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Original Research Paper

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A PROSPECTIVE COMPARITIVE STUDY TO EVALUATE THE EFFECTIVENESS OF VITAMIN D SUPPLEMENTATION IN DRY EYE SYNDROME

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ABSTRACT Dry eye disease (DED) is a multi-factorial ocular surface disorder characterized by a loss of tear film homeostasis and inflammation. Emerging evidence suggests that Vitamin D plays a crucial role in immune modulation and ocular surface health. To evaluate the clinical effectiveness of systemic oral Vitamin D supplementation in patients with Dry Eye Syndrome (DES) and concurrent Vitamin D deficiency. A prospective comparative study was conducted with 105 patients aged 30–60 years diagnosed with DES. Participants were allocated into three balanced groups (n=35 each): Group A (Normal baseline Vitamin D; managed with 0.5% carboxymethylcellulose [CMC] 4x/day), Group B (Deficient Vitamin D; managed with 0.5% CMC alone), and Group C (Deficient Vitamin D; managed With 0.5% CMC along with 2000 IU Vitamin D buccal spray daily). Parameters including Tear Break-up Time (TBUT), Schirmer's test type I, Ocular Surface Disease Index (OSDI) scores, and serum Vitamin D3 levels were tracked at Day 0, 15, 30, and 90. Vitamin D deficiency significantly exacerbates dry eye severity. Systemic correction of Vitamin D levels in deficient individuals provides profound therapeutic synergy with traditional tear substitutes, markedly expanding tear film stability, volume, and patient comfort.

KEYWORDS : Dry Eye Syndrome, Vitamin- D, Inflammation, Immunomodulation, Tear Film

INTRODUCTION

Dry eye disease (DED) or Dry Eye Syndrome (DES) is a widespread ocular condition that impacts Millions of individuals worldwide, with global prevalence rates varying significantly from 5% to 50% Across different geographical locations[1]. It is highly characterized by an unstable tear film and underlying Chronic inflammation of the ocular surface[2]. This condition greatly reduces patients' quality of life, leading To decreased work capability, impaired visual clarity, and learning productivity.

DES is traditionally divided into two distinct patho-physiological types[3]: (1) Aqueous deficiency dry eye, Wherein a decrease in tear production from the lacrimal glands occurs, encompassing both Sjogren's Syndrome and non-Sjogren's forms[4,5] and (2) Evaporative dry eye, primarily driven by inflammation of the Eyelid margins, meibomian gland dysfunction (MGD), and accelerated tear film thinning[4,5].

AIMS AND OBJECTIVES

- To Compare the association of dry eye syndrome in patient with normal and decreased Vitamin D Levels.
- To compare the effects of conventional treatment and conventional treatment along with Vitamin D supplements in dry eye syndrome.

MATERIALS AND METHODS

This prospective, comparative clinical study was carried out over a duration of one year in the Out-Patient Department (OPD) of Ophthalmology at Sant Parmanand Hospital, Civil Lines, New Delhi. A sample Size calculation was performed using reference parameters from prior literature (Seok Hyun Bae et al.)[6], Which established a post-supplementation standard deviation for TBUT of 2.60. Assuming a target Difference of 40% between the intervention and non-intervention groups, at 80% statistical power and a 5% significance level (alpha error), a minimum required cohort size of 33 patients per arm was derived. Factoring an anticipated 5% loss-to-follow-up rate, a total study population of 105 patients was enrolled And equally distributed across three arms (35 participants per group).

Inclusion and Exclusion Criteria

The study cohort was restricted to cooperative adult individuals aged 30 to 60 years presenting with Clinical symptoms of dry eye syndrome who provided written, informed consent. Rigid exclusion criteria Were enforced to eliminate confounding causes of ocular surface changes. Ocular exclusions consisted of Preexisting active pathologies such as glaucoma, uveitis, severe ocular allergy, pterygium, blepharitis, Active infections, advanced corneal disease, high-degree lid or eyelash structural abnormalities, Nasolacrimal apparatus blocks, contact lens wear within the preceding month, or any history of intraocular Surgery within the past six months.

Systemic exclusions encompassed immune-mediated conditions (e.g., Sjogren's syndrome, rheumatoid arthritis, lupus), systemic malignancies, hematological disorders, Hyperthyroidism, general malnutrition, chronic kidney disease, diabetes mellitus, major clinical Depression, pregnancy, lactation, or known hypersensitivity/allergy to Vitamin D compounds.

