EFFECT OF HYDRA THERAPY ON LIPID LAYER THICKNESS IN MEIBOMIAN GLAND DYSFUNCTION PATIENTS

Fareena Tehreem[1], Shakila Abbas[1], Idrees Khan[2], Tehreem Ahmad[1], Rabia Bushra Ehsan[1], Marium Muhammad Nadeem[1]

1: Department of Optometery, The University of Faisalabad

2: Department of Eastern Medicine, Superior University Lahore

ABSTRACT

Background: Meibomian gland dysfunction is characterized by inadequate or defective oil production from the meibomian glands, resulting in unstable tear film; various treatments like IPL therapy, artificial tears, ointments, and warm compresses are utilized for its management.

Aim: This study aimed to assess the effect of hydra therapy on tear film stability in patients with meibomian gland dysfunction. The objectives were to evaluate the thickness of the lipid layer before and after the application of hydra therapy and to assess the grading of meibomian gland dysfunction before and after hydra therapy.

Methodology: Longitudinal experimental design was employed to investigate the relationship between variables over time at the Islamabad Eye Centre from August 2022 to May 2023. Thirty patients of sixty eyes with meibomian gland disorder, were selected using non-probability purposive sampling with 3 sessions including 2 followups. Both genders were included, with patients aged 18 to 50. Excluded were patients with mild or moderate dry eye, contact lens users, and those unwilling to participate. Data for all parameters were collected using the Ocular Surface Analyzer, while symptoms were assessed using the OSDI Questionnaire. The results were analyzed using repeated measure ANOVA in SPSS version 29.

Results: The mean score on the LLT assessment increased from 14.16 nm in the pre-therapy session to 26.86nm in session 2, and then to 54.50nm in session 3. The p values on the TBUT assessment, MGD score assessment and OSDI were calculated as 0.000 indicating improved subjective symptoms of dry eye following the intervention. These changes were statistically significant, with p-value less than 0.05.

Conclusions: Hydra therapy was found to improve tear break-up time (TBUT), alleviate dry eye symptoms, increase lipid layer thickness, improve meibomian gland scores, stabilize the tear film, and result in decreased Ocular Surface Disease Index (OSDI) scores, indicating significant improvement in dry eye symptoms. The efficacy of hydra therapy was thoroughly examined and firmly established, highlighting its favorable effects on patients with dry eye.

Keywords: Dry eye syndrome, Meibomian Gland Dysfunction, Evaporative Dry Eye, OSDI

INTRODUCTION

The outer mucosal surfaces of the eye are covered by a special thin fluid layer called the tear film, which is around 3-micron meters thick and 3 micro litres in volume. It serves as the ocular surface's interaction with the outside world. The three layers that make up the lacrimal film are the lipid, aqueous, and mucus layer. These layers work together to maintain the health and lubrication of the eye. The lacrimal film is composed of three distinct layers, namely the lipid layer, the aqueous layer, and the mucus layer. The outermost layer is lipid layer which comprises oils that prevent the evaporation of tears. The second layer is the aqueous layer, that offers nutrients to the cornea and facilitate the removal of debris. Finally, the innermost layer is the mucus layer, which acts as an anchor to the ocular surface and ensures even distribution of tears, preventing the formation of dry spots. These layers collectively form a smooth and protective surface for the eye (1).

The lipid layer is the outermost layer and plays a crucial role in preserving the tear film by reducing surface tension and retarding the evaporation of the aqueous layer. When there is ideal lipid layer thickness it leads to better stability of tears on eye surface. It should ideally be between 30nm to 80nm which allows for smooth surface of the eyes with spread of ideal amount of tears. The meibomian glands, located in the tarsal plate of the eyelids, produce the lipid layer of the tear film intermittently as needed, to maintain the stability of the ocular surface by creating a smooth barrier that protects the eye from external environmental factors. The tear film has several important functions, including creating a smooth optical surface for clear vision and aiding in the re-spreading of tears following blinks. However, if the meibomian glands become affected, they may produce a defective oil layer or not enough lipid layer, which can result in complications of the eye surface. When the Meibomian glands produce a defective oil layer, it can cause the tears to evaporate too quickly, leading to dryness and discomfort. This can also result in inflammation, irritation, and destruction of the ocular surface over time. On the other hand, if the Meibomian glands do not produce enough lipid layer, the tears may not be able to spread evenly across the ocular surface, causing dry spots and further exacerbating dry eye symptoms. Hence, it is crucial to ensure the optimal operation of the meibomian glands and the lipid layer they produce to maintain the health and functionality of the tear film and to prevent any complications of the eye surface (2).

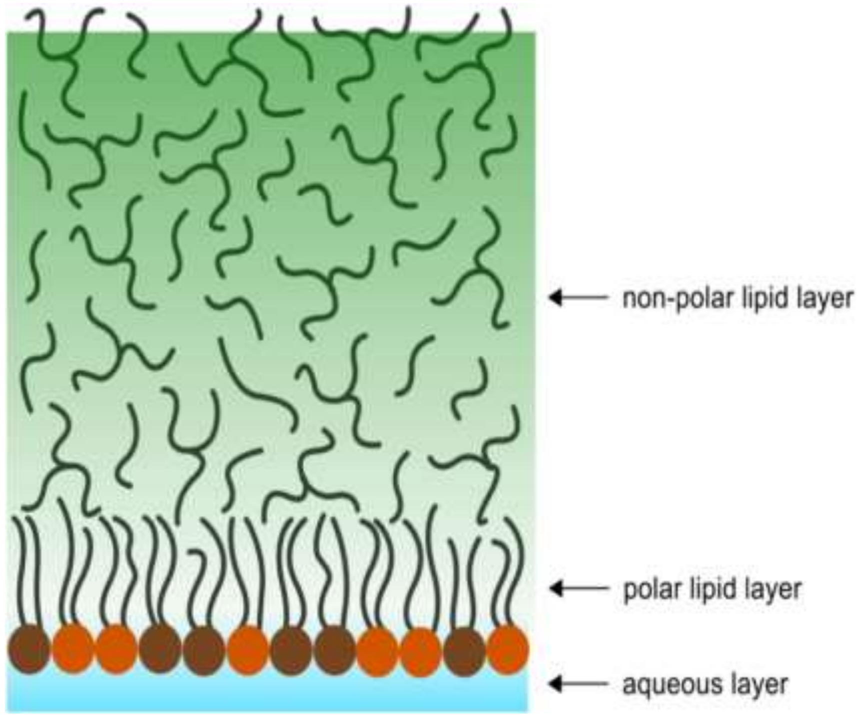

Figure 1.1: Scheme of Lipid Layer structure.

The middle layer of lacrimal film is positioned in the middle and has a critical function in safeguarding the ocular surface against bacterial infections. The lacrimal glands, located above the eyelids, secrete the aqueous layer, which comprises soluble antibacterial agents that lubricate and defend the ocular surface. The aqueous layer is vital in protecting and lubricating the ocular surface as it helps to eliminate any foreign objects that might be embedded in the cornea or conjunctiva. Moreover, the aqueous layer of the tear film includes a variety of vital components such as proteins, metabolites, inorganic salts, glucose, oxygen, and electrolytes that are necessary for eliminating debris and toxins and maintaining the health of the ocular surface. In summary, the aqueous layer of the tear film provides crucial lube and nutrients to the eye surface, helps eliminate bacteria and foreign objects, and is crucial for preserving the ocular health (3).

