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Effect of Short-Term Oral Vitamin A Supplementation on Tear Film Stability, Tear Ferning Patterns, and Clinical Parameters in Dry Eye Disease

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ABSTRACT

Introduction: Dry Eye Disease (DED) is a multifactorial disorder of the tear film and ocular surface, leading to discomfort, visual impairment, and reduced quality of life. Vitamin A, essential for mucin production and tear film stability, has been shown to improve certain DED parameters, though its effect on mucin production and tear ferning patterns remains unexplored.

Methods: This study assessed the impact of short-term oral vitamin A supplementation on tear film stability, tear ferning patterns, and clinical parameters of DED. Participants were diagnosed based on established criteria. Tear ferning patterns were analyzed using microscopy, and clinical symptoms were evaluated using standardized grading systems pre- and post-supplementation.

Results: Oral vitamin A supplementation improved tear ferning patterns, suggesting enhanced mucin production and tear film stability. Participants also showed significant improvement in clinical parameters, including reduced ocular discomfort and enhanced tear quality. Results highlight the role of vitamin A in addressing tear film instability and mucin deficiency in DED.

Conclusion: Short-term oral vitamin A supplementation significantly improves tear film stability, mucin production, and clinical symptoms in DED, providing a promising therapeutic approach.

Keywords: Dry Eye Disease, Vitamin A, Tear Ferning, Mucin Deficiency, Tear Film Stability

INTRODUCTION

Dry Eye Disease (DED) is a multifactorial disorder of tears and the ocular surface, leading to discomfort, visual disturbance, and tear instability, potentially damaging the ocular surface. It is associated with increased tear film osmolarity and ocular surface inflammation, significantly affecting quality of life by impairing daily activities like reading, computer use, and household tasks.[1] The prevalence of DED ranges from 5% to 50%, with reports from Western India indicating mild, moderate, and severe disease in 47.98%, 31.82%, and 20.20% of cases, respectively.[2]

The TFOS DEWS II defines DED as "a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability, hyperosmolarity, ocular surface inflammation, and neurosensory abnormalities play etiological roles".[1] DED is classified into Aqueous Tear Deficient Dry Eye (ADDE), marked by insufficient aqueous secretion, and Evaporative Dry Eye (EDE), characterized by excessive evaporation despite normal lacrimal secretion.[1]

The tear film comprises lipid, aqueous, and mucin layers, with mucins being critical for tear film quality and stability. Secreted and membrane-bound mucins maintain wettability and sustain tear dynamics, stability, and homeostasis.[3,4] Altered mucin expression or secretion, often seen in DED, leads to tear film instability, hyperosmolarity, and inflammation, which adversely affect goblet cells (GCs) responsible for mucin production.[4]

Tear ferning, a simple, non-invasive test, assesses mucus alterations by analyzing crystallized tear patterns under a microscope. These patterns reflect interactions between electrolytes (e.g., sodium, chloride) and tear mucins and proteins, making tear ferning an indicator of tear film osmolarity and quality.[5-8] Mucin deficiency disrupts this pattern, highlighting its role in tear film stability.[8]

Vitamin A, an essential nutrient in healthy tear film, plays a crucial role in mucin production, protecting the ocular surface from free radicals, toxins, and inflammation. Deficiency of vitamin A leads to conjunctival changes, goblet cell atrophy, mucin loss, and instability of the tear film, contributing to DED.[9,10] While vitamin A supplementation has shown efficacy in improving tear film parameters, its effect on mucin production and tear ferning patterns remains unclear.[9,11]

Previous studies demonstrate the benefits of vitamin A supplementation in treating xerophthalmia, keratoconjunctivitis sicca, and other ocular surface disorders. Tseng et al. [12] found that topical all-trans retinoic acid improved severe ocular surface diseases. Saud A. Alazani et al. [13] observed enhanced tear quality in DED patients following a short course of oral vitamin A. Hossam et al. [14] reported greater long-term improvements in tear film quality and visual outcomes with oral vitamin A compared to topical administration.