Furthermore, any patients receiving systemic medications documented to compromise tear film Mechanics (including antihistamines, antidepressants, oral contraceptives, decongestants, gabapentin, Sildenafil, anticholinergics, beta-blockers, postmenopausal estrogen therapy, or active diuretics) were Explicitly excluded.

Study Interventions and Framework

All enrolled participants underwent clear allocation into one of three defined groups at baseline (Day 0):

- Group A: Dry eye patients presenting with normal baseline serum Vitamin D levels ($30-80 Ng/mL$); managed solely with standard topical lubricant therapy (0.5% carbo-xymethylcellulose [CMC] eye drops, 4 times daily for 90 days).
- Group B: Dry eye patients presenting with baseline serum Vitamin D deficiency (<20 ng/mL); Managed identically with topical lubricant therapy (0.5% CMC eye drops, 4 times daily for 90 days) Without any systemic replenishment.
- Group C: Dry eye patients presenting with baseline serum Vitamin D deficiency (<20 ng/mL); Managed with topical lubricant therapy (0.5% CMC eye drops, 4 times daily) plus active systemic Supplementation via an oral buccal spray containing 2000 IU of Vitamin D, administered once daily From Day 1 to Day 90.

Clinical evaluations were conducted systematically across four scheduled visits: Visit 1 (Baseline, Day 0), Visit 2 (Day 15), Visit 3 (Day 30), and Visit 4 (Day 90). Every evaluation comprised Best-Corrected Visual Acuity (BCVA) recorded via standard Snellen projections (converted to logMAR scales), slit-lamp Biomicroscopy, non-contact tonometry for intraocular pressure (IOP) tracking, dilated fundus Examinations utilizing a 90D lens, and targeted objective dry eye assessments. Serum 25-hydroxy Vitamin D3 [25(OH)D]

parameters were quantified analytically twice—at baseline (Day 0) and at Completion (Day 90)—via chemiluminescence assays executed on a standardized Access 2 analyzer (Beckman Coulter).

Methodology of Dry Eye Parameter Diagnostics

To maximize reproducibility, diagnostic tests were performed in an invariant sequential sequence across Visits, maintaining a minimum 30-minute quiet interval between objective checks. Examinations were Strictly performed without local anesthetic agents. Tear Film Break-Up Time (TBUT) was analyzed first Via low-intensity slit-lamp illumination with a cobalt blue filtering frame following minimal instillation of A sodium fluorescein strip. Patients were instructed to blink naturally and then sustain an open gaze; the Interval from the last complete blink to the emergence of the primary black dry gap was clocked. This Maneuver was repeated three separate times per eye to establish a true mean value. Values under 10 Seconds were designated pathognomonic for tear film instability.

Schirmer's Test Type I was subsequently performed utilizing standardized, pre-calibrated filter strips (Whatman Filter Paper No. 41). The notched edge of the strip was folded and carefully hooked over the Lower eyelid margin at the outer one-third junction, avoiding any focal touch to the highly sensitive Cornea. Wetting lengths were documented precisely after exactly 5 minutes of passive sitting. In line with Conventional criteria, clinical grading metrics were handled as: >10 mm as normal physiological wetting, 5–10 mm as mild dryness, 2–5 mm as moderate deficiency, and <2 mm as severe dry eye state.

Subjective symptom severity indexing was performed utilizing the authorized 12-point Ocular Surface Disease Index (OSDI) questionnaire framework. The patient answered specific occurrences of light Sensitivity, grittiness, pain, blurred vision, or visual restrictions during night driving, reading, computer Work, and environmental distresses over the prior week. Calculations were strictly evaluated via the Validated formula: OSDI Score = [(Sum of specific question responses) * 25] / (Total number of validly Answered questions), scaling from 0 to 100.

RESULTS AND OBSERVATIONS

Statistical operations were performed via SPSS Version 21.0, treating p-values less than 0.05 as Significant. Continuous variable checks utilized Analysis of Variance (ANOVA) and Post-Hoc Bonferroni Adjustments for normally distributed arrays, and Kruskal-Wallis/Dunn's tests for non-parametric Structures.