The mucin layer is situated at the innermost layer of the tear film, and it is primarily generated by the goblet cells present in the conjunctiva. This layer is composed of electrolytes, mucins and water and is accountable for securing the tear film to the ocular surface. The goblet cells that produce the mucin layer are assumed to be neurogenic, indicating that they receive parasympathetic innervation from the nervous system. This innervation helps to regulate the secretion of mucins, ensuring the proper lubrication and protection of the ocular surface. Therefore, the mucin layer is a critical component of the tear film that is produced by goblet cells in the conjunctiva, and it is regulated by parasympathetic innervation to ensure adequate secretion (4).

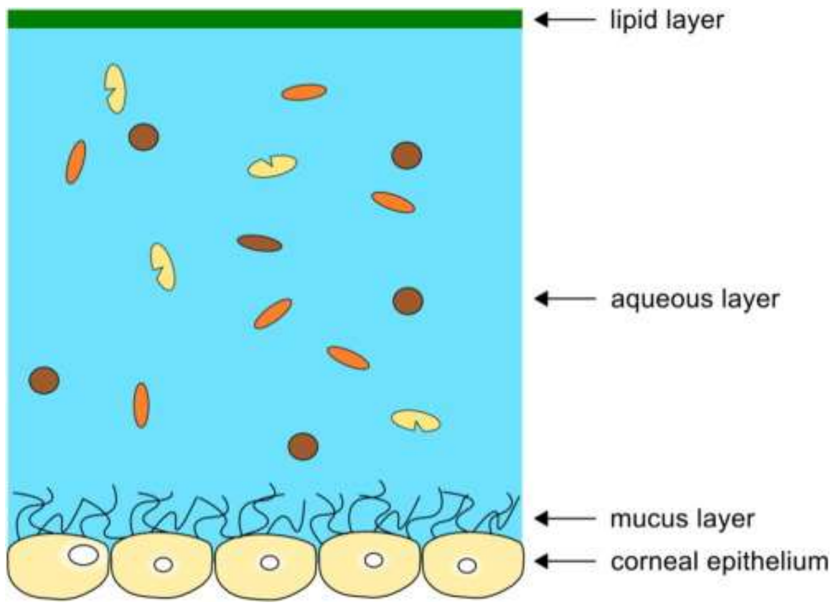

Figure 1.2: Scheme of the Tear film structure.

Dry eye is a prevalent eye related disorder that affects millions of people worldwide. It may occur due to many reasons such as environmental factors, problems with tear production or more evaporation of tears. The condition arises due to inadequate lubrication of the ocular surface, which leads to an unstable or insufficient tear film. Individuals with dry eye experience various symptoms, including discomfort, impaired or blurred vision, and a range of ocular surface issues such as epitheliopathy, inflammation, and neurosensory abnormalities. There are two primary types of dry eye: evaporative dry eye and aqueous deficient dry eye. Evaporative dry eye is caused by the malfunction of the meibomian glands, which are responsible for producing the oily layer of the tear film. In case of evaporative dry eye multiple factors can contribute to its development, including the natural aging process, hormonal fluctuations, and environmental influences.

On the other hand, aqueous deficient dry eye occurs when there is a decreased production of the aqueous layer of the tear film. This can be due to various factors such as autoimmune disorders, aging, or medication use.

Based on its underlying causes, such as unstable tear films, inflammation of surface of the eye, and meibomian gland dysfunction, dry eyes can be categorised. Tear film instability can be caused by poor blinking, exposure to dry or windy environments, or prolonged use of digital devices. Ocular surface inflammation can result from infections, allergies, or autoimmune disorders. Early diagnosis and treatment are crucial in managing the symptoms and preventing the progression of the disease, which can significantly impact an individual's quality of life (5).

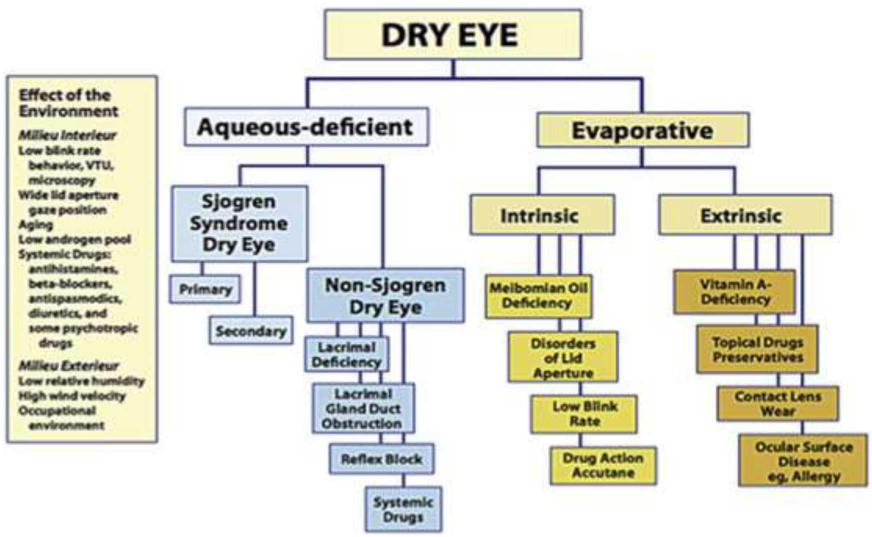

Figure 1.3: Major etiological causes of dry eye.

Dry eye disease (DED) is divided into two main subtypes: aqueous deficient and evaporative, with the latter being more prevalent. When there is more evaporation there will be reduction in appropriate tears formation which leads to unstability of outermost surface of eye. This kind of dry eye can be caused by a variety of factors including MGD, which is a common cause of evaporative dry eye. MGD occurs when the Meibomian glands in the eyelids become obstructed, leading to a reduction in the secretion of meibum, an essential component of the tear film. Tears evaporate out very quickly due to some reasons like environmental factors or Meibomian gland dysfunction. MGD causes changes in meibum quality and quantity, which can disrupt the ocular surface and result in evaporative dry eye in some people (6). The classification of MGD typically depends on the rate of gland secretion. Blockage or hypo secretion of the Meibomian glands are regarded as low-delivery conditions, whereas Meibomian gland hypersecretion is regarded as a high-delivery condition. They are further separated into primary causes and supplementary causes (7).

To avert further harm to the front of the eye, evaporating dry eye (EDE) must be diagnosed and treated as soon as possible. Some eye drops are efficient in managing lipid-deficient EDE by restoring the lipid layer of the tear film, reducing tear evaporation and improving tear stability. Treatment should be tailored to the individual needs of each patient, including a comprehensive evaluation of medical history and clinical examination to identify underlying causes. Other treatment options may include lifestyle modifications, such as adjusting one's environment, avoiding certain activities, and in some cases, oral medications or procedures to address underlying medical conditions contributing to EDE. A tailored treatment approach is essential to achieve optimal outcomes (6).

To treat evaporative dry eye, vectored thermal pulsation (VTP) is another option. It is reported that a single VTP treatment improves MG function and eye surface more than a traditional, twice-daily, 3-month program, on average. VTP is linked with better treatment outcomes for MGD (8). There is emerging research suggesting that eyewear designed to retain moisture can be a helpful addition to the treatment of evaporative dry eye. This type of eyewear is becoming increasingly available on the market and has been found to have a high rate of patient acceptance. By helping to maintain the moisture on the ocular surface, this type of eyewear can reduce the evaporation of tears and improve tear film stability, ultimately leading to relief of dry eye symptoms. There is more need to do research to understand further beneficial effects of this eye wear which is a latest innovation in treatment options (9).

