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ORIGINAL ARTICLE

Omega-3 Fatty Acid Supplementation on Lipid Profiles in Dialysis Patients: Meta-analysis

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Background and Aims. Studies of omega-3 supplementation in dialysis patients describe salutary effects on lipid profiles. However, study results have been inconsistent. The aim of this study was to evaluate the influence of omega-3 supplementation on serum lipids in chronic dialysis patients.

Methods. A systematic literature search was performed to identify the relevant randomized controlled trials (RCTs) that investigated the effects of omega-3 supplementation on dialysis patients. The outcomes included the levels of triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and albumin. Mean differences (MDs) and 95% confidence intervals (CIs) were calculated and heterogeneity was assessed with the I^2 test.

Results. A total of 678 patients from 14 trials were subjected to meta-analysis. Omega-3 supplementation could significantly decrease the levels of TG (MD, −34.8 mg/dL; 95% CI, −62.32 to −7.28) and LDL (MD, −7.15 mg/dL; 95% CI, −10.11 to −4.2). However, no statistically significant effects were observed for TC, HDL and albumin levels. In a subgroup meta-analysis, a statistically significant effect of omega-3 consumption on TG and LDL was observed in a short-term interventional duration and hemodialysis populations.

Conclusion. Our findings indicate that omega-3 supplementation significantly reduced serum TG and LDL level in dialysis patients. However, there is no conclusive evidence that it can modulate the TC, HDL and albumin level.

Key Words: Dialysis, Lipid, Meta-analysis, Omega-3.

Introduction

Chronic kidney disease (CKD) is strongly associated with an increased risk of cardiovascular disease (CVD), which still remains to be one of the major causes of morbidity and mortality in hemodialysis (HD) patient groups. Annual mortality rates from CVD in this population group are 20 times higher than in the general population (1,2). Although the pathogenesis of CVD in the CKD population is not clearly understood, a number of clinical and epidemiological studies have demonstrated that HD patient status has been strongly associated with lipid abnormalities (3,4). Further research has demonstrated that chronic inflammation is also a contributor to higher CVD incidence among HD patients (5). Moreover, a meta-analysis has shown a significant inverse relation between serum albumin and cardiovascular mortalities (6). Evidence supported the role of lipid-lowering therapy as a means to decrease cardiac death and atherosclerosis-mediated cardiovascular events in persons with CKD (7). In recent decades, the efficacy of pharmacologic interventions on lipid-lowering therapy has been

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extensively researched, especially the inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase (statins) are gaining widespread acceptance as a principal therapy for the primary and secondary prevention of atherosclerosis and CVD. However, current guidelines and some meta-analyses have provided evidence that the use of statins should not be recommended in dialysis-dependent CKD patients (8–12). Thus, the best strategies to treat dyslipidemia in the HD population remain to be established.

Omega-3 fatty acids included α-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), mainly obtained from fish and fish oils, and are a family of fatty acids that contain two or more double bonds. Several studies have shown that omega-3 fatty acids play an important role in many other health disorders such as prevention of arrhythmias, chronic heart failure, dyslipidemia regulation, modulation of blood pressure levels, progression of arteriosclerosis, rheumatological diseases and osteoporosis, mood depression, chronic kidney disease, chronic inflammatory diseases and others (13–15). Recently, several randomized controlled trials (RCTs) have confirmed the effects of omega-3 supplementation on HD patients. However, these studies have a modest sample size and convey inconsistent results. We therefore deemed a comprehensive systematic review and meta-analysis of RCTs to assess the influence of omega-3 supplementation on serum lipid profile in HD patients.

Materials and Methods

Literature Search and Inclusion Criteria

According to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (16), relevant RCTs were identified by searching PubMed, Embase databases and Cochrane Central Register of Controlled Trials (CENTRAL). All searches were up to date as of December 2013. The structured search strategies used the following format of search terms: (''kidney failure, chronic''[Mesh] OR 'dialysis' OR ''chronic renal failure'' OR 'hemodialysis' OR ''peritoneal dialysis'' OR ''kidney replacement therapy'') AND (''omega-3 fatty acids'' OR ''n-3 fatty acids'' OR ''fatty acid'' OR ''omega-3'' OR ''fish oil'' OR ''α-linolenic acid'' OR ''eicosapentanoic acid'' OR ''docosahexanoic acid''). Our searches were limited to English-language publications and human trials. In addition to electronic search original papers, we also reviewed the references of included RCTs to look for potentially eligible articles. Two investigators (XL and HH) independently did the literature search. Any disagreements were resolved by discussion and consensus.

For each of the relevant articles, full publications were retrieved for evaluation on the basis of criteria established a priori. The following inclusive selection criteria in PICOS order included: a) study population: patients (no matter how many patients recruited) who are receiving renal dialysis (including HD or peritoneal dialysis); b) intervention: omega-3 supplement (no matter what type and regimen applied); c) comparison intervention: placebo or no intervention; d) outcome measure: reported 'baseline' and 'end of intervention' mean and standard deviation values of lipid measurements and albumin for the active (omega-3) and control groups; and e) study design: only RCT reported in a full paper article, and non-randomized and cross-over studies were excluded.

Data Extraction and Outcome Measures

Two investigators independently collected the data, cross-checked and reached a consensus on all items. The following information was extracted from the included studies: first author's name, publication year, sample volume (intervention/control), dialysis modality, population information (mean age, gender and location), intervention group (types, grams per day), control group (placebo or other), duration of treatment. It should be emphasized that if the same population was reported in several publications, we only retained the most informative article or complete study to avoid duplication of information.

We were interested in the following outcomes or endpoints, including information on baseline and final concentrations (or net changes) of serum total cholesterol (TC), LDL cholesterol, HDL cholesterol, triglycerides (TG) and albumin. Studies that reported results in mmol/l were converted to mg/dL using the standard conversion factors (which was a division of the mmol/l value by 0.02586 for TC, LDL and HDL; and by 0.01129 for TG). These values were captured as the mean change from baseline to follow-up (with mean ± SD or mean ± SE, respectively).

Quality Scoring and Risk-of-Bias Assessment

We quantified the methodological qualities of studies using validated Jadad 5-point scale (17). Jadad scores ranged from 0 to 5 in which the Jadad score not more than 2 indicates the lowest quality and the score of at least 3 means the highest quality (18).

Risk-of-bias assessment was performed in accordance with guidelines outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (version 5.1.0) (19). For each study, we made judgments about risk of bias from each of the six domains of the tool. In all cases, an answer ''Yes'' indicated a low risk of bias, an answer ''No'' indicated high risk of bias, and if insufficient detail is reported of what happened in the study, the judgment would usually be ''Unclear'' risk of bias.

Statistical Analysis

For continuous data, mean differences (MDs) with 95% CIs were calculated. Clinical heterogeneity was assessed