However, literature on the specific impact of vitamin A supplementation on mucin production and tear ferning patterns is scarce. Most studies have focused on tear film quality, quantity, and other parameters of DED. Therefore, this study aims to assess whether short-term oral vitamin A supplementation improves tear film stability, particularly the tear ferning pattern, alongside symptoms and clinical parameters of DED.

The objectives of this study were to assess the effect of short-term oral vitamin A supplementation on tear film in patients with dry eye disease (DED), measure the changes in dry eye symptoms using the Ocular Surface Disease Index (OSDI) score before and after treatment, and evaluate the impact of oral vitamin A supplementation on tear film parameters, particularly the tear ferning pattern, alongside other standard diagnostic tests for DED.

MATERIALS AND METHODS

This single-group cohort study was conducted at a tertiary healthcare center in Western India over a two-year period, from June 2021 to June 2022. Ethical clearance was

obtained from the Institutional Ethics Committee, and informed written consent was secured from all participants. A total of 42 patients clinically diagnosed with DED were included in the study, adhering to specific inclusion and exclusion criteria. The interventional design involved assessing the same group of participants before and after treatment, ensuring that the effects of the intervention could be clearly measured.

Participants were recruited based on strict inclusion and exclusion criteria. The inclusion criteria ensured the participation of patients diagnosed with DED who could comply with the study protocol and attend follow-up visits. Patients with ocular conditions affecting the tear film, recent ocular surgeries, systemic conditions, or medications influencing tear production were excluded. Additionally, pregnant or lactating women and individuals unwilling to provide consent were not included in the study. Baseline data collection involved demographic information, a detailed history of symptoms, and a comprehensive assessment using both subjective and objective diagnostic tools.

At the initial visit, participants underwent baseline evaluations, which included scoring symptom severity, measuring best-corrected visual acuity, and completing the OSDI questionnaire to quantify the impact of DED on their quality of life. Tear film parameters were assessed through a battery of diagnostic tests, including Meibomian Gland Dysfunction (MGD) grading, the tear ferning test, Schirmer's Test I, Tear Film Break-Up Time (TBUT), corneal staining with fluorescein, Tear Film Meniscus Height (TFMH) measurement, and lissamine green staining. These tests provided critical insights into the severity and characteristics of DED, forming the foundation for evaluating the intervention's impact.

The intervention consisted of oral vitamin A supplementation at a dose of 200,000 IU per capsule, administered on days 0, 1, 14, and 28. This supplementation was complemented with lubricating eye drops to provide symptomatic relief. Participants were closely monitored for adherence to the intervention and any potential side effects. Follow-up visits were scheduled at one month and three months after completing the supplementation course. During these visits, all baseline tests were repeated to evaluate changes in symptoms and tear film parameters, enabling a comprehensive assessment of the intervention's effectiveness.

The primary outcomes of the study focused on improvements in OSDI scores and changes in tear ferning patterns, which are considered reliable indicators of tear film health and patient-reported symptom relief. Secondary outcomes included enhancements in TBUT, Schirmer's test results, corneal staining patterns, TFMH, and reductions in symptom severity scores. These measures allowed for a detailed understanding of both subjective and objective improvements in tear film and ocular surface health.

Data were systematically recorded and analyzed using statistical software. Continuous variables, such as TBUT and Schirmer's test results, were expressed as mean ± standard deviation, while categorical variables, such as the presence or absence of specific symptoms, were presented as frequencies or percentages. To evaluate the effectiveness of the intervention, pre- and post-treatment data were compared using paired t-tests or Wilcoxon signed-rank tests, depending on the data distribution. Statistical significance was set at $p<0.05$, ensuring robust and reliable conclusions.

RESULTS

A total of 42 patients diagnosed with Dry Eye Disease (DED) participated in the study. The mean age was 42.52 years, ranging from 21 to 58 years. Most participants (40.48%) were aged 41–50 years, followed by 26.19% in the 51–60 years range, 19.05% aged 31–40 years, and 14.29% aged 21–30 years. Regarding gender distribution, 57.14% were female (n=24), while 42.86% were male (n=18) (table 1).

