MÆDICA - a Journal of Clinical Medicine

JOURNAL CLUB

Omega-3 fatty acid supplementation and total homocysteine levels in end-stage renal disease patients

Stefania MAGDA, MD

Cardiology and Internal Medicine Department,
Emergency University Hospital, Bucharest, Romania

Cardiovascular disease (CVD) is a major cause of morbidity and mortality in patients with renal failure. In addition to classical risk factors for CVD, end-stage renal disease (ESRD) patients have uraemia-specific risk factors: volume overload and hypertension, anaemia, altered calcium-phosphate metabolism, elevated levels of specific uraemic toxins and chronic inflammatory processes. High levels of the uraemic total homocysteine (tHcy) is a strong predictor of cardiovascular events in patients with pre-existing morbid conditions, including renal failure. Original research previously published suggested that fish oil (FO) supplementation is correlated with decreased tHcy levels in high-risk populations, therefore reducing morbidity and mortality.

The purpose of the present study (double-blind, permuted-randomized and placebo controlled experimental protocol) was to examine the effect of an omega 3 fatty acid (n-3) supplementation on tHcy levels in ESRD patients undergoing chronic haemodialysis.

Sixty-nine patients were recruited. Exclusion criteria were: abnormalities of electrolyte, liver function or complete blood count, history of gastrointestinal bleeding in the last 6 months, anticoagulation therapy with antiplatelet medication, life-expectancy of less than 6 months, pregnancy, malignant hypertension, or history of haemodialysis or previous medication non-compliance.

ESRD patients were followed while supplementing n-3 (34 patients) or placebo (corn oil, 35 patients) prospectively for 6 months. Additionally, all patients received vitamin supplements (B6, B12 and folic acid). Participants donated blood for analysis at baseline and at 6 months. There was no statistically significant difference between the groups at baseline regarding age, gender, smoking history, diabetic status, months on dialysis, ethnicity, medication usage and tHcy levels.

There were no statistically significant differences between the two groups in the mean changes from baseline at 6 months or between the two groups tHcy values at 6 months. Age was significant ($p = 0.02$), indicating that older participants had a trend towards a percentage decrease in tHcy from baseline to 6 months. Daily administration of 6 g of n-3 fatty acids containing 160 mg of eicosapentaenic acid (EPA-0.96 g/day) and 100 mg of docosahexaenoic acid (DHA- 0.6 g/day) had no effect on tHcy levels when compared with control.

Potential reasons for this nonsignificant result may be found in a dose–response relationship, the advanced stage of disease in the sample population or the lack of a significant relationship between fatty acids and tHcy. Patients with ESRD have significant morbid conditions such as altered lipid metabolism and have higher risk for CVD and related outcomes. tHcy levels are significantly elevated in ESRD patients with levels four times higher than healthy population. Hyperhomocysteinemia may have been elevated for too long, with supplementation occurring too late in the morbid condition. Supplementation may have been more effective if started upon initiation of dialysis. There is also the possibility that n-3 supplementation may have no effect on tHcy levels.

Limitations: Patient compliance was monitored through the standard practice of „pill counting", which might be insufficient. Because of the impossibility of quality checking of each individual supplement, amounts of DHA and EPA may have varied.

In conclusion, the results of the present study show that the administration of n-3 supplementation was not better than placebo in lowering tHcy levels in an ESRD population. Future studies are needed to clarify the mechanism by which fatty acids may lower tHcy levels, whether a dose–response relationship between fatty acid supplementation and tHcy levels exists, and examine how stage of disease progression affects intervention success.

Comment on the paper:
Kristen Beavers, Daniel Beavers, Rodney Bowden, et al – Omega-3 fatty acid supplementation and total homocysteine levels in end-stage renal disease patients, *Nephrology* 2008; 13:284-288