One potential treatment option for individuals with Meibomian gland dysfunction (MGD) is Intense pulse light therapy. IPL therapy applies light at specific wavelengths to the lower eyelid, which can improve Meibomian gland function and reduce swelling linked with DED. The therapy typically consists of multiple sessions, with the number of sessions depending on the severity of the MGD-associated dry eye. Symptoms of dry eyes can be reduced and tear film stability may become better with IPL treatment in some patients with MGD-associated dry eye. However, it is important to note that IPL therapy is not suitable for all individuals with DED and should be evaluated on a case-by-case basis by a qualified healthcare professional (10).

Aqueous Deficient Dry Eye is a type of dry eye that is characterized by reduced tear production from the lacrimal glands. This lack of tears leads to dryness and discomfort in the eyes, as well as other symptoms such as burning, grittiness, and irritation. A comprehensive evaluation, including a thorough medical history and clinical examination, can help to identify the underlying causes of dry eye symptoms and guide the appropriate treatment plan for aqueous deficient dry eye. Treatment options may include the use of artificial tears, prescription medications, and in severe cases, surgical interventions. It is important to consult with an eye care professional for proper diagnosis and management of aqueous deficient dry eye. Therapy of aqueous deficiency dry eye includes artificial tears and topical lubricants which have historically been used to initiate DED treatment. For more moderate to severe cases, topical anti-inflammatory drugs such corticosteroids and cyclosporine a 0.05% are frequently utilized (11). The ocular surface disease index a most known dry eye assessment questionnaire. With 12 components and a final score ranging from 0 which means no symptoms to 100 reffering to severe symptoms. The OSDI is a commonly used tool to evaluate DED. The questionnaire's 12 items are divided into three subscales. With the help of the OSDI questionnaire, doctors can quickly identify ocular surface changes in a population and begin therapy, care, and monitoring (12).

The Ocular Surface Analyzer is a diagnostic instrument that is often used for the diagnosis of dry eye disease. It is similar to a slit lamp in some ways and is considered an effective method for assessing the ocular surface. It measures various parameters, such as tear meniscus height, tear breakup time (visible and infrared), radial scan of the cornea, lipid layer thickness, Meibomian gland score, and upper and lower lid gland openings by everting the eyelids. The first step in the examination is measuring the tear meniscus height by magnifying the eye at 16x and capturing the measurement, which should be at least 1mm in height. Then, the tear breakup time is assessed by asking the patient to blink twice and then keeping their eyes open for 22-24 seconds. Dry spots are recorded during this time if present. The values beyond normal ranges are 3 seconds to 6 seconds. It should ideally be 8-10 seconds without appearance of dry spots in the eye. The lipid layer thickness is measured by focusing and defocusing the instrument, and the patient is instructed to blink at least three times. The spread of the lipid layer over the ocular surface is then calculated. Ideally it should be between 60-micron meters to 80-micron meters. Non-contact infrared meibography is a method for analyzing MG dropout to explore MG malfunction. Meibomian gland scoring governs the Meibomian gland functioning. 0 is normal, gland loss <=1/3 is score 1, score 2 loss = 1/3 to 2/3 and score 3 loss> 2/3. Score 3 is worse in which there is maximum Meibomian glands loss.

Gland openings are checked on 10x magnification with stages of normal, mild, moderate and severe. In normal, blepharon is clear and transparent, in mild cases, there is gland opening buldge, in case of moderate eye lid margin of mucus membrane disappear and cornification occurs, and in severe cases, eye lid irregularity, gland opening disappears, and new vessels formed (13).

Figure 1.4: Ocular surface analyzer.

Applying heat therapy is one of the main methods used to improve Meibomian gland function in the treatment of MGD. This therapy involves applying heat to the eyelids to open blocked Meibomian gland ducts and improve the flow of meibum. By improving Meibomian gland function, the quality and quantity of the tear film can be improved, which can lead to relief of dry eye symptoms. Heat therapy can be applied in various ways, including the use of warm compresses, heated eye masks, or specialized devices that deliver controlled heat to the eyelids. Hydra therapy is the latest treatment option. Goggles form a seal with the periocular skin and has the appearance of swimming goggles. The goggle chambers are lined with a ring of moist cotton. The water evaporates after 15 minutes of preheating, releasing hot steam that is 42 degrees when it reaches the eyes. Heat gets transferred to the eyelids as steam when put over the eyes. The device is utilized for one 15-minute treatment session with total 3 sessions mainly in severe dry eye cases. After heat application for 15 minutes a Meibomian gland expresser is used to remove all the defected lipid layer and a new lipid layer generates naturally with ideal thickness between 60-80-micron meters (14).

Figure 1.5: Steam eye goggles with temperature 42 degrees centigrade.

OBJECTIVES

To assess the effect of hydra therapy on tear film stability in meibomian gland dysfunction patients.

To assess the thickness of lipid layer before and after application of hydra therapy in Meibomian gland dysfunction patients.

To assess the grading of meibomian gland dysfunction before and after hydra therapy.

MATERIALS AND METHODS

3.1: Study Design

In this study, a longitudinal experimental design was employed to investigate the relationship between two or more variables over a period of time.

3.2: Place of Study

The study in question was conducted in the Islamabad Eye Centre, located in the bustling city of Islamabad, Pakistan.

3.3: Duration of Study

The duration was from August 2022 to May 2023. This duration allowed for the collection of extensive and comprehensive data, ensuring that all aspects of the research were thoroughly investigated and analyzed.

3.4: Sample Size

For the purpose of this study, thirty patients including sixty eyes were taken who were having Meibomian Gland Disorder . Rao Soft formula was used to calculate the sample size of this study.

3.5: Sampling Technique

In this study Non-Probability Purposive Sampling technique is used.

3.6: Inclusion Criteria

- Both gender patients were participants in the study.
- Patients with Meibomian Gland Dysfunction who had hydra therapy were included in this study.
- Age was from 18 to 50.
- People who were having severe dry eye were taken as participants in this study.

3.7: Exclusion Criteria

- People who were willing to participate in the study.
- Those who had mild and moderate dry eye were excluded.
- Contact lens users were excluded.
- Patients with hormonal imbalances, pregnant ladies and lactating mothers were excluded.

- Patients with convergence and accommodation anomalies were excluded.

3.8: Data Collection Tools

- Ocular Surface Analyzer (OSA) SLM Ophthalmic Slit Lamp, Chongqing Kanghuaruiming.
- OSDI Questionnaire

Figure 3.1: Ocular Surface Analyzer.

