INPLASY

Effectiveness of Omega-3 Intake in Managing Dry Eye Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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ADMINISTRATIVE INFORMATION

Support - Non financial support.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 September 2023 and was last updated on 25 September 2023.

INTRODUCTION

Review question / Objective To investigate the treatment effect of Omega-3 on dry eye syndromes.

Rationale Omega-3 fatty acids, an antioxidant, can shift the balance of eicosanoid production toward a less inflammatory state. It has been suggested to reduce symptoms of dry eye disease in some clinical studies. However, the clinical effectiveness was inconclusive. Therefore, we would like to perform a systematic review and meta-analysis to investigate the treatment effect of omega-3 on dry eye syndromes.

Condition being studied PICO were defined as below: P, human participants; I, Omega-3 intake; C, placebo or non-omega-3 oil; and O, alterations in the score of dry eye outcomes, tear break-up time (TBUT), Schirmer test, osmolarity, and corneal fluorescein staining (CFS).

METHODS

Search strategy The literature search for this study was independently performed by two authors using the PubMed, Embase, ClinicalTrials.gov, Cochrane CENTRAL, and Web of Science electronic databases from inception up to the search date (March 16, 2023). Keywords included ("keratoconjunctivitis sicca" OR "dry eye" OR "dry eye disease") AND ("omega-3" OR "fatty acid" OR "n-3").

Participant or population Human participants.

Intervention Omega-3 supplement.

Comparator Placebo.

Study designs to be included Randomized controlled trials.

Eligibility criteria Inclusion criteria for this study were as follows: human-involved randomized

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controlled trials (RCTs); RCTs that provided quantitative assessments before and after omega-3 intake; trials that used a placebo control (without any age or treatment duration restrictions); and studies offering accessible information on dry eye evaluations both before and after the intervention or any alterations in the outcome measures.

Information sources The literature search for this study was independently performed by two authors using the PubMed, Embase, ClinicalTrials.gov, Cochrane CENTRAL, and Web of Science electronic databases from inception up to the search date (March 16, 2023). Keywords included ("keratoconjunctivitis sicca" OR "dry eye" OR "dry eye disease") AND ("omega-3" OR "fatty acid" OR "n-3").

Main outcome(s) The primary outcomes, such as dry eye symptom score, tear break-up time, Schirmer test, osmolarity, and corneal staining, were the changes in the scores of dry eye symptom following omega-3 supplements or placebo regimens. The validity and appropriateness of the outcome measurement used in each trial were also examined by checking the pertinent references. If there were more than one scoring system for symptom evaluation in a single trial, the index test included for meta-analysis was decided by the consensus of two authors.

Additional outcome(s) Meta-regression analysis focused on the effects of daily omega-3 dosage, EPA percentage of omega-3, and different treatment durations to determine whether the symptom-reducing effects of omega-3 were associated with these factors.

Data management Data from the chosen studies were extracted by two authors, including demographic information, study design, specifics of the omega-3 and placebo treatments, and outcome values. If multiple time points for post-treatment data were available, the results at the intervention's conclusion were used for statistical evaluation. Data extraction and conversion, along with consolidation of results from distinct study arms using varying omega-3 dosages, were performed following the Cochrane Handbook for Systematic Reviews of Interventions guidelines and related medical publications.

Quality assessment / Risk of bias analysis The Cochrane Risk of Bias tool (version 2, RoB 2, London, United Kingdom) was used to assess the methodological quality of the included studies. This tool comprises 6 primary elements for assessing the quality of the study: randomization process, intervention adherence, missing outcome data, outcome measurement, selective reporting, and overall risk of bias.

Strategy of data synthesis Owing to the diverse target groups in the studies reviewed, the present meta-analysis was performed using a random-effects model , facilitated by Comprehensive Meta-Analysis software version 4 (Biostat, Englewood, NJ, USA). Differences with a two-tailed $p < 0.05$ were considered to be statistically significant.
Study outcomes, such as changes in dry eye symptoms and CFS scores, were quantified using the Hedges' g statistic along with the associated 95% confidence intervals (CIs). Effect sizes with Hedges' g values of 0.2, 0.5, and 0.8 were respectively considered as small, moderate, and large. Other outcomes, such as TBUT, Schirmer's test, and osmolarity, were assessed using standardized mean difference (SMD) along with the associated 95% CI.
To determine the level of heterogeneity between the studies, the I2 and Cochran's Q statistics were utilized. Heterogeneity was classified as low, moderate, or high at I2 values of 25%, 50%, and 75%, respectively.

Subgroup analysis Meta-regression analysis focused on the effects of daily omega-3 dosage, EPA percentage of omega-3, and different treatment durations to determine whether the symptom-reducing effects of omega-3 were associated with these factors.

Sensitivity analysis To ensure the reliability of the meta-analysis, sensitivity analyses were conducted with the "leave-one-out" method. This method assessed whether excluding a specific trial from the analysis led to a statistically significant change in the overall effect size.

Language restriction No language limit.

Country(ies) involved Taiwan.

Other relevant information None.

Keywords Omega-3, dry eye disease, clinical trials, meta-analysis, systematic review.

Dissemination plans None.

Contributions of each author
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