Baseline characteristics, including age, gender distribution, and chief symptomatic presentations, were Exceptionally homogenous across the three study arms, with no significant differences detected (p>0.05). The global sample (N=105) demonstrated a mean age of 40.75±9.91 years (p=0.306 across groups) and Was predominantly composed of female patients (63.81% female vs. 36.19% male, p=0.457). The primary Driving complaints reported at baseline were localized ocular pain (27.62%) and distinct sensations of Severe dryness (20.00%). Routine baseline metrics for the anterior segment, adnexa, intraocular pressure (mean 15.08±2.35 mmHg, p=0.504), and structural fundus checks were within normal limits (WNL) for All participants.

Table 1: Baseline Demographic Metrics and Clinical Segment Profiling

Parameter	Group A (n=35)	Group B (n=35)	Group C (n=35)	Total (N=105)	p-value
30 to 40 years	20 (57.14%)	18 (51.43%)	24 (68.57%)	62 (59.05%)	0.516†
41 to 50 years	7 (20.00%)	6 (17.14%)	6 (17.14%)	19 (18.10%)	A vs B: 0.720†
51 to 60 years	8 (22.86%)	11 (31.43%)	5 (14.29%)	24 (22.86%)	A vs C: 0.568†
Mean Age ± SD	41.29 ± 10.82	42.26 ± 10.30	38.71 ± 8.40	40.75 ± 9.91	0.306‡
Female	25 (71.43%)	20 (57.14%)	22 (62.86%)	67 (63.81%)	0.457†
Male	10 (28.57%)	15 (42.86%)	13 (37.14%)	38 (36.19%)	B vs C: 0.626†
Mean IOP ± SD	15.04 ± 2.30	15.43 ± 2.42	14.77 ± 2.34	15.08 ± 2.35	0.504‡
Visual Acuity (logMAR)	0.18 ± 0.17	0.06 ± 0.12	0.11 ± 0.17	0.12 ± 0.16	0.002§

Table 2: Longitudinal Evolution of Tear Break-up Time (Seconds)

Visit Timeline	Group A (n=35)	Group B (n=35)	Group C (n=35)	Total Dataset	p-value
Baseline (Day 0)	3.94 ± 1.43	4.17 ± 1.31	4.33 ± 1.96	4.15 ± 1.58	0.596‡
Follow-up Day 15	5.57 ± 1.63	4.81 ± 1.35	5.87 ± 1.93	5.42 ± 1.70	0.026‡ (B vs C)*
Follow-up Day 30	7.83 ± 1.80	5.01 ± 1.65	8.41 ± 2.11	7.09 ± 2.37	<0.0001‡ (A/C vs B)*
Final Visit (Day 90)	11.09 ± 2.31	6.36 ± 3.16	12.10 ± 2.59	9.85 ± 3.68	<0.0001‡ (A/C vs B)*

Visit Timeline	Group A (n=35)	Group B (n=35)	Group C (n=35)	Total Dataset	p-value
Baseline (Day 0)	5.39 ± 1.91	5.90 ± 2.35	5.14 ± 1.85	5.48 ± 2.06	0.293‡
Follow-up Day 15	7.60 ± 2.19	6.43 ± 3.77	8.60 ± 4.54	7.54 ± 3.71	0.048‡ (B vs C)*
Follow-up Day 30	9.96 ± 2.41	6.97 ± 4.20	11.30 ± 4.40	9.41 ± 4.16	<0.0001‡ (A/C vs B)*
Final Visit (Day 90)	13.34 ± 3.20	7.96 ± 4.65	15.53 ± 4.62	12.28 ± 5.26	<0.0001‡ (A/C vs B)*

Table 4: Longitudinal Shift in Mean OSDI Objective Discomfort Scores

Visit Timeline	Group A (n=35)	Group B (n=35)	Group C (n=35)	Total Dataset	p-value
Baseline (Day 0)	44.23 ± 9.39	44.57 ± 9.52	47.17 ± 11.11	45.32 ± 10.03	0.409‡
Follow-up Day 15	31.76 ± 8.12	34.99 ± 10.83	30.81 ± 9.95	32.52 ± 9.77	0.173‡
Follow-up Day 30	24.92 ± 7.33	28.51 ± 12.47	19.67 ± 9.44	24.37 ± 10.53	0.001‡ (B vs C)*
Final Visit (Day 90)	17.73 ± 6.94	23.91 ± 12.71	12.84 ± 3.94	18.16 ± 9.71	<0.0001‡ (A/B/C vs)*