3.9: Data Collection Method

This involved administering questionnaires, conducting assessments, and performing a therapeutic procedure known as hydra therapy. The instruments used in the data collection process included the OSA device, OSDI questionnaire, and tools for assessing thickness of lipid layer, stability of tear film, and scoring of meibomian glands. After taking consent from the patient data from the patients was gathered by using OSA & OSDI questionnaire. Lipid layer thickness, tear film stability and MGD grading score was assessed before 1st session of hydra therapy and before 2nd session and before 3rd session, and after 3rd session. Before 1st and after last session OSDI questionnaire was be filled by the patients to gather the information regarding improvement in symptoms leading to recovery. The Ocular Surface Analyzer is a diagnostic instrument that is often used for the diagnosis of dry eye disease. It is similar to a slit lamp in some ways and is considered an effective method for assessing the ocular surface. The first step in the examination is measuring the tear meniscus height by magnifying the eye at 16x and capturing the measurement, which should be at least 1mm in height. Then, the tear breakup time is assessed by asking the patient to blink twice and then keeping their eyes open for 22-24 seconds. Dry spots are recorded during this time if present. The values beyond normal ranges are 3 seconds to 6 seconds. It should ideally be 8-10 seconds without appearance of dry spots in the eye. The lipid layer thickness is measured by focusing and defocusing the instrument, and the patient is instructed to blink at least three times. The spread of the lipid layer over the ocular surface is then calculated. Ideally it should be between 60-micron meters to 80-micron meters. Non-contact infrared meibography is a method for analyzing MG dropout to explore MG malfunction. Meibomian gland scoring governs the Meibomian gland functioning. 0 is normal, gland loss <=1/3 is score 1, score 2 loss = 1/3 to 2/3 and score 3 loss> 2/3. Score 3 is worse in which there is maximum Meibomian glands loss. Gland openings are checked on 10x magnification with stages of normal, mild, moderate and severe. In normal, blepharon is clear and transparent, in mild cases, there is gland opening buldge, in case of moderate eye lid margin of mucus membrane disappear and cornification occurs, and in severe cases, eye lid irregularity, gland opening disappears, and new vessels formed. The OSDI questionnaire was employed to assess the improvement in symptoms leading to recovery after the hydra therapy sessions. The questionnaire was administered to the patients before the first session and after the last session, enabling the comparison of symptom improvement over the treatment period. The OSDI questionnaire comprises questions addressing visual symptoms, functional limitations, and environmental triggers associated with dry eye disease. The thickness of the oily layer of tear film was assessed before the first session of hydra therapy, before the second session, before the third session, and after the third session. A non-invasive technique used to measure the thickness of lipid layer. Tear film stability was evaluated using a method like the tear breakup time (TBUT) test. The TBUT measurement was performed at the same time points as the lipid layer thickness assessment. A slit-lamp bio microscope equipped with fluorescein dye and a cobalt blue filter was used to visualize the tear film and determine the TBUT. The severity of meibomian gland dysfunction was assessed using a standardized grading system. The evaluation was conducted before the first session, before the second session and before the third session. The grading system, such as the meibomian gland expressibility and the meibomian gland dropout scale, was used to categorize the severity of MGD.

Hydra therapy, a therapeutic procedure for treating dry eye disease, was administered to the patients consisting of three sessions. The exact protocol and technique of hydra therapy were followed as per the established guidelines. Briefly, the procedure involved the application of heat between 38- 42 degree centigrade, followed by gentle massage of the eyelid margins to express the meibomian glands with expresser and facilitate the release of meibum. The therapy was performed during three sessions, with a specified interval of 15 days between each session.

The patients were scheduled for follow-up visits at specific intervals to monitor their progress and assess the effectiveness of the hydra therapy. The follow-up visits were conducted after the first session, after the second session, and after the completion of the third session. During these visits, the assessments mentioned earlier (lipid layer thickness, tear film stability, and MGD grading score) were performed. The patients were also requested to complete the OSDI questionnaire after the last session to evaluate the overall improvement in symptoms leading to recovery.

3.10: Data Analysis Method

In this study, the data analysis process was conducted using IBM SPSS Version 29 software, which is a widely used statistical analysis tool in the social sciences. Repeated measure ANOVA test was applied to rule out the results of the study.

3.11: Ethical Considerations

Verbal and written consent will be obtained from patients who have been adequately informed of the study's objectives and design, have been given enough time to consider all options, have volunteered to attend to the subject, and wanted to provide all the necessary details by exchanging informations with the help of questions.

RESULTS

This study included a total of thirty patients consisting of sixty eyes having dry eye in meibomian gland dysfunction patients about 18 to 50 years of age. Patients who had hydra therapy were kept on two follow ups after the first session. Total three sessions were included in this treatment for meibomian gland dysfunction. Results were analyzed by using repeated measure ANOVA test.

4.1: Age of Patients

A total of the 30 patients included in the sample were above 15 to 50 years who underwent hydra therapy treatment for meibomian gland dysfunction. Out of this range, the minimum age and maximum with which patients presented were found to be 15 years and 50 years. The mean value and standard deviation of the age were found to be 32.07 ± 7.79. These results are presented in Table 4.1, which summarizes the minimum, maximum, mean and standard deviation.

Table 4.1: Age of the Patients of Meibomian Gland Dysfunction.

Age of the patients with Meibomian Gland Dysfunction	N	Minimum	Maximum	Mean	Std. Deviation
	30	19	47	32.07	7.79

4.2: Gender of Patients

The patients participated in the study having MGD were of both genders including 40% female patients (N=12) and 60% male patients (N=18). Maximum population was consisting of males.

Table 4.2: Gender of the Patients with Meibomian Gland Dysfunction.

	Frequency	Percent	Valid Percent	Cumulative Percent
Female	12	40.0	40.0	40.0
Male	18	60.0	60.0	100.0
Total	60	100.0	100.0	

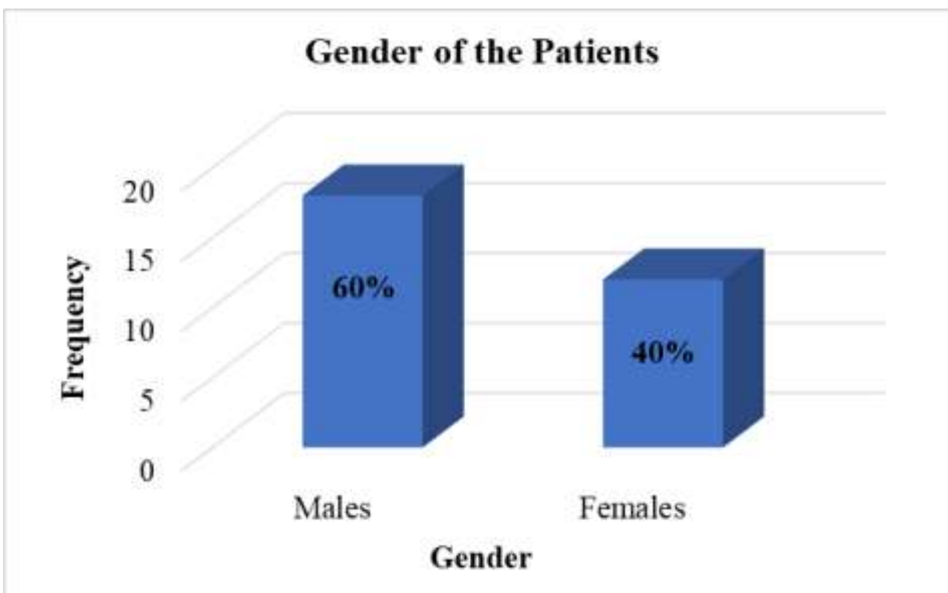

Figure 4.1: Gender of the patients with Meibomian Gland Dysfunction.

4.3: Assessment of Lipid Layer Thickness (LLT) in Meibomian Gland Dysfunction Patients

The lipid layer thickness (LLT) was analyzed using repeated measure ANOVA test. The results of this study indicate that the hydra therapy treatment had a significant effect on the participant's scores over the course of three sessions. As shown in Table 4.3, the mean score on the LLT assessment increased from 14.16 ± 2.93 in the pre-therapy session to 26.86 ± 4.85 in session 2, and then to 54.50 ± 13.20 in session 3. These changes were statistically significant, with p-value less than 0.05 which suggests that the intervention had a significant effect on LLT following the three hydra therapy sessions as described in table 4.3.

Table 4.3: Mean Values of LLT on Assessment in MGD patients.