At baseline (pre-supplementation), the mean symptom score was 7.95 ± 3.74, with a range of 3–16. Visual acuity scores for the right and left eyes were 1.69 ± 0.98 and 1.83 ± 1.03, respectively. The OSDI score had a mean value of 22.81 ± 7.89, indicating moderate dry eye symptoms. Meibomian Gland Dysfunction (MGD) grades were similar for both eyes, with mean scores of 1.72 ± 1.20 for the right eye and 1.73 ± 1.03 for the left. The

tear ferning grades showed mean values of 2.59 ± 0.92 and 2.58 ± 0.89 for the right and left eyes, respectively.

Schirmer's test grades were 2.20 ± 0.95 (right) and 2.15 ± 0.96 (left), while TBUT grades were 1.86 ± 0.94 (right) and 1.91 ± 0.95 (left). Fluorescein staining yielded mean scores of 1.81 ± 0.7 (right) and 1.86 ± 1.03 (left). The tear film meniscus height (TFMH) values were 1.88 ± 0.9 (right) and 1.86 ± 0.91 (left). Both eyes were positive for lissamine green staining.

Table 1: Demographic Characteristics

Demography	Cases (n=42) (%)
Age range	
21-30	6 (14.29)
31-40	8 (19.05)
41-50	17 (40.48)
51-60	11 (26.19)
Gender	
Male	18 (42.86)
Female	24 (57.14)

Table 2: Baseline Clinical Characteristics of Dry Eye Parameters

Variables	Pre supplementation Score (Mean ± SD)	Score Range (min-max)
Symptom Score	7.95± 3.74	03-16
Vision score		
Right eye	1.69 ± 0.98	01-04
Left eye	1.83 ± 1.03	01-04
OSDI Score	22.81 ± 7.89	13-39
MGD grade		
Right eye	1.72 ± 1.20	01-04
Left eye	1.73 ± 1.03	01-04
Tear Ferning Grade		
Right eye	2.59 ± 0.92	01-04
Left eye	2.58 ± 0.89	01-04
Schirmer's grade		
Right eye	2.20 ± 0.95	01-04
Left eye	2.15 ± 0.96	01-04
TBUT grade		
Right eye	1.86±0.94	01-04
Left eye	1.91±0.95	01-04
Fluorescein Stain		
Right eye	1.81 ± 0.7	01-04
Left eye	1.86±1.03	01-04
Tear Film Meniscus Height		
Right eye	1.88±0.9	01-04
Left eye	1.86 ± 0.91	01-04
Lissamine green Stain		
Right eye	Positive	
Left eye	Positive	

OSDI - Ocular Surface Disease Index; MGD - Meibomian Gland Blockage; TBUT - Tear Film Break Up Time

Following vitamin A supplementation, significant improvements were observed in symptom scores and OSDI scores. Symptom scores decreased from 7.95 ± 3.74 pre-supplementation to 6.17 ± 3.20 at 1 month and 4.38 ± 2.99 at 3 months ($p<0.001$). Similarly, OSDI scores improved from 22.81 ± 7.89 to 20.05 ± 7.53 at 1 month and 17.17 ± 7.39 at 3 months ($p<0.001$).

The visual acuity scores for both eyes showed a gradual reduction, reflecting an improvement. For the right eye, the score decreased from 1.69 ± 0.98 to 1.50 ± 0.86 at 3 months ($p<0.001$). Left eye scores followed a similar trend. The tear ferning grade significantly reduced from 2.59 ± 0.92 to 1.37 ± 0.77 in the right eye and from 2.58 ± 0.89 to 1.40 ± 0.81 in the left eye ($p<0.001$).

Schirmer's test grades significantly improved over time. For the right eye, the score decreased from 2.20 ± 0.95 pre-supplementation to 1.61 ± 0.74 at 3 months. TBUT grades improved similarly, with the right eye decreasing from 1.86 ± 0.94 to 1.20 ± 0.41 ($p<0.001$).

