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EFFECT OF LOW-LEVEL LIGHT THERAPY IN PATIENT WITH DRY EYES

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Abstract

OBJECTIVE: *To compare the effect of conventional therapy and low-level light therapy (LLLT) with near-infrared light-emitting diodes (LED-LLLT) for the treatment of dry eye*

STUDY DESIGN: *Quasi-experimental study.*

PLACE AND DURATION OF THE STUDY: *Tertiary Care Hospital Rawalpindi, from July 2023 to Dec 2023.*

METHODOLOGY: *A 1:1 allocation ratio was used to randomly assign 54 patients to either LED-LLLT (n = 27) or conventional therapy (n = 27). For a total of three treatment sessions, the Low-level light therapy group got Low-level light therapy once a week for three weeks. The change in fluorescein corneal staining (FCS) scores served as the primary outcome measure. Changes in the ocular surface disease index (OSDI) score and tear film break-up time (TBUT) were the secondary goals. These were evaluated before the start of treatment and four weeks later.*

RESULT: *There was a marked improvement in primary end point (FCS) in LLLT group than in the conventional therapy group. Secondary end points, TBUT, OSDI also showed more improvement in values in LLLT group than in conventional therapy group.*

CONCLUSION *Compared to traditional therapy, the use of LED-LLLT for dry eye treatment seems to be safer and more effective*

INTRODUCTION

Ocular surface disease is a common cause of morbidity in patients presenting to the out patient department, affecting upto 33% of the population worldwide[1]. Symptoms such as watering, itching, stinging, burning, foreign body sensation, sensitivity to light commonly plague patients lives. Dysfunction of the meibomian gland is the most frequent cause of dry eyes illness. The goal of the current study is to assess how well LLLT works to treat dry eye condition.[1] Twenty on the lower lid and twenty on the upper lid are meibomian glands, which are modified sebaceous glands. In order to keep tears from evaporating, they release meibum, an oily material that coats the topmost layer of the tear film. It has a significant antibacterial role in addition to lubricating.[2] Chronic abnormalities of the meibomian glands that cause tear film instability and eye discomfort are known as meibomian gland dysfunction (MGD).[3] treatment strategies include topical lubricants, warm compresses and mild anti

inflammatory agents. A considerable portion of patients, however are resistant to conventional treatment strategies, therefore newer therapies are now being proposed.[4]Several therapies have been proposed for the management of MGD. These device based therapies can be classified as: eyelid warming; lid warming and massaging; light based; electrotherapy; nerve stimulators. [5] this study focuses on Low-level light therapy (LLLT), which is a non-invasive therapy to reduce inflammation and discomfort secondary to dry eye disease.[6] Red light LLLT works by atraumatic cellular photoactivation through the release of LED light. LLLT works by the use of a specific wavelength of light, resulting in penetrating of therapeutic levels of light. This aids in cellular repair and better functioning of cells. It is postulated that LLLT works by promoting cellular function by increasing the production of ATP in the mitochondria and increasing the expression of transcription factors. .[7] The purpose of the current study was to determine the effectiveness of LLLT in treating dry eye patients utilizing LED-LLLT.

Methodology

From July 2023 to December 2023, this quasi-experimental investigation was carried out at the Tertiary Care Hospital in Rawalpindi. The College of Physicians and Surgeons' Research Evaluation Unit gave its approval to the study protocol (CPSP/REU/OPL-2021-124-2293). Following each patient's signed informed consent, Tertiary Care Hospital Rawalpindi participants were enrolled in the study. The CONSORT criteria were followed in reporting this study.

Patients were assigned at random in a 1:1 allocation ratio to either Low-level light therapy or conventional treatment using a computer-generated list of random numbers. The intervention was unknown to the individual and the researcher. Using OpenEpi Software online for cohort studies, a total sample size of 54 (27 in each group) was calculated with a two-sided significance level (1-alpha):95, a power (1-beta, % likelihood of detecting):80, and an odds ratio of 10.8 for the risk of dry eye condition with keratoconus.

