n-3脂肪酸はMI後の心血管イベントを減少させなかった

ALPHA OMEGA：低用量のn-3脂肪酸の有益性は心筋梗塞後患者のうちサブグループにおいてのみ認められた

ALPHA OMEGA: Beneficial effect of low doses of n-3 fatty acids only found in sub-groups of post-MI patients

心筋梗塞（MI）後患者を対象とした多施設プラセボコントロールトライアル（Alpha Omega Trial）の結果、低用量n-3脂肪酸を添加マーガリンの形で投与しても主要な心血管イベントは減少させなかったことが示された。計4,837人（60～80歳）の患者が4種類のマーガリン：EPA+DHA（400mg/day）、ALA（2g/day）、EPA+DHAとALA、またはプラセボのいずれかを添加）のうちの1つを40ヵ月間毎日摂取する群に無作為に割り付けられた。参加者らは98%が抗血栓薬を、90%が降圧薬を、86%が脂質低下薬で十分治療されていた。おそらく患者に対する治療が優れていたため、心血管死亡率は予測のわずか半分であった。そのために主要な心血管イベントが脂肪酸群とプラセボ群とで同等であった可能性がある。ALAを摂取した女性においては一次エンドポイントが27%低下し、ボーダーラインの有意差であった。糖尿病患者ではEPA+DHAを摂取した者において心血管死亡率が50%と有意に低下した。EPA+DHAとALAを摂取した糖尿病患者においても不整脈関連イベントが同様に50%低下した。このトライアルは2010年European Society of Cardiology学会のホットラインセッションで発表され、New England Journal of Medicineオンライン版に掲載された。

Full Text

Results from the Alpha Omega Trial, a multicentre, placebo-controlled trial in men and women following myocardial infarction (MI), suggest that low doses of n-3 fatty acids given in the form of enriched margarines do not reduce the overall rate of major cardiovascular events.

Results from the study - in which patients received a 400 mg per day supplement of the fish oil fatty acids EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) and 2 grams of the plant-derived fatty acid alpha-linolenic acid (ALA) via enriched margarines - showed that these supplementary n-3 fatty acids did not reduce major cardiovascular events in the overall patient population. Among sub-groups, there was a borderline significant reduction in major cardiovascular events in women who received ALA, and, in patients with diabetes, n-3 fatty acids were protective against ventricular arrhythmia-related events.

N-3 (or omega-3) fatty acids can be divided in two main classes: EPA and DHA from fish, and ALA from plant foods such as soybean oil and walnuts. "Several intervention studies in cardiac patients have shown that a daily intake of 1-2 grams of EPA + DHA via fish oil capsules reduced mortality from coronary heart disease by 20%," said principal investigator Professor Daan Kromhout from Wageningen University, the Netherlands.

"Epidemiological studies in healthy populations have also suggested that 250 mg EPA + DHA or eating fish once or twice a week can lower the risk of CVD by a similar amount. For ALA, there is less evidence of a cardioprotective effect. We designed the Alpha Omega Trial as a dietary intervention study to examine the effect of low doses of n-3 fatty acids on major cardiovascular events."

A total of 4837 men and women aged 60-80 years were enrolled in the trial. They had all suffered a myocardial infarction approximately four years before the study began. They were randomly assigned to daily use of one of four margarines for 40 months: containing extra EPA + DHA (400 mg/day); ALA (2 g/day); both EPA + DHA and ALA; or placebo. The margarines were similar in taste and appearance for all four treatment groups and were used by the trial participants on bread instead of their regular margarine or butter; compliance and double blinding were maintained throughout the study period.

The primary endpoint of the trial, which was completed in November 2009, was major cardiovascular events (MACE) of morbidity and mortality, and cardiac procedures (PCI and CABG). Important secondary endpoints were fatal coronary heart disease and ventricular arrhythmia-related events defined as sudden death, cardiac arrest and cardioverter-defibrillator placement.

"The patients in this trial were very well treated," said Professor Kromhout, "with 98% on antithrombotic agents, 90% on antihypertensive drugs, and 86% on lipid lowering drugs. We found that cardiovascular mortality rate in the study population was only half that expected, probably because of their excellent treatment. This may also be why the rate of major cardiovascular events during follow-up was no lower in the fatty acid groups than in the placebo group.

"However, we did see a 27% borderline significant reduction in primary endpoint in women who received ALA. We also carried out an exploratory analysis in patients with diabetes, and this showed a significant 50% reduction in CHD mortality in patients who received EPA + DHA. For both, EPA + DHA and ALA a similar 50% reduction was observed in the number of arrhythmia-related events in diabetic patients."

The trial results were presented during a Hotline session at ESC 2010 and published simultaneously online in the New England Journal of Medicine.

The Alpha Omega trial was carried out in collaboration with 32 hospitals, approximately one-third of all hospitals in the Netherlands, and with grants from the Netherlands Heart Foundation, National Institutes of Health, USA, and Unilever R&D, the Netherlands.

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