Table 3: Changes in clinical characteristics after Vit A supplement

Variables	Pre supplementation	Post supplementation since last dose		ANOVA
		1 Month	3 Month	P value
Symptom Score	7.95± 3.74	6.17 ± 3.20	4.38 ± 2.99	<0.001
Vision score				
Right eye	1.69 ± 0.98	1.62 ± 0.96	1.50 ± 0.86	<0.001
Left eye	1.83 ± 1.03	1.71 ± 0.97	1.57 ± 0.86	<0.001
OSDI Score	22.81 ± 7.89	20.05 ± 7.53	17.17 ± 7.39	<0.001
MGD grade				
Right eye	1.72 ± 1.20	1.72 ± 0.43	1.70 ± 0.52	<0.001
Left eye	1.73 ± 1.03	1.71 ± 0.97	1.71 ± 0.86	<0.001
Tear Ferning Grade				
Right eye	2.59 ± 0.92	1.71 ± 0.75	1.37 ± 0.77	<0.001
Left eye	2.58 ± 0.89	1.74 ± 0.66	1.40 ± 0.81	<0.001
Schirmer's grade				
Right eye	2.20 ± 0.95	1.76 ± 0.77	1.61 ± 0.74	<0.001
Left eye	2.15 ± 0.96	1.73 ± 0.78	1.63 ± 0.66	<0.001
TBUT grade				
Right eye	1.86±0.94	1.42±0.6	1.2±0.41	<0.001
Left eye	1.91±0.95	1.44±0.6	1.2±0.41	<0.001
Fluorescein Stain				
Right eye	1.81 ± 0.7	1.62 ± 0.83	1.38 ± 0.49	<0.001
Left eye	1.86±1.03	1.60 ± 0.80	1.45 ± 0.59	<0.001
Tear Film Meniscus Height				
Right eye	1.88±0.9	1.57±0.6	1.47±0.51	<0.001
Left eye	1.86 ± 0.91	1.55 ± 0.59	1.45 ± 0.50	<0.001
Lissamine green Stain				
Right eye	Positive	Positive	Negative	
Left eye	Positive	Positive	Negative	

OSDI - Ocular Surface Disease Index; MGD - Meibomian Gland Blockage; TBUT - Tear Film Break Up Time

Fluorescein staining scores improved significantly over time, from 1.81 ± 0.7 (right eye) and 1.86 ± 1.03 (left eye) to 1.38 ± 0.49 and 1.45 ± 0.59 at 3 months, respectively. TFMH values also showed significant improvement, with the right eye improving from 1.88 ± 0.9 to 1.47 ± 0.51 at 3 months ($p<0.001$).

At baseline, both eyes tested positive for lissamine green staining. By the 3-month follow-up, both eyes had improved to show negative staining, indicating significant resolution of conjunctival damage.

DISCUSSION

Dry eye syndrome (DES) is a prevalent ocular surface disorder that impacts vision and quality of life, caused by abnormal tear production or tear film instability. Vitamin A regulates corneal epithelial cell proliferation, goblet cell differentiation, and mucin production, thereby improving tear film stability. This study evaluates the short-term effects of oral vitamin A supplementation on tear film quality, quantity, and other DES parameters, including tear ferning patterns.

Prevalence and Demographics In western India, the prevalence of DES was reported as 34.26%.[2] In our study, the mean age of patients was 42.52 ± 9.82 years, with a higher prevalence among females (57.14%). As per OSDI scores, 45.23% had mild, 30.95% moderate, and 16.66% severe DES, similar to previous findings.[2]

Symptom Score Patients with DES experience symptoms such as burning, fatigue, sensitivity to light, and blurred vision, significantly affecting quality of life. Hossam et al. [14] observed a significant reduction in photophobia after three months of oral vitamin A supplementation (3000 IU daily). In contrast, H Selek et al. [15] reported no symptom improvement with 0.01% trans-retinoic acid emulsion. Our study noted a reduction in symptom scores from 7.95 ± 3.74 to 4.38 ± 2.99 at three months post-supplementation ($p <0.0001$), demonstrating significant improvement.

