

COMPARATIVE EVALUATION OF THE EFFICACY OF VITAMIN A SUPPLEMENTATION VERSUS ARTIFICIAL TEAR LUBRICANTS IN THE MANAGEMENT OF DRY EYE DISEASE AMONG TYPE 2 DIABETES PATIENTS

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Abstract

Background: Dry eye disease is a common complication of type 2 diabetes mellitus, but no studies have directly compared the effect of vitamin A supplementation with artificial tears in people with type 2 diabetes mellitus (T2DM) to date.

Objective: To compare the efficacy of vitamin A supplementation versus artificial tear lubricants in the management of dry eye disease among type 2 diabetes patients.

Methods: A prospective, parallel-group randomized controlled trial was conducted in Sighton Optix Eye Center. Patients with type 2 diabetes mellitus (T2DM) and mild-to-moderate dry eye disease were recruited and randomly assigned to Hylo artificial tears (n=37) or Retin A vitamin A 10,000 IU (n=37) for six weeks. Sample size was calculated using G*Power 3.1.9.4 (effect size d=0.70, $\alpha=0.05$, power=95%). Eligible participants were aged 40–70 years with T2DM, OSDI 13–32, TBUT ≤ 10 seconds, Schirmer I ≤ 10 mm/5 min. Baseline and post-treatment assessments included OSDI, TBUT, and Schirmer I testing. Data were analyzed using SPSS version 27. Data was tested for normality using the Kolmogorov-Smirnov test with Lilliefors correction. Changes over time and between-group differences were evaluated using repeated-measures general linear modeling with Bonferroni-adjusted comparisons. Statistical significance was set at $p < 0.05$.

Result: Hylo and Retin A had significant effects on reducing dry eye symptoms and clinical signs in T2DM patients during 6 weeks. However, Hylo was significantly more effective, producing lower Week 6 OSDI scores (9.97 ± 2.12 vs. 14.76 ± 2.58 ; $F = 76.25$, $p < 0.001$), greater TBUT improvement in both eyes (mean difference: -1.43 and -1.52 seconds; both $p < 0.001$), and higher Schirmer values (mean difference: -1.49 and -1.28 mm; both $p < 0.001$). Significant between-group differences were also observed for left-eye Schirmer values at Week 6 ($F=6.01$, $p=0.017$) and right-eye TBUT at Week 2 ($F=7.07$, $p=0.010$).

Conclusion: Both vitamin A and artificial tears improved dry eye outcomes in patients with type 2 diabetes mellitus, but Hylo demonstrated significantly greater improvements in symptoms, tear-film stability, and tear secretion after 6 weeks.

Introduction

Type 2 diabetes mellitus (T2DM) is one of the major non-communicable diseases worldwide.[1] The 11th edition of the International Diabetes Federation's (IDF) Diabetes Atlas estimates that 589 million persons worldwide, aged 20 to 79, have diabetes. (11.1% of this age group).[2] The global burden is expected to increase substantially because of population ageing, urbanization, obesity, and sedentary lifestyles, particularly in low- and middle-income countries.[3-6]

Diabetic dry eye disease (DED) is a highly prevalent ocular surface complication that can cause chronic discomfort, visual disturbance, reduced quality of life, and corneal morbidity.[7] DED is defined by the TFOS DEWS II consensus as a multifactorial disease characterized by loss of tear-film homeostasis, with tear-film instability, hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities contributing to its pathogenesis.[8] The pathogenesis of diabetic DED is complex and involves multiple overlapping mechanisms. Chronic hyperglycemia can impair lacrimal gland structure and function, resulting in reduced aqueous tear production.[9] Meibomian gland dysfunction can alter the lipid layer of the tear film and increase evaporative loss, producing a mixed aqueous-deficient and evaporative dry eye pattern. Tear-film breakup time is consequently one of the commonly reported abnormal clinical findings in diabetic DED.[10] Artificial tears remain the mainstay and first-line treatment for DED.[11] They primarily supplement the aqueous or lipid components of the tear film and provide symptomatic relief; however, they are considered palliative rather than disease-modifying therapy and do not directly address epithelial damage, mucin deficiency, inflammation, or glandular dysfunction.[12] Evidence from systematic reviews also indicates no clear consensus that one artificial tear formulation is superior to

another. These limitations highlight the need for adjunctive treatments that target underlying ocular surface abnormalities.[13]

Vitamin A and its derivatives have an established role in maintaining ocular surface health. Vitamin A contributes to epithelial integrity, mucin synthesis, and goblet cell function, while topical retinoids have demonstrated beneficial effects on epithelial abnormalities and ocular surface healing in experimental models.[14] Clinical studies in patients with DED have reported improvements in tear-film stability, corneal staining, and goblet cell-related function following retinol palmitate treatment. However, direct evidence comparing vitamin A supplementation with artificial tears specifically in patients with T2DM remains limited.[15]

Therefore, comparative clinical evaluation is needed to determine whether vitamin A supplementation provides additional benefits over conventional artificial tear lubricants in managing diabetic dry eye. This study aims to address this evidence gap and evaluate the potential role of vitamin A as an adjunctive or alternative treatment for ocular surface disease in patients with T2DM.

