Atrial fibrillation: recurrence not prevented by omega-3 fatty acid supplements

The FORWARD randomised controlled trial found that omega-3 fatty acid supplementation did not prevent recurrent atrial fibrillation. This is consistent with the limited role for omega-3 fatty acid supplements outlined in various NICE guidance on cardiovascular disease.

Overview and current advice

Several pieces of NICE guidance discuss omega-3 fatty acid supplementation in the prevention of cardiovascular disease. NICE clinical guidelines on lipid modification (currently being updated), familial hypercholesterolaemia (FH) and type 2 diabetes (currently being updated) recommend against prescribing these supplements for the primary prevention of cardiovascular disease. For people with type 2 diabetes and refractory hypertriglyceridaemia, a trial of highly concentrated, licensed omega-3 fish oils can be considered if lifestyle measures and fibrate therapy have failed.

For the secondary prevention of cardiovascular disease, NICE guidance gives a limited role for omega-3 fatty acid supplements. The NICE clinical guideline on MI: secondary prevention (currently being updated) advises that omega-3 fatty acid supplements licensed for secondary prevention can be considered in people who have had an MI within 3 months and are not achieving 7 g of omega-3 fatty acids per week from oily fish in their diet. These recommendations were based on results from the GISSI-Prevenzione Investigators (GISSI-P) trial, which showed a benefit from treatment with omega-3 fatty acid supplements within 3 months of an MI1, possibly through an antiarrhythmic effect2.

The NICE clinical guideline on management of atrial fibrillation (AF) from 2006 contains no information on omega-3 fatty acid supplements. This guideline is currently being updated, but the scope does not refer to omega-3 fatty acid supplements.

See the NHS Evidence topic page on AF for a general overview of the condition.
New evidence

The double-blind, placebo-controlled, randomised controlled trial (RCT) FORWARD assessed the efficacy of omega-3 fatty acid supplements for the prevention of recurrent AF\(^3\). The study included 586 people from 42 Argentinean centres who had previously had symptomatic AF but had recovered normal sinus rhythm (mostly through cardioversion). They were randomised to 1 g per day of omega-3 fatty acids or placebo for 12 months, in addition to any other treatment prescribed for AF.

Supplementation with omega-3 fatty acids did not reduce the primary endpoint of time to first recurrence of symptomatic AF. At the end of follow-up, 56 of 297 people (18.9%) in the placebo group and 69 of 289 people (24.0%) in the omega-3 group had recurrent symptomatic AF (hazard ratio [HR] 1.28, 95% confidence interval [CI] 0.90 to 1.83, \(p=0.17\)). There was also no statistically significant difference between the groups in the proportion of people who died or experienced the composite cardiovascular morbidity/mortality endpoint.

This RCT was stopped early because of slow recruitment and low event rates, and was therefore not statistically powered for the endpoints studied. However, the findings were similar to those from OPERA, a double-blind, placebo-controlled RCT assessing the effect of omega-3 fatty acids for the prevention of postoperative AF\(^4\). In OPERA, short-term perioperative supplementation with omega-3 fatty acids did not reduce the risk of postoperative AF in 1516 patients undergoing cardiac surgery.

Commentary

These trials of omega-3 fatty acid supplements in AF add to other studies that have questioned the cardiovascular benefits of fatty acid supplementation in both primary and secondary prevention. A meta-analysis of 14 randomised, double-blind, placebo-controlled trials of omega-3 fatty acid supplements in people with a history of cardiovascular disease found no reduction in the risk of cardiovascular events or all-cause mortality\(^5\). See the NICE Medicines Evidence Commentary Cardiovascular disease: omega-3 fatty acid supplements in secondary prevention for details.

A larger meta-analysis of 20 RCTs (including open label trials, those not controlled with placebo, and trials in primary prevention) found similar results\(^5\). Omega-3 fatty acid supplements did not reduce the risk of all-cause mortality, cardiac death, sudden death, MI or stroke. This larger meta-analysis included the ORIGIN study, which included people with early type 2 diabetes who also had cardiovascular risk factors\(^6\). ORIGIN found that daily supplementation with 1 g of omega-3 fatty acids for 6 years did not reduce the rate of cardiovascular events or mortality compared with placebo. See the Eyes on Evidence commentary Omega 3 fatty acids have no effect on cardiovascular outcomes in high-risk people with type 2 diabetes for details.

Annually, approximately 645,000 items of omega-3 fatty acid compounds (Omacor and Maxepa) are prescribed in primary care in England, at a cost of about £15.4 million. However, the variation between Primary Care Trusts (PCTs) is marked, and there may be wider variation still at practice level. In the year to September 2012, the lowest prescribing PCT prescribed 259 items of omega-3 fatty acid compounds at a cost of £7363. This compared with 17,457 items and £378,312 in the highest volume, and highest cost, prescribing PCTs respectively (data provided by NHS Prescription Services, NHS Business Services Authority, December 2012).

Omega-3 fatty acid supplements are a key therapeutic topic identified to support the QIPP medicines use and procurement work stream. This highlights therapeutic areas where there are potential opportunities for maintaining or improving quality and improving value. Releasing resources from one area of health care whilst maintaining or improving quality of care means those resources are available, for example, for the prescribing of innovative medicines.
Study sponsorship

Funding was through unrestricted grants provided by the companies that supplied the study drugs: SPA Società Prodotti Antibiotici, Milan, Italy; and Sigma Tau, Rome, Italy. These companies did not have representatives on the Steering Committee for the FORWARD study.

References


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