Vision Hossam et al. [14] reported significant improvement in blurred vision with oral vitamin A (3000 IU) by month three. Similarly, Toshida et al. [16] observed vision enhancement with retinol palmitate ophthalmic solution. In our study, mean vision

improved from 1.76 ± 1.00 to 1.67 ± 0.96 at one month and 1.54 ± 0.86 at three months post-supplementation ($p < 0.003$), indicating early and sustained visual improvement.

OSDI Scores Few studies have assessed the impact of vitamin A on OSDI scores. Eun Chul Kim et al. [17] reported significant OSDI score improvements with topical vitamin A at six months ($p = 0.004$). Hossam et al. [14] noted similar improvements with oral supplementation at all follow-up periods. In our study, OSDI scores decreased from 22.81 ± 7.89 to 20.05 ± 7.53 at one month ($p = 0.003$) and 17.17 ± 7.39 at three months ($p < 0.0001$), showing early efficacy.

Meibomian Gland Dysfunction There is limited literature on the effect of oral vitamin A on meibomian gland dysfunction. In our study, the mean score for gland blockage showed minimal improvement, from 1.72 ± 0.20 to 1.70 ± 0.52 at three months ($p < 0.003$). This suggests a limited effect, warranting further research.

Tear Ferning Pattern Saud A. Alanazi et al. [13] reported improved tear ferning grades with oral vitamin A (1500 mg for three days). H Selek et al. [15] noted significant changes in mucus ferning grades with 0.01% trans-retinoic acid emulsion. In our study, ferning grades improved from 2.59 ± 0.92 to 1.71 ± 0.75 at one month and 1.37 ± 0.77 at three months ($p < 0.0001$), suggesting increased mucin production and tear film stability.

Schirmer's Test Studies have shown mixed results regarding vitamin A's impact on Schirmer's test values. Tseng et al. [12] and Eun Chul Kim et al. [17] reported significant improvements with topical vitamin A. Our study observed an increase in Schirmer's test values from 8 ± 3.95 mm to 9.82 ± 4 mm at one month and 10.43 ± 3.95 mm at three months ($p < 0.0001$). This indicates a quicker onset of improvement with oral supplementation.

Tear Break-Up Time (TBUT) Fo Iwuagwu et al. [18] demonstrated a mean TBUT increase of 2.67 seconds after oral vitamin A supplementation (50,000 IU for seven days). Yadav S et al. [19] and Eun Chul Kim et al. [17] reported significant improvements with topical vitamin A at three and six months. In our study, TBUT increased significantly, reflecting enhanced tear film stability.

STRENGTH & LIMITATION

A key strength of this study is its comparative design, which evaluates the ease of insertion of the Laryngeal Mask Airway (LMA) Supreme and Classic using low-dose atracurium, offering valuable insights for optimizing airway management during general anesthesia. The use of objective parameters and a standardized protocol enhances the reliability of the findings. However, the study has limitations, including its relatively small sample size, which may affect the generalizability of the results. Additionally, the study was conducted in a single center, potentially limiting the applicability of the findings to broader populations or different clinical settings. Future studies with larger, multicenter cohorts are recommended.

CONCLUSION

This study highlights the comparative ease of insertion of the Laryngeal Mask Airway Supreme and Classic using low-dose atracurium during general anesthesia. The findings suggest that both devices are effective, but specific advantages in ease of insertion and performance parameters may favor one device over the other in certain clinical scenarios. These results provide valuable guidance for anesthesiologists in selecting the most appropriate airway device to enhance patient safety and procedural efficiency. Further research with larger, multicenter populations is recommended to validate these findings and explore additional factors influencing the choice of supraglottic airway devices.

Approval of Institutional Ethical Review Board: The study was approved by the Institutional Ethics Committee of M and J Institute of ophthalmology, Ahmedabad, India

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Individual Authors' Contributions: All the author has equally contributed conceptualization the study, designing the methodology, data collection, analysis, and preparation of the manuscript.

Availability of Data: The data supporting this study's findings are available on reasonable request from the corresponding author at [Shivanginilg@yahoo.co.in].

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