	Mean	Std. Deviation	N
Pre- Therapy [LLT]	14.1667	2.93527	60
FOLLOW-UP 1 [LLT]	26.8667	4.85193	60
FOLLOW-UP 2 [LLT]	54.5000	13.20311	60

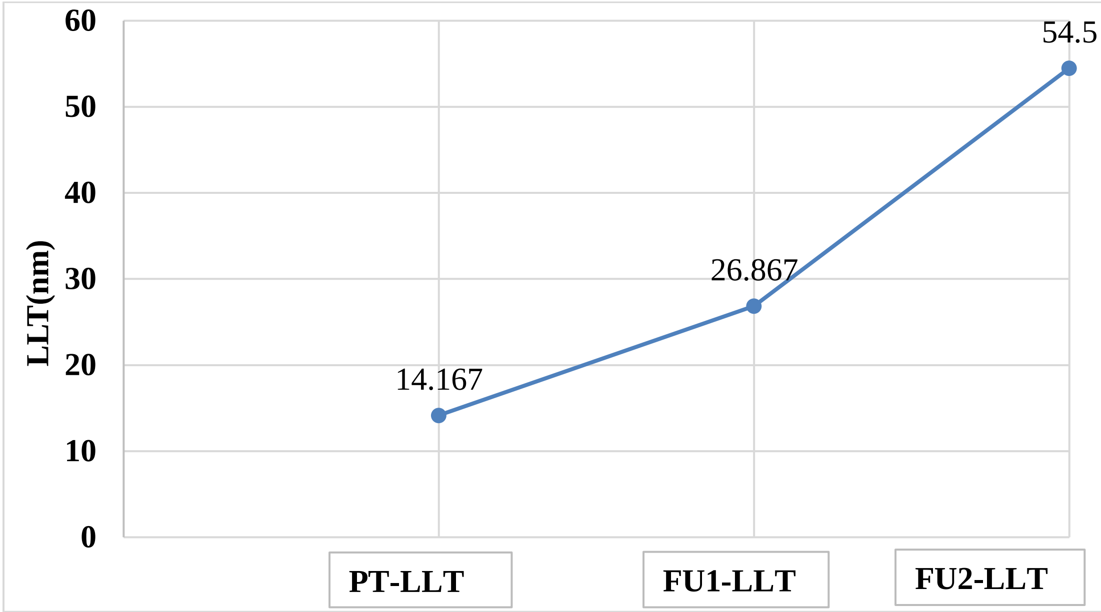

Figure 4.2: Mean Value Graph of Variable Progression of LLT in every follow-up from baseline.

Table 4.4: Repeated Measure Analysis for LLT.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Sphericity Assumed	51033.378	2	25516.689	376.279	.000
Greenhouse-Geisser	51033.378	1.257	40605.348	376.279	.000

Pair wise comparison of LLT in patients with meibomian gland dysfunction also showed that there were significant results between baseline, first and second follow-up. P value <0.05 indicated that the results were significant among follow-ups as described in Table 4.5.

Table 4.5: Pairwise Comparisons for Lipid Layer Thickness (LLT).

(I) factor1		Mean Difference (I-J)	Std. Error	Sig.[b]
1	**2**	-12.700*	.770	.000
	3	-40.333*	1.633	.000
2	**1**	12.700*	.770	.000
	3	-27.633*	1.876	.000
3	**1**	40.333*	1.633	.000
	2	27.633*	1.876	.000

4.4: Assessment of Tear Breakup Time (TBUT) in Meibomian Gland Dysfunction Patients

The tear breakup time was analyzed using repeated measure ANOVA test. The results of this study indicate that the hydra therapy treatment had a significant effect on the participant's scores over the course of three sessions. As shown in Table 4.6, the mean score on the TBUT assessment increased from 4.80 ± 1.27 in the pre-therapy session to 8.75 ± 1.79 in session 2, and then to 16.50 ± 2.49 in session 3. The p value was less than 0.05 which suggest that the intervention had a significant effect on TBUT.

Table 4.6: Mean Value of TBUT on assessment in MGD patients.

	Mean	Std. Deviation	N
PRE-THERAPY [TBUT]	4.8050	1.27604	60
FOLLOW-UP 1 [TBUT]	8.7500	1.79098	60
FOLLOW-UP 2 [TBUT]	16.5000	2.49406	60

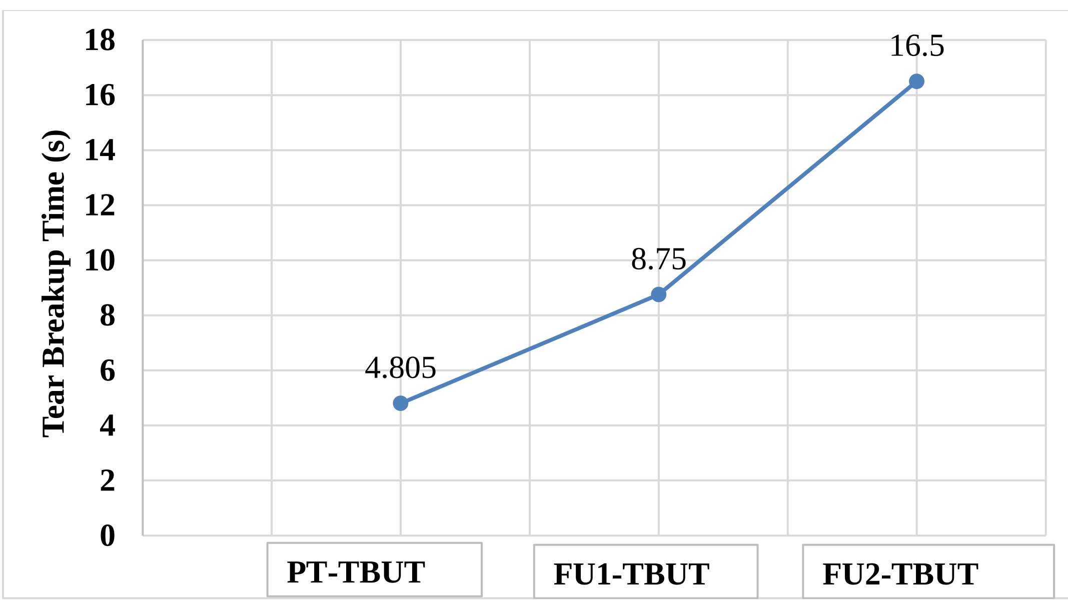

Figure 4.3: Mean Value Graph of TBUT over Time.

Table 4.7: Repeated Measure Analysis for TBUT in MGD patients

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Sphericity Assumed	4247.971	2	2123.986	599.600	.000
Greenhouse-Geisser	4247.971	1.333	3187.445	599.600	.000

The Table 4.8 shows the pairwise comparisons for the Tear Break-Up Time (TBUT) variable. Comparing TBUT level 1 to level 2, the mean difference is -3.945 (expressed as TBUT level 1 minus TBUT level 2). The standard error associated with this mean difference is 0.198. The significance level (Sig.) is reported as .000, indicating a highly significant difference.

Table 4.8: Pairwise Comparisons of TBUT Scores.

(I) TBUT	(J) TBUT	Mean Difference (I-J)	Std. Error	Sig.[b]
1	**2**	-3.945*	.198	.000
	3	-11.695*	.365	.000
2	**1**	3.945*	.198	.000
	3	-7.750*	.426	.000
3	**1**	11.695*	.365	.000
	2	7.750*	.426	.000

4.5: Assessment of Meibomian Gland Score (MGD) in Meibomian Gland Dysfunction Patients

The Meibomian Gland Score was analyzed using repeated measure ANOVA test. The results of this study indicate that the hydra therapy treatment had a significant effect on the participant's scores over the course of three sessions. As shown in Table 4.6, the mean score on the MGD score assessment decreased from 0.52 ± 0.20 in the pre-therapy session to 0.19 ± 0.17 in session 2, and then to 0.01 ± 0.02 in session 3. The p value was less than 0.05 which suggest that the intervention had a significant effect on Meibomian Gland Dysfunction Scores as described in Table 4.9.