Patients had to be 20 years of age or older, diagnosed with keratoconjunctivitis sicca, or dry eye syndrome, and exhibit symptoms of dry eye (irritability, redness, discharge, impaired vision, and easily fatigued eyes) during the screening examination in order to be eligible. 1. A conjunctivo-corneal inflammation-indicating score of 316 dots on the Oxford grading scale for fluorescein corneal staining (FCS); 2. a tear film break-up time (TBUT) of no more than five seconds. 3. greater than thirteen on the OSDI scale. Conditions that were excluded included anterior ocular disease, and intraocular or refractive surgery, including LASIK, during the three months prior. Patients with glaucoma, blepharitis, uveitis, SJ syndrome, or any other conditions affecting tear fluid were also excluded, as were those taking immunosuppressants, steroids, antihistamines that altered the tear fluid dynamics. Pregnant or nursing women, as well as those receiving additional dry eye therapies, were excluded.

During the course of treatment, each patient received one drop of sodium hyaluronate ophthalmic suspension in each eye four to six times daily. Additionally, the patients undergoing conventional therapy were given topical mild steroid eye drops (flouromethalone eye drops) three times a day for three weeks. The findings were assessed using changes in the Focal Corneal Stain (FCS), TBUT, and Ocular Surface Disease Index scores at week four. Both at baseline and four weeks later, these parameters were assessed.

Following corneal staining with a fluorescein strip (fluorescein sodium I.P. 1 mg), the A slit-lamp microscope fitted with a cobalt blue filter was used to study FCS. Additionally, TBUT was ascertained by staining cornea with fluorescein strip and timing the onset of a dry patch three times after a typical blink.

At Tertiary Care Hospital Rawalpindi, patients received low-level light therapy (LLLT) from the Equinox eye equipment, ESW Vision, France, during their scheduled appointments. In order to induce mithochondrial light absorption, LLLT of red light, which uses light emitting diodes to emit near infrared light at a specified wavelength (600–1100 nm), was employed. Each session lasted for ten minutes.

During the procedure ,patients were advised to close both eyes and they were made to wear a mask emitting LED energy source for 10 minutes.Patients in the conventional therapy group were advised top[ical weak steroid eye drops (flouromethalone o.i %) ,three times a day along with topical lubricating eye drops

(polyethylene 400(0.4%)+ propylene glycol 0.3%), 4 times a day for 4 weeks .

The statistical techniques and data analysis were carried out with SPSS version 20. At week 4, the mean differences in the LLT and placebo groups' results were assessed. Using the Kolmogorov-Smirnov Test, the normality of the data distribution was evaluated. To compare the parameters before and after therapy, the Wilcoxon sign rank test was employed. Results are displayed as mean values with standard deviation, while percentages (%) are used to represent categorical variables. The p-value was deemed statistically significant if it was ≤0.05.

Result

The mean age of the participants enrolled in the study was 40.81 (SD+10.43) ranging between 20-55 years. 24 (44.4%) were males and 30(55.6%) were females. The baseline characteristics of the participants for both LLLT and conventional therapy group is given in Table 1.

Characteristic	LLT group Mean (SD)	LLT group	Conventional therapy group	Conventional therapy group
	Right eye	Left eye	Right eye	Left eye
Fluorescein corneal staining (FCS)	1.22 (0.42)	1.33 (0.48)	1.22 (0.42)	1.33 (0.48)
Ocular surface disease index (OSDI)	39.27 (11.95)		39.59 (11.88)	
Tear break-up time (TBUT)	4.59 (1.6)	4.52 (1.19)	4.56 (1.739)	4.33 (1.44)

Table 1: Baseline characteristics of the study participants (n=27) as means and standard deviation (SD)

The LLLT group showed significant improvements in fluorescein corneal staining (FCS), ocular surface disease index (OSDI) and tear break-up time (TBUT), compared to the conventional therapy group. The results of the clinical outcomes of the study are summarized in Table 2.