Methods

This study was designed as a randomized controlled, prospective, parallel-group study conducted at Cairns Railway Hospital over a period of six months following synopsis approval. The study population comprised patients aged 40–70 years with Type 2 Diabetes Mellitus presenting with symptoms of dry eye disease. A total sample of 74 participants was calculated using G*Power Software version 3.1.9.4, based on an effect size of 0.7, alpha error of 0.05, and 95% statistical power, with 37 participants allocated to each treatment group. Participants were recruited using non-probability consecutive sampling. Eligible participants had dry eye symptoms for at least one month, an OSDI score of 13–32, TBUT

≤10 seconds, Schirmer I test ≤10 mm/5 minutes and provided written informed consent. Patients with Type 1 diabetes, uncontrolled systemic disease, severe dry eye, recent ocular surgery or laser procedures, contact lens use, active ocular infection or inflammation, use of other topical ophthalmic medications, systemic autoimmune diseases associated with severe dry eye, medications affecting tear production, or pregnancy/lactation were excluded. Ethical approval was obtained from the Institutional Ethical Review Committee of The Superior University, and written informed consent was obtained from all participants. Confidentiality and anonymity were maintained, and participants were informed of their right to withdraw from the study at any time. Following screening, eligible participants underwent baseline assessment including demographic and medical history, OSDI questionnaire, TBUT, and Schirmer I test. Participants were randomly assigned to two groups: Group A received Vitamin A supplementation (RETIN A, 10,000 IU capsule/day), while Group B received artificial tear lubricants (Hylo four drops/day) for six weeks. OSDI, TBUT, and Schirmer I measurements were reassessed at baseline, Week 2, and Week 6 using the same standardized procedures. Data were recorded on a structured proforma, coded to maintain confidentiality, and analyzed using SPSS version 27. Continuous variables were summarized as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Data normality

was assessed using the Kolmogorov-Smirnov test with Lilliefors correction. A Linear Mixed Model was used to assess repeated OSDI, TBUT, and Schirmer measurements, evaluating the effects of time, treatment group, and group-by-time interaction. Bonferroni-adjusted pairwise comparisons were performed where appropriate, and a p-value <0.05 was considered statistically significant. Results were presented using tables and graphs to demonstrate differences in dry eye symptoms, tear-film stability, and tear production between the two treatment groups.

Results

OSDI scores were comparable at baseline between the Hylo and Retin A groups (23.19 ± 4.50 vs. 24.97 ± 3.11 ; $p = 0.051$), but significantly lower scores were observed in the Hylo group at week 2 (15.92 ± 3.85 vs. 21.30 ± 2.76 ; $p < 0.001$) and week 6 (9.97 ± 2.12 vs. 14.76 ± 2.58 ; $p < 0.001$). TBUT progressively increased in both groups, with a significant between-group difference in the right eye at week 2 (9.81 ± 1.02 vs. 8.46 ± 1.48 seconds; $p = 0.010$). Similarly, Schirmer test values increased substantially in both groups throughout follow-up. In the right eye, differences between groups were not statistically significant at baseline, week 2, or week 6; however, in the left eye, a significant difference was observed at week 6, with higher values in the Hylo group than the Retin A group (15.22 ± 1.11 vs. 12.68 ± 1.47 mm; $p = 0.017$).

Table 1: Descriptive Statistics for Demographic Data

		Age (years)	Duration of Type 2 Diabetes Mellitus (years)
Study Groups	Visits	Mean ± SD	Mean ± SD
Hylo	Baseline	50.19 ± 5.72	16.59 ± 5.41
	2 Weeks	50.19 ± 5.72	16.59 ± 5.41
	6 Weeks	50.19 ± 5.72	16.59 ± 5.41
Retin A	Baseline	50.65 ± 5.31	16.41 ± 4.06
	2 Weeks	50.65 ± 5.31	16.41 ± 4.06
	6 Weeks	50.65 ± 5.31	16.41 ± 4.06

The table shows that the two study groups were comparable in terms of baseline demographic

data. In the Hylo group, the mean age was 50.19 ± 5.72 years and mean duration of type

2 diabetes mellitus was 16.59 ± 5.41 years. These values remained unchanged at the 2-week and 6-week visits. Similarly, in the Retin A group, the mean age was 50.65 ± 5.31 years

and mean duration of diabetes was 16.41 ± 4.06 years, with the same values reported at 2 and 6 weeks.