Table 4.9: Mean values of MGD scores in Meibomian Gland Dysfunction Patients.

	Mean	Std. Deviation	N
PRE-THERAPY [MGD]	.5227	.20882	60
FOLLOW-UP 1 [MGD]	.1910	.17714	60
FOLLOW-UP 2 [MGD]	.0162	.02799	60

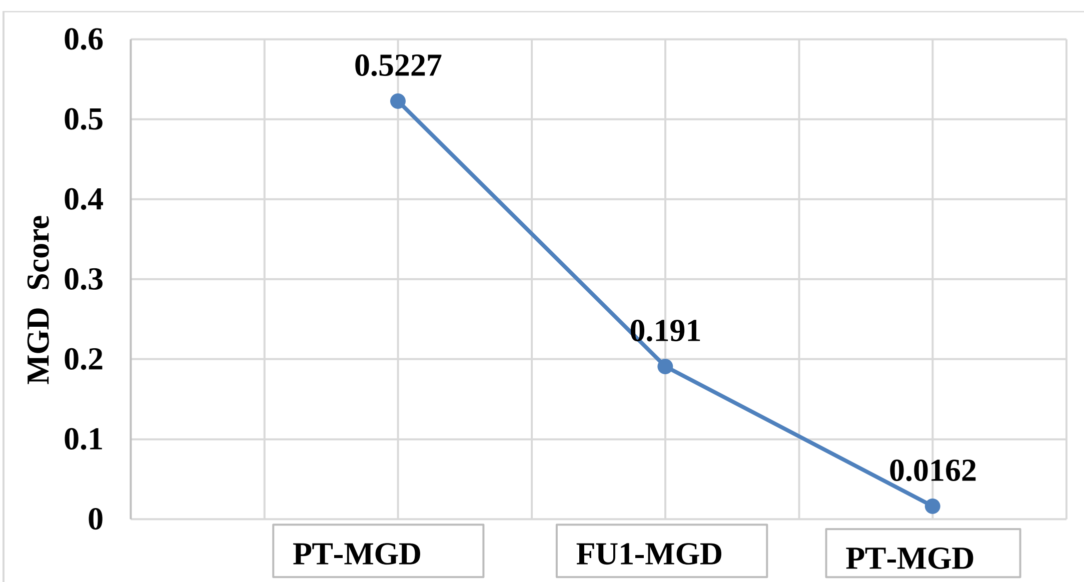

Figure 4.4: Mean Value Graph Showing Decrease in MGD Score from Baseline to Follow-Up 2.

Table 4.10: Repeated Measure Analysis for MGD.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Sphericity Assumed	7.942	2	3.971	222.064	.000
Greenhouse-Geisser	7.942	1.924	4.129	222.064	.000

The Table 4.8 shows the pairwise comparisons for the Meibomian Gland Dysfunction score variable. The significance level (Sig.) is reported as .000, indicating a highly significant difference.

Table 4.11: Pairwise Comparisons for Meibomian Gland Dysfunction (MGD).

(I) MGD	(J) MGD	Mean Difference (I-J)	Std. Error	Sig.[b]
1	**2**	.332*	.025	.000
	3	.507*	.026	.000
2	**1**	-.332*	.025	.000
	3	.175*	.022	.000
3	**1**	-.507*	.026	.000
	2	-.175*	.022	.000

4.6: Assessment of Ocular Surface Disease Index (OSDI) in Meibomian Gland Dysfunction Patients

The table 4.12 presents the mean values of the OSDI scores for the patients with Meibomian Gland Dysfunction (MGD) at different time points. The OSDI scores significantly decreased from 40.1000 at pre-therapy to 10.4083 at follow-up 2, indicating improved subjective symptoms of dry eye following the intervention.

Table 4.12: Mean Values of OSDI on assessment in Meibomian Gland Dysfunction Patients.

	Mean	Std. Deviation	N
PRE-THERAPY [OSDI]	40.1000	5.93667	60
FOLLOW-UP 1 [OSDI]	27.4000	3.18471	60
FOLLOW-UP 2 [OSDI]	10.4083	1.06760	60

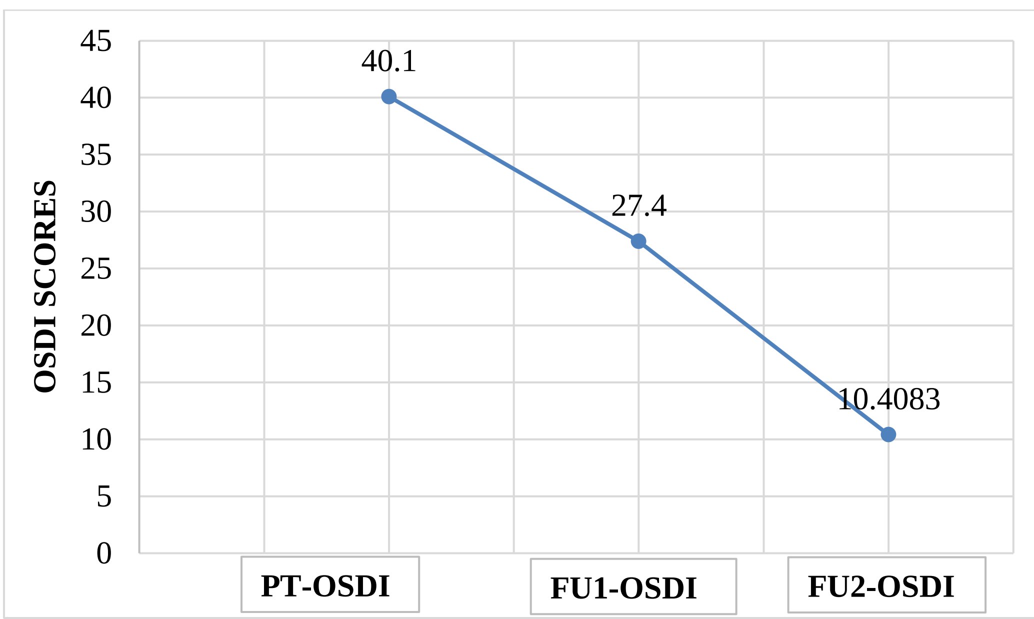

Figure 4.5: Linear Graph Illustrating Reduction in Dry Eye Scores Assessed by OSDI Questionnaire.

Table 4.13: Repeated Measure Analysis for Ocular Surface Disease Index (OSDI) in Meibomian Gland Dysfunction patients.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Sphericity Assumed	26632.036	2	13316.018	893.728	.000
Greenhouse-Geisser	26632.036	1.499	17764.828	893.728	.000

The table 4.10 shows significant mean differences in Ocular Surface Disease Index (OSDI) scores between different time points (1 and 2, 1 and 3, and 2 and 3) with p-values < 0.001, indicating significant changes in subjective symptoms of dry eye. The mean differences range from 12.700 to 29.692, suggesting improvement in ocular surface health with deterioration in OSDI scores over the course of the study.

Table 4.14: Pairwise Comparisons for Ocular Surface Disease Index (OSDI).

