n-3 fatty acids and cardiovascular disease in patients treated with chronic haemodialysis

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ABSTRACT

The present work was carried out at the Department of Nephrology, Aalborg Hospital and the department of Preventive Cardiology, Aalborg Hospital.

Patients treated with chronic haemodialysis (HD) have a very high mortality from cardiovascular disease (CVD). Both the traditional risk factors for CVD and more specific risk factors related to ESRD, such as oxidative stress, specific alterations in lipid metabolism, chronic inflammation and accumulation of uraemic toxins contribute to the increased risk of CVD.

n-3 polyunsaturated fatty acids (PUFA), derived from fish are essential fatty acids that incorporate into the cell membranes of the human body. Evidence exists from epidemiological and interventional studies that n-3 PUFA might be effective as secondary prevention of CVD. A wide range of possible mechanisms of action from n-3 PUFA have been suggested from animal and human studies, such as antiatherosclerotic, antithrombotic, antiinflammatory, antihypertensive, and antiarrhythmic effects. In patients with ESRD, there are no previous data regarding the effects of long-term supplementation with n-3 PUFA.

We hypothesized that supplementation with n-3 PUFA would:

1. Reduce the number of cardiovascular events and deaths, when given as secondary prevention of CVD.
2. Decrease serum triglycerides and increase HDL-cholesterol.
3. Increase time domain measures of heart rate variability (HRV).

We investigated our hypotheses in a randomised placebo controlled design, including 206 patients treated with chronic HD randomized to 1.7 g of n-3 PUFA or a control treatment.

1. After a median follow-up of 558 days (219-730), there was a very high event rate 121/206 (59%). No significant effect was seen on the primary outcome, which was a composite of the total number of cardiovascular events and deaths. Supplementation with n-3 PUFA significantly reduced the number of MI as a secondary outcome.
2. Supplementation with n-3 PUFA for three months reduced serum triglycerides but did not significantly increase HDL-cholesterol.
3. In a sub-study of 30 patients, supplementation with n-3 PUFA did not significantly affect time domain measurements of HRV.

In conclusion, supplementation with n-3 PUFA for two years did not reduce the total number of cardiovascular events and deaths in HD patients. However, a significant reduction in the number of MI was found in the n-3 PUFA group. This finding might be due to antithrombotic, antiinflammatory or antioxidative effects from n-3 PUFA. Further research designed to explore these possible mechanisms in HD patients and larger intervention studies designed to investigate the effect of n-3 PUFA with MI as the primary outcome would be of interest.