Table 2: Comparative Statistics for Ocular Surface Disease Index (OSDI)

Comparative Statistics OSDI				
Visit	Study Group	Mean $\pm$ Std. Deviation	F	P-Value
Baseline	Hylo	23.19 ± 4.50	3.94	0.051
	RETIN A (10000 iu)	24.97 ± 3.11		
Week 2	Hylo	15.92 ± 3.85	47.66	< 0.001
	RETIN A (10000 iu)	21.30 ± 2.76		
Week 6	Hylo	9.97 ± 2.12	76.25	< 0.001
	RETIN A (10000 iu)	14.76 ± 2.58		

The comparative analysis of Ocular Surface Disease Index (OSDI) scores demonstrated no statistically significant difference between the Hylo and Retin A groups at baseline, with mean scores of 23.19 ± 4.50 and 24.97 ± 3.11 , respectively ($F = 3.94$, $p = 0.051$). At week 2, the mean OSDI score decreased to 15.92 ± 3.85 in the Hylo group compared with $21.30 \pm$

2.76 in the Retin A group, showing a statistically significant between-group difference ($F = 47.66$, $p < 0.001$). By week 6, OSDI scores further declined to 9.97 ± 2.12 in the Hylo group and 14.76 ± 2.58 in the Retin A group, with a highly significant difference ($F = 76.25$, $p < 0.001$).

Table 3: Comparative Statistics for Tear Break Up Time (TBUT)

Comparative Statistics TBUT					
Eye	Visit	Study Group	Mean $\pm$ Std. Deviation	F	P-Values
Right Eye	Baseline	Hylo	6.08 ± 1.27	2.004	0.161
		RETIN A (10000 iu)	5.89 ± 1.09		
	Week 2	Hylo	9.81 ± 1.02	7.07	0.01
		RETIN A (10000 iu)	8.46 ± 1.48		
	Week 6	Hylo	15 ± 1.51	1.768	0.188
		RETIN A (10000 iu)	12.7 ± 1.85		
Left Eye	Baseline	Hylo	6.28 ± 1.42	0.543	0.464
		RETIN A (10000 iu)	6.23 ± 1.21		
	Week 2	Hylo	9.81 ± 1.13	0.634	0.428
		RETIN A (10000 iu)	8.19 ± 1.24		
	Week 6	Hylo	15.32 ± 1.20	2.634	0.109
		RETIN A (10000 iu)	12.78 ± 1.70		

In the right eye, baseline TBUT was comparable between the Hylo and Retin A groups (6.08 ± 1.27 vs. 5.89 ± 1.09 seconds; $F = 2.004$, $p = 0.161$). At week 2, TBUT increased to 9.81 ± 1.02 seconds in the Hylo group and 8.46 ± 1.48 seconds in the Retin A group, showing a statistically significant

difference ($F = 7.07$, $p = 0.010$). By week 6, TBUT further increased to 15.00 ± 1.51 and 12.70 ± 1.85 seconds, respectively; however, the between-group difference was not statistically significant ($F = 1.768$, $p = 0.188$). Similarly, in the left eye, baseline TBUT was comparable between groups (6.28 ± 1.42 vs.

6.23 ± 1.21 seconds; $F = 0.543$, $p = 0.464$). At week 2, TBUT increased to 9.81 ± 1.13 seconds in the Hylo group and 8.19 ± 1.24 seconds in the Retin A group, with no statistically significant difference ($F = 0.634$, $p = 0.428$). At

week 6, TBUT reached 15.32 ± 1.20 and 12.78 ± 1.70 seconds, respectively, again without a significant between-group difference ($F = 2.634$, $p = 0.109$).

