Assessment of the effect of vitamin E supplementation on the ocular tear film Study Protocol

Background

The tear film is a thin, multilayered structure that protects and lubricates the ocular surface while maintaining optical clarity. Disturbances in its composition or stability are central to the pathophysiology of dry eye disease, a condition characterized by discomfort, visual disturbance, and reduced quality of life. Oxidative stress is increasingly recognized as a key contributor to tear film instability and ocular surface damage. Vitamin E, a fat-soluble antioxidant composed of tocopherols and tocotrienols, protects cellular membranes from free radical damage and has shown promise in supporting ocular health. Previous studies have suggested that systemic antioxidant supplementation may improve tear parameters, but evidence for short-term oral vitamin E use in healthy young adults remains limited.

Objectives

This nonrandomized interventional clinical trial aims to determine the effect of short-term oral vitamin E supplementation on tear film parameters such as non-invasive tear breakup time (NITBUT), tear meniscus height (TMH), tear ferning (TF), and subjective dry eye symptoms using the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire.

Methods

Participants

This nonrandomized interventional clinical trial will be conducted at King Saud University. We will recruit a total sample of 64 healthy adults aged 18–30 years to provide 90% power at a 95% confidence level and a significance level of 0.05. Before measurements began, we will inform participants of the study's purpose, procedures, risks, and benefits, and they will provide written informed consent. We will assign each subject a number from 1 to 64, written on sealed envelopes. We will divide subjects into two groups: 1–32 will receive vitamin E supplementation, and 33–64 will receive the placebo for 3 consecutive days. We will recruit adults with no ocular

disease, who do not wear contact lenses and have no history of ocular surgery. Exclusion criteria will include participants with systemic diseases such as hypertension or diabetes, pregnant or breastfeeding women, those taking medications that affect tear physiology, and individuals with known hypersensitivity to vitamin E.

Participants in the study group will take a vitamin E capsule (400 IU; 400 mg softgel) daily for three consecutive days. We will obtain baseline measurements before supplementation and follow-up measurements 24 hours after the third dose (2 visits total). The control group will receive placebo capsules for comparison, and we will obtain measurements on days 1 and 4.

All participants will first complete the SPEED questionnaire. We will then conduct the NITBUT test, followed by the TMH and TF tests. We will measure NITBUT and TMH using the EASYTEAR View+ device. After three days of supplementation, participants will return for Visit 2, where the same assessments will be repeated 24 hours after the final dose. Five minutes will be allowed between tests. Both participants and the examiner will be blinded to the type of artificial tears used in this double-masked study. All tests will be performed in the right eye.

Vitamin E

Vitamin E 400 IU (400 mg) softgels are fat-soluble antioxidant supplements commonly used to support skin, hair, and immune health and protect cells from oxidative stress. We'll purchase them from a local pharmacy.

Placebo Capsules

The placebo group will receive Zeebo Tablets, Pure Honest Placebo, Dietary Supplement 45 White Tablets (Zeebo Effect LLC, South Burlington, USA; Amazon). The placebo capsules contain inert microcrystalline cellulose, a natural dietary fiber.

The SPEED Questionnaire

The SPEED questionnaire tracks the frequency and severity of dry eye symptoms over time, with scores ranging from 0 to 28. Scores of 5 to 7 indicate moderate symptoms, while scores above 8 indicate severe symptoms.

EASYTEAR View+

EASYTEAR View+ (EASYTEAR SRL, Via Maioliche, Trento, Italy) measures NITBUT and TMH scores. It is a noninvasive, simple, and convenient device.

The NITBUT Test

The NITBUT test measures tear film stability by indicating how long it takes for the lines to blur. It is calculated in seconds, from the first appearance of a dry spot in the tear film until the last blink. A NITBUT of less than 10 seconds suggests dry eye. For each participant, NITBUT will be measured three times in the right eye, and the results will be averaged.

The TMH Test

The TMH test measures tear film volume and the height, in millimeters, of the triangular cross-section between the lower lid margin and the cornea. A measurement below 0.2 mm indicates dry eye. We measured TMH three times in each participant's right eye and calculated the average.

The TF Test

The TF test involves collecting a small tear sample (1 L) from the lower meniscus of the right eye using a glass capillary tube (10 L). The sample will be dried for 10 min at 23 °C with humidity below 40%. We used an Olympus DP72 digital microscope to observe and capture TF images at 10× magnification. TF patterns will be graded on a five-point scale. A TF grade of 2 is considered indicative of dry eye. Grade 0 indicates flawless ferns with no gaps, whereas Grade 4 indicates no ferns. As the TF grade increases, tear quality deteriorates. Two examiners graded the ferns in the dried tears, and their average grade was calculated and rounded to the nearest decimal place.

Statistical Methods

Data will be collected using Microsoft Excel 2024 and analyzed with the Statistical Package for the Social Sciences. A correlation coefficient will measure the strength of the association

between two or more variables. The Kolmogorov–Smirnov test will assess the dataset's normality by examining its distribution. The Wilcoxon signed-rank test will assess whether score differences between the study and control groups are statistically significant, enabling a robust comparison. We will examine between-sex differences in tear film parameters and subjective dry eye symptoms using the Mann–Whitney U test. The Kruskal–Wallis test, with gender as the grouping variable, will examine between-sex differences in demographic characteristics, subjective symptoms, and tear film parameters. In addition, Spearman's rho will be calculated to assess correlations among the parameters and provide insight into their relationships.