 2: Percentage of responders who had a reduction of >4.5 in ocular surface disease index score on day 30

Table 1: Change of OSDI in patients with dry eyes from baseline to subsequent follow-up visits

Parameters	Change from baseline to day 15 (n=64)	Change from baseline to day 30 (n=63)
Mean (SD)	−3.8 (3.13)	−9.6 (4.80)
95% CI	(−4.62, −3.06)	(−10.79, −8.38)
P-value	<0.0001 (S)	<0.0001 (T)

P-value was calculated using paired t-test (T)/signed rank test (S).
CI: Confidence interval; OSDI: Ocular surface disease index; SD: Standard deviation

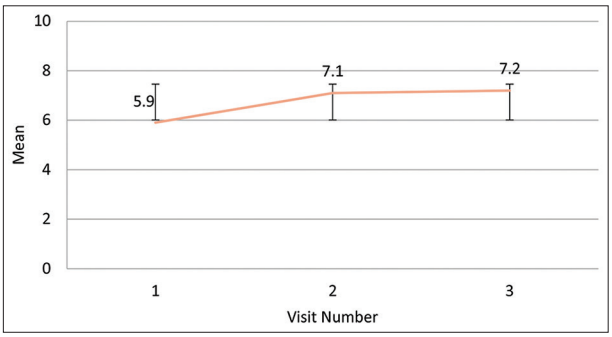

Figure 3: Change in tear film break-up time from baseline to day 30. *P*-value, OD: 0.0001 (s), 0.7866 (w), OS: 0.0002 (s), Mean of eyes: <0.0001 (s) at day 30. (s)

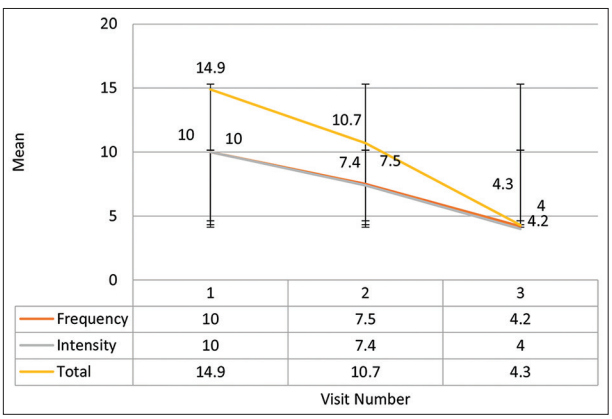

Figure 4: Decrease in computer vision syndrome questionnaire score from baseline to day 30. *P*-value, Frequency: <0.0001(s), Intensity: <0.0001(s), Total: <0.0001(s), at day 30

Discussion

Effective treatment of DED includes the restoration of the ocular surface by reducing damage, maintaining tear film homeostasis, alleviating signs and symptoms of dry eye, and maintaining visual function. Artificial tears are the first-line treatment for DED care because they protect the ocular surface, maintain tear film stability, and restore the natural tear film, while also enhancing patients' comfort, vision, and quality of life.[12] Ideally, artificial tears should effectively improve signs and symptoms of DED and for that, they must spread in an even and uniform manner, reduce friction during blinks, cause negligible visual disturbance, and be safe to use.[13] In the current study, with the use of PEG/PG with HPG lubricating eye drops in patients with CVS-associated dry eye, significant reduction in the mean OSDI score ($P < 0.0001$) was seen from baseline to Days 15 and 30. These reductions in the OSDI score may indicate the beneficial effect of PEG/PG with HPG lubricating eye drops. The mean total CVS-Q score showed a significant reduction ($P < 0.0001$) from baseline (intragroup) to Days 15 and 30, indicating an improvement in dry eye symptoms with the use of PEG/PG with HPG lubricating eye drops. The TFBUT scores exhibited a significant increase in visits 2 and 3 compared to the baseline score, which might be indicative of the efficacy of PEG/PG with HPG.

Our findings are in line with the study by Davitt *et al.*[14] who observed that the use of artificial eye drops significantly decreased the mean scores of the dry eye symptoms and OSDI compared to baseline. The study findings indicated that the use of PEG/PG with HPG lubricant QID for 6 weeks was effective and well-tolerated in patients with dry eyes. Numerous other studies have shown that PEG/PG plus HPG is successful in reducing the

Table 2: Change of TFBUT in patients with dry eyes from baseline to subsequent follow-up visits

Parameters	Change from baseline to day 15 (*n*=64)	Change from baseline to day 30 (*n*=63)
OD		
Mean (SD)	1.2 (3.12)	1.3 (2.59)
95% CI	(0.42, 1.98)	(0.68, 1.99)
P-value	0.0050 (S), 0.9522 (W)	0.0001 (S), 0.7866 (W)
OS		
Mean (SD)	1.2 (3.15)	1.4 (2.61)
95% CI	(0.34, 2.12)	(0.71, 2.02)
P-value	0.0239 (S)	0.0002 (S)
Mean of eyes		
Mean (SD)	1.2 (3.56)	1.3 (2.35)
95% CI	(0.43, 2.01)	(0.76, 1.94)
P-value	0.0081 (S)	<0.0001 (S)