Table 4: Comparative Statistics for Schirmer Test

Comparative Statistics Schirmer Test					
Eye	Visit	Study Group	Mean ± Std. Deviation	F	P-Value
Right Eye	Baseline	Hylo	5.49 ± 1.43	0.185	0.668
		RETIN A (10000 iu)	5.78 ± 1.32		
	Week 2	Hylo	10.57 ± 1.14	2.939	0.091
		RETIN A (10000 iu)	8.54 ± 1.48		
	Week 6	Hylo	15 ± 1.51	0.821	0.368
		RETIN A (10000 iu)	12.62 ± 1.80		
Left Eye	Baseline	Hylo	5.51 ± 1.35	0.059	0.809
		RETIN A (10000 iu)	5.97 ± 1.28		
	Week 2	Hylo	9.97 ± 1.40	0.24	0.626
		RETIN A (10000 iu)	8.54 ± 1.48		
	Week 6	Hylo	15.22 ± 1.11	6.013	0.017
		RETIN A (10000 iu)	12.68 ± 1.47		

In the right eye, baseline Schirmer values were comparable between the Hylo and Retin A groups (5.49 ± 1.43 vs. 5.78 ± 1.32 mm; $F = 0.185$, $p = 0.668$). At week 2, the values increased to 10.57 ± 1.14 mm in the Hylo group and 8.54 ± 1.48 mm in the Retin A group, although the difference was not statistically significant ($F = 2.939$, $p = 0.091$). At week 6, Schirmer values further increased to 15.00 ± 1.51 and 12.62 ± 1.80 mm, respectively, with no significant between-group difference ($F = 0.821$, $p = 0.368$). Similarly, in the left eye, baseline values were 5.51 ± 1.35 mm for Hylo and 5.97 ± 1.28 mm for Retin A ($F = 0.059$, $p = 0.809$). At week 2, values increased to 9.97 ± 1.40 and 8.54 ± 1.48 mm, respectively ($F = 0.240$, $p = 0.626$). By week 6, Schirmer values reached 15.22 ± 1.11 mm in the Hylo group and 12.68 ± 1.47 mm in the Retin A group, with a statistically significant between-group difference ($F = 6.013$, $p = 0.017$).

Discussion

The present study demonstrated that both Hylo and Retin A significantly improved dry-eye symptoms and clinical parameters in patients with type 2 diabetes mellitus over six weeks. Although the groups were comparable in age and diabetes duration, the Retin A group had higher baseline OSDI scores, which may have influenced treatment response. The significantly greater reduction in OSDI with Hylo (estimated marginal mean difference −4.46 points, 95% CI: −5.87 to −3.04; $p < 0.001$) suggests that Hylo may provide superior symptomatic relief in diabetic dry eye. In a recent systematic review and meta-analysis study published in 2026 analysed 3469 patients from 39 RCTs and concluded that HAC products with intermediate concentrations (around 0.15 – 0.18%) significantly improved

patient reported symptoms associated with dry eye.[16]

Tear film findings are consistent with previous evidence showing that sodium hyaluronate improves TBUT and overall tear-film stability, although the magnitude of benefit may vary according to the study population, treatment formulation, duration, and comparator. In contrast, previous studies of retinol palmitate have shown modest and sometimes non-significant improvements in TBUT suggesting that its primary benefit may result from improving ocular-surface epithelial health rather than directly enhancing tear production. The greater improvement observed with Hylo in the present study may therefore reflect its stronger lubricating and tear-film stabilizing properties in patients with diabetic dry eye disease.[17]

The Schirmer test findings are consistent with a recent systematic review of randomized controlled trials reported consistent improvements in Schirmer values following hyaluronate therapy. In contrast, previous studies of topical retinol palmitate found no significant effect on Schirmer values, suggesting that vitamin A primarily improves corneal and conjunctival epithelial function rather than directly increasing lacrimal gland secretion. This difference in therapeutic mechanisms may explain the greater improvement in tear volume observed with Hylo in the present study.[18]

A key aspect of the present study is that the improvements of both groups of treated participants were significant. Thus it is not fair to conclude that Retin A was ineffective on the basis of these results. Retin A may explain its improvement due to the biological effect of Vitamin A on maintaining health of the ocular-surface epithelial cells. Topical retinol palmitate has been shown clinically to have beneficial effects on some subjective disorders and it has been suggested that it may be beneficial in epithelial healing.[19]

Clinically, sodium hyaluronate demonstrated broader improvement in both subjective symptoms and objective tear-film parameters, while Retin A also showed significant benefits and may remain useful for ocular-surface epithelial recovery. Findings from Sun et al.

similarly showed benefits with both treatments, although differences in underlying disease, formulation, baseline ocular-surface status, and treatment duration may explain variations between studies. The Japanese retinol palmitate study further supports the present findings by demonstrating modest TBUT improvement, no significant Schirmer effect, and limited symptomatic benefit.[20]

Conclusion

The present study demonstrated that both Hylo (sodium hyaluronate artificial tears) and Retin A 10,000 IU effectively improved dry-eye parameters in adults with type 2 diabetes mellitus. However, Hylo demonstrated a significantly greater therapeutic benefit than Retin A, particularly in reducing symptoms and improving tear-film stability and tear production.

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