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Eyes on Evidence
expert commentary on important new evidence

Omega-3 fatty acids have no effect on cardiovascular outcomes in high-risk people with type 2 diabetes

The ORIGIN study found that supplementation with 1g per day of omega-3 fatty acids did not reduce the rate of cardiovascular events or the risk of dying from these events or from any cause in people with, or at high risk of, type 2 diabetes who also had evidence of cardiovascular disease.

Overview: Having type 2 diabetes, impaired fasting glucose or impaired glucose tolerance is a known risk factor for cardiovascular disease. However, it is unclear whether dietary supplementation with omega-3 fatty acids (also known as n–3 fatty acids) reduces the rate of cardiovascular events in these people.

Current advice: NICE guidance on type 2 diabetes recommends that omega 3 fish oil preparations should not be prescribed for the primary prevention of cardiovascular disease in people with type 2 diabetes. This recommendation does not apply to people with hypertriglyceridaemia receiving advice from a healthcare professional with special expertise in blood lipid management. A trial of highly concentrated, licensed omega-3 fish oils may be considered for people with refractory hypertriglyceridaemia if lifestyle measures and fibrate therapy have failed.

NICE guidance on the secondary prevention of myocardial infarction (MI) recommends that patients should be advised to consume at least 7 g of omega-3 fatty acids per week from 2 to 4 portions of oily fish. For patients who have had an MI within 3 months and who are not achieving 7 g of omega-3 fatty acids per week, prescribers may consider providing at least 1 g daily of omega-3-acid ethyl esters treatment licensed for secondary prevention post MI for up to 4 years. This guidance is currently being updated.

See the NHS Evidence topic page on type 2 diabetes for a general overview of the condition. A NICE Pathway brings together all related NICE guidance and associated products on diabetes in a set of interactive topic-based diagrams.

New evidence: The ORIGIN study, a large randomised controlled trial (RCT), recruited 12,536 people with impaired fasting glucose, impaired glucose tolerance or type 2 diabetes (taking no or only 1 oral glucose-lowering drug). Trial participants were aged at least 50 years and had evidence of cardiovascular disease: at baseline 59% of the patients had had a MI or stroke or had undergone revascularisation. Participants were randomised to receive supplementation with 1 g of omega-3 fatty acids (Omacor) daily or placebo.

Over a median of 6.2 years, omega-3 fatty acids did not significantly reduce the rate of death from cardiovascular causes, compared with placebo (9.1% versus 9.3% respectively, p=0.72). Use of supplementation also had no significant effect on the rates of major vascular events (e.g. MI or stroke), death from any cause, death from arrhythmia or any other predefined study outcome. Triglyceride levels were reduced by a mean of 0.16 mmol/litre in people receiving omega-3 fatty acids compared to those receiving placebo (p<0.001). There was no significant effect on other lipids. The rate of adverse events was similar in both groups (The ORIGIN trial investigators 2012).

Although it is a large, robust study, ORIGIN does have some limitations. For example, it is possible that the 1 g daily dose of omega-3 fatty acids used was too low to show an effect. However, the dose was chosen on the basis of previous studies (GISSI-Prevenzione Investigators 1999, GISSI-HF Investigators 2008) that did show a benefit of omega-3 fatty acids over placebo. Participants in these studies had had an MI within the previous 3 months or had heart failure and, being at higher baseline risk, may have been more likely to benefit from omega-3 treatment than patients in the ORIGIN study. Also, participants in the ORIGIN study were taking more

cardioprotective therapies than those in the earlier studies which may have reduced the incidence of cardiovascular events and, therefore, the statistical power of the study to detect a difference between omega-3 fatty acids and placebo.

Commentary: "It is unclear how these findings relate to dietary recommendations to eat more oily fish. As well as increasing intake of omega-3 fatty acids, eating more fish is associated with an increase in other nutrients and a reduction in the consumption of other foods such as red meats, which may also affect cardiovascular risk. NICE guidance advises that people who have experienced an MI should consume at least 7 g of omega-3 fatty acids per week from two to four portions of oily fish. In ORIGIN, median weekly dietary intake was about 1.5 g, which may have been different from intake in earlier studies that showed a benefit of omega-3 supplementation

"Other large studies are underway, which might help to clarify the role of omega-3 fatty acid supplementation in people with diabetes. For example, a UK RCT, the ASCEND study, (n=15,480, median 7.5 years follow-up) aims to determine whether 100 mg aspirin daily versus placebo and/or supplementation with 1 g daily omega-3 fatty acids or placebo prevents serious vascular events (non-fatal MI, non-fatal stroke or death from vascular causes) in patients with type 1 or type 2 diabetes who are not known to have occlusive arterial disease. It will also assess the effects on serious bleeding or other adverse events. However, results are not expected until 2017. In the meantime, the ORIGIN study supports current NICE guidance on type 2 diabetes, which advises that omega-3 fish oil preparations should not be prescribed for the primary prevention of cardiovascular disease in people with type 2 diabetes. Furthermore, NICE guidance on the secondary prevention of MI is currently being updated and will consider this issue within the update." **– Richard Paisey, Consultant Physician in Diabetes and Research Clinical Lead, Torbay Hospital.**

About this article: This article appeared in the December 2012 issue of the Eyes on Evidence newsletter. This free monthly newsletter from NICE Evidence outlines interesting new evidence and what it means for current practice. They do not constitute formal NICE guidance. The opinions of contributors do not necessarily reflect the views of NICE.

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