(S): *P*-value was calculated using paired sample *t*-test (T)/signed rank test (S). (W): *P*-value was calculated using Two Sample t-test (T)/Wilcoxon Signed Rank Test (W). CI: Confidence interval, OD: Right eye, OS: Left eye, SD: Standard deviation, TFBUT: Tear breakup time

Table 3: Change of CVS-Q score

Parameters	Change from baseline to day 15 (*n*=64)	Change from baseline to day 30 (*n*=63)
Frequency		
Mean (SD)	−2.4 (2.01)	−5.7 (2.29)
95% CI	(−2.91, −1.90)	(−6.29, −5.14)
P-value	<0.0001(S)	<0.0001(S)
Intensity		
Mean (SD)	−2.5 (1.87)	−5.8 (2.04)
95% CI	(−2.95, −2.02)	(−6.34, −5.31)
P-value	<0.0001(S)	<0.0001(S)
Total		
Mean (SD)	−4.1 (4.18)	−10.6 (4.18)
95% CI	(−5.17, −3.08)	(−11.66, −9.55)
P-value	<0.0001 (T)	<0.0001 (S)

P-value was calculated using paired *t*-test (T)/Signed Rank Test (S). CI: Confidence interval, CVS-Q: Computer vision syndrome questionnaire, SD: Standard deviation

signs and symptoms of DED (conjunctival hyperemia, central corneal staining, and ocular surface staining) for a longer period of time (3–5 weeks).[12,15]

Although artificial tears are the gold standard for treating DED, they have a short retention time in the eye resulting in temporary relief of symptoms. HPG gellable lubricant eye drops are a gelling polymer formulation that aids in retaining the solution for a longer period. With the instillation of PEG/PG with HPG, the alteration of HPG from low-viscosity liquid to gel occurs because of the pH difference in the drop bottle and eye, which aids in the effective improvement of DED symptoms.[16] Further studies are warranted to establish the efficacy of PEG/PG with HPG following long-term use.

In our study, we found a significant improvement in TFBUT from baseline to 30-day follow-up. This was in agreement with the study by Abusharha *et al*. where a 32% increase in TFBUT was reported with the use of PEG/PG with HPG eye drops. This is an important observation as the protective layer created by PEG/PG with HPG increases TFBUT and in turn, maintains tear film stability, controls the tear evaporation rate, and prevents further moisture loss from the eye. All of these further contribute to lowering optical abnormalities caused by CVS and increasing the visual quality in patients with dry eye.[16]

There were no AEs observed for PEG/PG with HPG lubricating eye drops in any patient. Our study thus indicates that short-term treatment with PEG/PG with HPG lubricating eye drops is safe to be used in patients with dry eye symptoms due to CVS. This was in accordance with a previous randomized controlled, 6-week study on 113 patients on DED, which demonstrated a reduction in dry eye symptoms with the use of PEG/PG with HPG without any safety concern.[14] The safety of using PEG/PG with HPG eye drops has also been confirmed by other studies.[12,15] All these studies are short-term studies (3–12 weeks). However, with advances in technology and changes in our lifestyle, screen time will rise as the use of computers, laptops, and smartphones is inevitable in our everyday life. Hence, long-term studies to establish the safety of using PEG/PG with HPG for DED are much needed.

Computer use has evolved into a 21st-century necessity, and the pandemic significantly increased its usage. However, even 3 h, a day of computer usage reportedly increases the incidence of CVS. Every year, there are 1 million new instances of CVS.[4] The prevalence of DED in India is between 18.5% and 54.3%, which is greater than the worldwide prevalence of DED.[17] Although it has not yet been proven that using computers permanently damages the eyes, research has shown that short-term discomfort of the eyes lowers work efficiency and, in turn, productivity. Several studies have shown a link between prolonged computer use, poor workstation postures, and CVS;[18-22] however, there is very little information on the effectiveness and safety of using artificial tears to treat the vision issues associated with prolonged computer use.

Our study is one of the first studies conducted in patients with dry eye symptoms associated with CVS in India to assess the effectiveness and safety of PEG/PG with HPG lubricating eye drops in the reduction of DED symptoms in these patients. Although the sample size of the study is <100 to generalize the results to a wider population, it is noteworthy to report the preliminary findings that may stimulate researchers to design further studies with larger sample sizes and more diverse population groups.

Conclusion

The study suggested that short-term treatment with PEG/PG with HPG was effective for treating dry eye symptoms associated with CVS. No new safety findings emerged from this study.

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Conflict of Interest

The authors declared no conflict of interest.

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