Characteristic	LLT group	LLT group	Conventional therapy group	Conventional therapy group
	Right eye	Left eye	Right eye	Left eye
Fluorescein corneal staining (FCS)	0	0.11 (0.32)	1.11(0.32)	1.22 (0.58)
Ocular surface disease index (OSDI)	29.61 (8.67)		36.35 (11.68)	
Tear break-up time (TBUT)	8.78 (1.31)	8.81 (0.88)	5.93 (1.64)	5.7 (1.20)

Table 2: Results of clinical outcomes following the 4-week therapy (n=27) as means and standard deviation (SD).

The scores for the right and the left eye for each individual were combined so total number in each group was 54. Kolmogorov-Smirnov test showed atypical distribution and non-parametric Wilcoxon sign rank test was used to compare the parameters at baseline and after therapy. Table 3 compares baseline and post-treatment scores for va~~~~rious ocular health parameters in the LLT group. Ocular surface disease index (OSDI), tear break-up time (TBUT), and fluorescein corneal staining (FCS) all showed significant improvements, with p-values of 0.00 indicating statistical significance.

Characteristic	Baseline score Mean (SD)	Post-procedure score Mean (SD)	p-value*
Fluorescein corneal staining (FCS)	1.28 (0.45)	0.06 (0.23)	0.00
Ocular surface disease index *(OSDI)	39.26 (11.83)	29.61(8.59)	0.00
Tear break-up time (TBUT)	4.56 (1.40)	8.8 (1.11)	0.00

Table 3: Comparison of baseline and post-treatment mean scores for various ocular health parameters in the LLLT group. (n=54). *p-value <0.05 was taken as significant.

Figure 1 shows a comparison of the OSDI and TBUT in the LLLT group whereby a considerable improved was observed in these parameters.

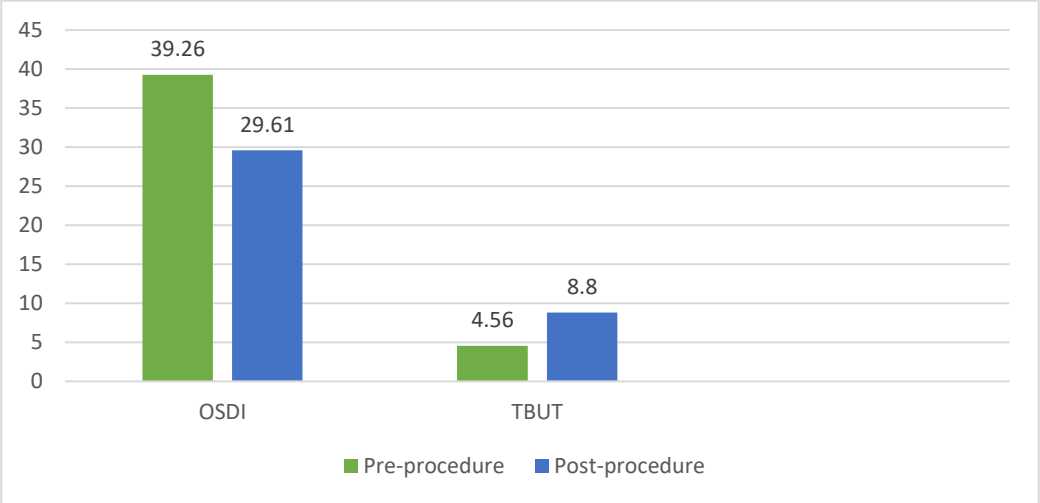

Figure 1: Comparison of OSDI and TBUT in the LLLT group.

Discussion

This study assessed the impact of LED-based low-level light therapy (LLLT) on patients with dry eye disease, revealing beneficial outcomes in symptom improvement. Low-level light therapy (LLLT), also known as photobiomodulation, is a treatment method used in dermatology and various other medical applications. Its biological effects are believed to occur through the absorption of energy by cell membranes, organelles and molecules, depending on the light wavelength. It has been demonstrated that athermal and non-invasive photoactivation, which uses light-emitting diodes at particular wavelengths, can restore injured or compromised cells and improve the function of healthy cells.[9]