(I) OSDI	(J) OSDI	Mean Difference (I-J)	Std. Error	Sig.[b]
1	**2**	12.700*	.808	.000
	3	29.692*	.792	.000
2	**1**	-12.700*	.808	.000
	3	16.992*	.458	.000
3	**1**	-29.692*	.792	.000
	2	-16.992*	.458	.000

CHAPTER 5

DISCUSSIONS

The main findings of this study demonstrate the significant effects of hydra therapy on various measures related to ocular health and dry eye symptoms. Marta et al published a study in 2022 regarding treatment options for improvement in LLT with therapy having low light in case of treatment options of meibomian gland disorder. In this study involving 62 eyes of 31 patients (61.3% female, mean age 66.94 ± 9.08 years). The mean OSDI scores improved from 45.02 which was severe to 22.35 which was moderate at interval of two to three weeks and then it improved to 8.24 after six months interval. No patients got any side effects from it. LLT grades significantly improved ($p < 0.001$) after IPL plus LLL treatment (15). In comparison to the previous study, this study on hydra therapy in Meibomian gland dysfunction patients offers a more targeted approach specifically addressing the dysfunction of the Meibomian glands. By focusing on hydra therapy, which is a specific intervention designed to improve oil glands functioning and alleviate symptoms of dry eyes, this study provides a more specialized and effective treatment option for this particular patient population.

In comparison to previous studies, the analysis of lipid layer thickness in this study revealed a substantial increase in LLT scores over the three therapy sessions. The mean score on the LLT assessment increased from 14.1667 ± 2.93 in the pre-therapy session to 26.86 ± 4.85 in session 2, and then to 54.50 ± 13.20 in session 3. These changes were statistically significant, with p-value of 0.000 which suggests that the intervention had a significant effect on LLT following the three hydra therapy sessions. The significant changes observed in LLT scores further support the effectiveness of hydra therapy in enhancing ocular health.

In 2020, Pult et al published the study regarding improvement in ocular surface health with Low-level light therapy in the treatment of Meibomian gland dysfunction. Twenty two eyes of 11 patients were included in this study. The impact of Low-Level Laser Therapy and lower eyelids was examined in individuals suffering from meibomian gland disorder. The participants in this study underwent Low-Level Laser Therapy (LLLT) using a specific device called from Espansione Group, located in Bologna, IT. The treatment protocol involved four consecutive applications of LLLT, with each application lasting for 15 minutes. There was a gap of 48 to 72 hours between each session. There was significant difference in mean scores which was 33.73 before and after treatment it was found to be 19.15 with p value less than 0.005. Before treatment MGD median score was 12 points and 10.5 points after treatment. Significant improvement was seen before treatment it was 4.5 seconds and after treatment it was found to be 6.5 seconds with p value less than 0.005. Meiboscore was 2 before treatment and 1.5 after the treatment with p value less than 0.05. To assess the efficiency of effect of the mask, thermography was performed after the initial session. Two to four days after the completion of all four treatment sessions, various parameters including visual acuity (VA), tear film quality, lower eyelid condition, Meibomian gland (MG) function, meibography, and dry eye syndrome (DES) were re-evaluated. The application of LLLT demonstrated a notable improvement in both dry eye symptoms and tear film quality. However, the treatment did not have a noticeable impact on the appearance and morphology of the lower eyelids. It was observed that the warming effect produced by the LLLT device was more pronounced on the upper eyelid compared to the lower eyelid. In comparison to previous studies, the results of tear breakup time (TBUT) assessments showed a notable increase in TBUT scores following hydra therapy. The mean score on the TBUT assessment increased from 4.80 ± 1.27 in the pre-therapy session to 8.75 ± 1.79 in session 2, and then to 16.50 ± 2.49 in session 3. The p value was 0.000 which suggest that the intervention had a significant effect on TBUT. This increase in TBUT scores signifies improved tear film stability, which is crucial for preventing tear evaporation and alleviating dry eye symptoms (16).

Tao et al in 2020 published a study on treatment option of azithromycin in case of Meibomian gland dysfunction for improvement in Meibomian gland scoring. A systematic review of studies on management of meibomian gland disorder with azithromycin was conducted to assess its effectiveness. Symptom scores significantly improved after administering both oral azithromycin (OA) and topical azithromycin (TA). Eyelid signs, Meibomian gland plugging, meibum quality, and tear secretion also showed distinct improvements. Significant improvements for tear break-up time (TBUT) and corneal staining (CS) were achieved by TA (TBUT: $P = 0.02$; CS: $P = 0.02$) but not by OA (TBUT: $P = 0.08$; CS: $P = 0.14$). Other measurements for evaluating the quality of tear film, the pooled TBUT also increased distinctly from baseline values after applying TA with $Z = 2.41$, $P = 0.02$; $SMD = -1.20$, 95% with confidence interval from −2.17 to −0.22) but not after administering OA which showed $Z = 1.74$, $P = 0.08$; $SMD = -0.35$, 95% with confidence interval from −0.75–0.04. However, tear secretion distinctly increased after applying both TA with p value of 0.01 having SMD of −0.34 and 95% confidence interval from −0.60 to −0.08 and OA with p value of 0.01 having SMD −0.44 and confidence interval 95% from −0.79 to −0.10. Adverse event rates were 25% for TA and 7% for OA. Additionally, TA showed comparable effectiveness to oral doxycycline (OD) in symptom relief. Overall, azithromycin, both oral and topical, effectively treated MGD by improving symptoms, clinical signs, and tear film stability, with topical use showing superiority in short-term tear film quality improvement (17).

In comparison to old studies, the analysis of Meibomian Gland Dysfunction (MGD) scores demonstrated a significant decrease in MGD scores over the three therapy sessions. The mean score on the MGD score assessment decreased from 0.52 ± 0.20 in the pre-therapy session to 0.19 ± 0.17 in session 2, and then to 0.01 ± 0.02 in session 3. The p value was observed to be 0.000. This decrease indicates an improvement in Meibomian gland function, which is often impaired in individuals with dry eye disease. The significant effect of hydra therapy on MGD scores highlights its efficacy in addressing Meibomian gland dysfunction and its impact on dry eye symptoms.

Choi et al in 2019 published a study on Meibum expressibility improvement as a therapeutic target of intense pulsed light treatment in Meibomian gland dysfunction and its association with tear inflammatory cytokines. A total of thirty participants underwent three IPL treatment sessions, which included various examinations and assessments such as tear film lipid layer interferometry, meibography, tear sampling, slit-lamp examination, and completion of the OSDI questionnaire. The OSDI score after three treatment sessions decreased from the baseline score by 18.2 for each additional meibum expressibility score at baseline and increased from the baseline by 4.5 for each additional second of TBUT at baseline. Following IPL treatment, meibum quality, expressibility, lid margin abnormality, tear film break-up time (TBUT), ocular surface staining, and OSDI scores significantly improved. Participants with poor meibum expressibility and shorter

TBUT improved more on the OSDI. Tear IL-4, IL-6, IL-10, IL-17A, and TNF levels decreased after IPL, and meibum expressibility improved with lower IL-6 and TNF levels. The change in IL-2 level was not significant with p value of 0.117 by applying Kruskal-Wallis test. Although a slight increasing trend in IL-6, IL-17A, and TNF-α levels was observed after the third IPL session, the difference was not statistically significant (IL-6, $P = 0.904$; IL-17A, $P = 0.394$; TNF-α, $P = 0.875$). A positive correlation was observed between the changes in meibum expression and changes in IL-6 with $r = 0.59$, p value of 0.02 and TNF-α with $r = 0.755$, $p = 0.01$ levels. Finally, IPL treatment improved meibomian gland function, stabilized the tear film, and reduced ocular surface inflammation. Patients with obstructive MGD and tear instability, on the other hand, were more likely to experience ocular discomfort relief after IPL treatment (18).