Table- 5 Analysis of Serum 25-Hydroxy Vitamin D3

Timeline	Group A (n=35)	Group B (n=35)	Group C (n=35)	Total Sample	Statistical Significance (p-value)
Baseline (Pre-Study)	28.07 ± 6.31 Med: 25.23 Range: 20.55–48.00	14.01 ± 3.28 Med: 15.24 Range: 7.59–18.84	14.47 ± 3.43 Med: 15.25 Range: 6.95–19.20	18.85 ± 7.96 Med: 16.45 Range: 6.95–48.00	p < 0.0001 (A vs B <0.0001; A vs C <0.0001; B vs C: 0.905)
Day 90 (Post-Study)	30.60 ± 6.50 Med: 28.64 Range: 21.54–49.00	15.23 ± 3.30 Med: 15.81 Range: 7.50–19.80	25.60 ± 4.63 Med: 25.00 Range: 13.00–35.70	23.81 ± 8.11 Med: 24.00 Range: 7.50–49.00	p < 0.0001 (A vs B <0.0001; A vs C: 0.0002; B vs C <0.0001)

DISCUSSION

This prospective hospital-based study evaluated the relationship of DES with Vitamin D deficiency by Tracking multiple clinical indices over 90 days. Age-related distribution showed that 59.05% (n = 62) of The sample was between 30 and 40 years of age. This high concentration in younger adult cohorts matches.

The findings of Jeewan S Titiyal et al[7]., whose large-scale epidemiological work in Northern India reported a 32% dry eye prevalence, with the 21–40 age bracket identified as the most commonly affected group.

Regarding gender, our data showed a higher percentage of female participants (63.81%, n = 67) than male Participants (36.19%, n = 38). This distribution is consistent with findings by Hyojin Kim et al[32]. and Maria Borrelli et al[33]., which indicate higher dry eye symptom severity and OSDI indices in female subjects.Tear film stability, measured via TBUT, improved significantly by Day 90 in patients with normal Baseline Vitamin D levels receiving topical lubrication (Group A) compared to those with uncorrected Vitamin D deficiency (Group B). This aligns with Demirci et al[10]., who reported significantly higher Baseline TBUT values in healthy

individuals (18.1 ± 0.5 seconds) than in Vitamin D-deficient subjects (8.8 ± 0.6 seconds). Notably, after 90 days of systemic Vitamin D supplementation, Group C achieved a Mean TBUT of 12.10 ± 2.59 seconds, whereas the uncorrected deficient group (Group B) remained Severely tracking at 6.36 ± 3.16 seconds ($p < 0.0001$). These results match those of P. Watts et al[11]. and Nikita Jain et al[12]., which demonstrated substantial improvements in tear break-up profiles following Systemic Vitamin D combinations.

Schirmer's Test Type I wetting parameters showed a similar pattern. Patients with normal baseline Vitamin D levels (Group A) achieved significantly higher clinical improvements under standard topical Lubrication than those with uncorrected deficiency (Group B). This supports the findings of Yildirim et al[13]., who demonstrated lower overall Schirmer scores in premenopausal women with baseline Vitamin D Deficiency. Systemic supplementation in Group C led to a significant increase in mean Schirmer wetting From 5.14 ± 1.85 mm to 15.53 ± 4.62 mm by Day 90, whereas Group B showed minimal recovery (7.96 ± 4.65 mm, $p < 0.0001$). Similar increases in aqueous tear volume following Vitamin D replenishment were Reported by P. Watts et al[11]. and Bae et al[6].

Furthermore, uncorrected continuous systemic deficiency was associated with persistent subjective ocular Discomfort and limited symptom resolution in Group B. This supports findings by Demirci et al[10]. Demonstrating elevated OSDI scores in patients with deficient Vitamin D status. Systemic replenishment In Group C led to a substantial reduction in final mean OSDI scores (12.84 ± 3.94) compared to Group B (23.91 ± 12.71, $p < 0.0001$), with 97.14% of patients achieving full clinical normalization. These findings Match the multi-group comparative results published by Nikita Jain et al[12].

CONCLUSIONS

Exacerbation of Pathology: Systemic deficiency of Vitamin D can worsen the subjective and objective symptoms of Dry Eye Syndrome.

Therapeutic Efficacy: Systemic replenishment with oral Vitamin D in deficient states significantly improves objective tear break-up time (TBUT), Schirmer's Type I aqueous secretion, and subjective OSDI clinical scores.

Clinical Recommendation: To optimize clinical outcomes, serum Vitamin D screening should support standard diagnostic workups for DES, and systemic correction should be integrated alongside conventional topical lubricants.

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