Because of its analgesic, anti-inflammatory, and biostimulatory properties, dermatologists, plastic surgeons, and other experts frequently use LLLT. Recent research has shown that LLLT alone can effectively treat chalazia, and that LLLT plus intense pulsed light (IPL) therapy can effectively treat meibomian gland dysfunction.[10]

While LLLT has traditionally used laser-based light sources, there has been a growing shift toward using light-emitting diode (LED) arrays for LLLT over the past decade. LED-based LLLT has some advantages compared to laser-based LLLT. Although LEDs are non-coherent, high-quality LEDs produce nearly monochromatic light, with over 98% of the photons at the target wavelength, and their design ensures photons travel in roughly the same direction, though not perfectly aligned. This means that LED light cannot be focused to a point like lasers can. LEDs are also safer because their non-coherent light disperses, meaning the eye can only absorb a small amount of the emitted light. Additionally, LEDs can be arranged in flat panels, allowing them to cover larger areas of tissue more easily and without requiring precise positioning.[1]

A recent prospective study comparing LLLT combined with IPL to tear substitutes found that device-assisted therapy was superior to topical treatments.[11] Recent animal studies in rabbits have shown promising results.[12] The decrease in pro-inflammatory cytokines such as TNF alpha and IL-6 may be the cause of this. The neutralization of TNF alpha may be one way that light therapy reduces inflammation on the ocular surface in people with dry eye.[13] Interestingly, this impact seems to be dose-dependent, which could account for our patients' rapid improvement in ocular surface condition. LLT's main medical applications include preventing tissue damage, lowering pain and inflammation, encouraging the regeneration of different tissues and neurons, and speeding up tissue healing.[14] The eyelid tissue was exposed to low-intensity yellow and near-infrared light as part of the LLLT procedure used in this investigation. Combining heat tissue penetration with ten minutes of continuous LLT exposure is another possible method. One to two millimeters of the eyelid tissue can be penetrated by the 633 nm light wavelength that is released. This suggests a potential way whereby LLLT influences the meibomian glands.[15]

Light therapy improved every clinical outcome that was directly related to MGD. At the end of the 4-week treatment, our OSDI score dropped by 24.6%, but After a single therapy, Stonecipher and colleagues reported a decline of up to 57%;[16] however, it was unclear how long after treatment the OSDI score was calculated. The OSDI score decreased by 44% following 4 weeks of treatment, according to another study.[17] Differences in patient characteristics, treatment procedures, and the timing of score evaluations may be the cause of the diversity in OSDI score reductions. Another possible explanation for the observed disparities is the severity of the condition at the beginning of the trial.

According to Stonecipher and colleagues16, TBUT increased from 4.4 to 8.0 seconds following therapy, which is consistent with our study's findings of 4.56 and 8.8, both of which fall within the normal range.[16] In our study, we used an LED-based matrix module with a wavelength of 600-1100nm, which provided effective penetration depth and was well tolerated by the eye tissues.[18]

We did not find any adverse effects in the subjects in our investigation. Up to 13% of treated participants experienced discomfort, redness, or swelling, according to another study. 19. It is noteworthy that although the patients in our study continued to use topical medications and practice eyelid hygiene, the OSDI scores showed that these therapies were ineffective for their dry eye condition. However, the outcomes might have been impacted by these continued treatments.

One limitation of the study is the short follow-up duration, which may not fully capture the long-term effects or durability of the treatment benefits. Additionally, the results may not be broadly applicable due to a potentially small or non-representative sample size, which could limit the generalizability of the findings.

Conclusion

The study demonstrates that LLLT, specifically using an LED-based matrix module with wavelengths of 600-1100 nm significantly improves symptoms of dry eye disease. The treatment was well tolerated by patients, with notable enhancements in ocular surface conditions observed over the treatment period. Evidence is increasingly supporting the safety and effectiveness of LLLT for ophthalmic tissues, and we believe our study contributes to this growing body of knowledge.

However, the study's short follow-up duration and potential limitations in sample size warrant further investigation to assess the long-term efficacy and broader applicability of these findings. Future research with extended follow-up and larger, more diverse samples is needed to confirm and expand upon these results

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