In comparison to previous studies, the assessment of OSDI scores revealed a substantial reduction in OSDI scores after hydra therapy intervention. The OSDI scores significantly decreased from 40.1000 at pre-therapy to 10.4083 at follow-up 2, indicating improved subjective symptoms of dry eye following the intervention. This reduction indicates an improvement in subjective symptoms of dry eye, aligning with the overall goal of enhancing patients' quality of life. The significant improvement in OSDI scores supports the effectiveness of hydra therapy in alleviating dry eye symptoms and enhancing patients' subjective experience.

These findings align with existing literature and theories that emphasize the importance of tear film stability, lipid layer quality, Meibomian gland function, and subjective symptom relief in dry eye management. The observed patterns and trends in the data provide valuable insights into the effectiveness of hydra therapy as a comprehensive approach for addressing the multifactorial nature of dry eye syndrome.

5.1: Conclusions

- It was concluded that by having hydra therapy TBUT improves with which dry eye symptoms also improve.
- After hydra therapy, lipid layer thickness has significantly increased due to which tear film became stable.
- With hydra therapy, meibomian gland scores have significantly increased which resulted in stability of tear film and stable ocular surface.
- OSDI scores decreased after the hydra therapy which indicates the improvement in dry eye symptoms after hydra therapy.

5.2: Limitations

- Difficulty in collecting the data at followups as some patients did not came for followups because of which those patients had to be excluded at the end. It took some extra time.
- It was very difficult to ensure that all the patients get consistently all the three sessions of hydra therapy because they were belonging to some other cities.

5.3: Recommendations

- This study has resulted in significantly improved tear film with ideal tear breakup time which results into effective approaches for alleviating dry eye symptoms and improving patient's quality of life. Lipid layer thickness significantly improved with three sessions of hydra therapy which helped to relieve the dry eye symptoms with better ocular surface health. Meibomian gland scores have significantly improved so it's recommended to take hydra therapy for the meibomian gland dysfunction patients for betterment of ocular health. OSDI scores also showed significant decrease which showed improvement in dry eye symptoms after every session of hydra therapy.
- It is recommended for those dry eye patients who are not getting any beneficial effects from other treatment options such as artificial tears and ointments as it provides a better and quicker relieve in dry eye symptoms.
- It is a cost effective therapy with which patients of dry eye can get beneficial effects for better tear film stability.
- This study recommends to arrange awareness programs for the general population as maximum of the population don't know about the latest treatment options.

- Hydra therapy emerges as a favorable option for dry eye management, addressing the multifactorial nature of the condition by improving tear film stability, lipid layer thickness, meibomian gland function, and subjective symptom relief.
- In addition to objective clinical measures, future research should incorporate comprehensive patient-reported outcome measures to capture the subjective experiences and quality of life improvements resulting from hydra therapy. This includes assessing the impact of the intervention on factors such as visual comfort, daily activities, and overall satisfaction. Integrating patient perspectives will provide a more holistic understanding of the effectiveness and patient-centered outcomes of hydra therapy.
- Building on the findings of this study, researchers can explore the development of novel interventions or refinements of hydra therapy. This may involve incorporating advanced technologies, such as targeted drug delivery systems, precision medicine approaches, or personalized treatment algorithms based on individual patient characteristics. Innovative interventions can further optimize the outcomes and expand the treatment options available for individuals with dry eye syndrome.

REFERENCES

(1). Dartt DA, Willcox MD. Complexity of the tear film: importance in homeostasis and dysfunction during disease. Experimental eye research. 2013 Dec; 117(1): 1-3.

(2). Xu X, Li G, Zuo YY. Biophysical properties of tear film lipid layer I. Surface tension and surface rheology. Biophysical Journal. 2022 Feb 1; 121(3): 439-50.

(3). Chang AY, Purt B. Biochemistry, tear film. InStatPearls 2021 Jun 15. StatPearls Publishing.

(4). Hodges RR, Dartt DA. Tear film mucins: front line defenders of the ocular surface; comparison with airway and gastrointestinal tract mucins. Experimental eye research. 2013 Dec 1; 117(1): 62-78.

(5). Tsubota K, Pflugfelder SC, Liu Z, Baudouin C, Kim HM, Messmer EM et al. Defining dry eye from a clinical perspective. International journal of molecular sciences. 2020 Dec 4; 21(23): 9271

(6). Rolando M, Merayo-Lloves J. Management Strategies for Evaporative Dry Eye Disease and Future Perspective. Current Eye Research. 2022 Jun 3; 47(6): 813-23.

(7). Chhadva P, Goldhardt R, Galor A. Meibomian gland disease: the role of gland dysfunction in dry eye disease. Ophthalmology. 2017 Nov 1; 124(11): 20-6.

(8). Blackie CA, Coleman CA, Holland EJ. The sustained effect of a single-dose vectored thermal pulsation procedure for meibomian gland dysfunction and evaporative dry eye. Clinical Ophthalmology. 2016 Jul 26: 1385-96.

(9). Waduthantri S, Tan CH, Fong YW, Tong L. Specialized moisture retention eyewear for evaporative dry eye. Current eye research. 2015 May 4; 40(5): 490-5.

(10). Dell SJ. Intense pulsed light for evaporative dry eye disease. Clinical Ophthalmology. 2017 Jun 20: 1167-73.

(11). Sy A, O'Brien KS, Liu MP, Cuddapah PA, Acharya NR, Lietman TM et al. Expert opinion in the management of aqueous Deficient Dry Eye Disease (DED). Bmc

Ophthalmology. 2015 Dec; 15(1): 1-6.

(12). Zhang XM, Yang LT, Zhang Q, Fan QX, Zhang C, You Y et al. Reliability of Chinese web-based ocular surface disease index questionnaire in dry eye patients: a randomized, crossover study. International journal of ophthalmology. 2021; 14(6): 834.

(13). Sanchez-Gonzalez MC, Capote-Puente R, Garcia-Romera MC, De-Hita-Cantalejo C, Bautista-Llamas MJ, Silva-Viguera C et al. Dry eye disease and tear film assessment through a novel non-invasive ocular surface analyzer: The OSA protocol. Frontiers in Medicine. 2022; 9.

(14). Olafsson J, Lai X, Landsend EC, Olafsson S, Parissi E, Utheim OA et al. TheraPearl Eye Mask and Blephasteam for the treatment of meibomian gland dysfunction: a randomized, comparative clinical trial. Scientific Reports. 2021 Nov 17; 11(1): 22386.

(15). Marta A, Baptista PM, Heitor Marques J, Almeida D, José D, Sousa P et al. Intense pulsed plus low-level light therapy in meibomian gland dysfunction. Clinical Ophthalmology. 2021 Jun 28: 2803-11.

(16). Pult H. Low-level light therapy in the treatment of meibomian gland dysfunction. Investigative Ophthalmology & Visual Science. 2020 Jun 10; 61(7): 99.

(17). Tao T, Tao L. Systematic review and meta-analysis of treating meibomian gland dysfunction with azithromycin. Eye. 2020 Oct; 34(10): 1797-808.

(18). Choi M, Han SJ, Ji YW, Choi YJ, Jun I, Alotaibi MH et al. Meibum expressibility improvement as a therapeutic target of intense pulsed light treatment in meibomian gland dysfunction and its association with tear inflammatory cytokines. Scientific reports. 2019 May 21; 9(1): 1-8.