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Omega-3 fatty acid compounds and other fish oils

This is one of a number of bulletins providing further information on medicines that should be given a low priority, are poor value for money, are suitable for self care or for which there are safer more suitable alternatives. This guidance will support Clinical Commissioning Groups (CCGs) in taking action on items that should not routinely be prescribed in primary care or on the NHS. Further bulletins, including the overarching Low Value Medicines information bulletin are available on the PrescQIPP website: https://www.prescqipp.info/drop-list/headline-areas/the-prescqipp-drop-list#low-value-medicines-lvm

This bulletin focuses on omega-3 fatty acids which are found primarily in certain fish but there are some plant and nut sources too. The available evidence to support their use is limited and of poor quality. Consequently, they are not recommended for routine prescribing on the NHS.

Recommendations

- Omega-3 fatty acids and other fish oils are not recommended for routine prescribing on the NHS as the evidence to support their efficacy is not strong enough and they are not considered to be cost-effective.
- Patients already being prescribed these preparations should be reviewed and prescriptions stopped. No new prescriptions for omega-3 fatty acids or other fish oils should be commenced.
- Consider switching patients taking omega-3 fatty acid compounds for hypertriglyceridaemia to prevent myocardial infarction (MI) to evidence based treatment, in line with National Institute for Health and Care Excellence (NICE) clinical guideline 71 (CG71). For patients with severe hypertriglyceridaemia consider the risk of acute pancreatitis and ensure local treatment guidelines are available.
- Use in patients with schizophrenia is unlicensed and should be reviewed in conjunction with a specialist with a view to stopping prescribing if no benefit has been achieved.
- Patients wishing to take these products should be advised to increase their dietary intake or purchase them over the counter. Further advice is available at: https://www.bda.uk.com/foodfacts/omega3.pdf Community pharmacists will be able to assist patients in obtaining a suitable preparation.

Background

The NHS England guidance on 'Items which should not routinely be prescribed in primary care' lists products that are regarded as low priority for funding, poor value for money or for which there are safer alternatives (https://www.england.nhs.uk/publication/items-which-should-not-be-routinely-prescribed-in-primary-care-guidance-for-ccgs/). Omega-3 fatty acid compounds feature on the list as items of low clinical effectiveness, where there is a lack of robust evidence of clinical effectiveness or there are significant safety concerns.[1]

Clinical evidence

Omega-3 fatty acids are long-chain polyunsaturated fatty acids which are essential fatty acids and must be obtained from the diet. They have an important role as eicosanoid precursors (prostaglandins, leukotrienes, and thromboxanes) and as components of cell membranes. The main dietary omega-3 fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) which are primarily derived from marine fish.[2]

Because fatty acids are an integral component of cell membranes, their use has been suggested in a wide range of clinical conditions. Potential therapeutic uses include prevention of cardiovascular events, hypertriglyceridaemia, depression, attention deficit hyperactivity disorder (ADHD), schizophrenia, dry eyes, atrial fibrillation, hypertension, psoriasis, atopic eczema, autism, osteoarthritis, pre-menstrual syndrome, lupus, prostate cancer prevention and non-alcoholic fatty liver disease.[2]

Prevention of cardiovascular events

Of the increasing number of available licensed preparations of omega-3 fatty acid compounds, some are licensed as an adjunct to diet and/ or statins for hypertriglyceridaemia and others are also licensed as an adjunctive therapy in secondary prevention in those who have had a myocardial infarction (MI). Use in other indications is unlicensed. The different products vary in the ratio of EPA/DHA fatty acids they contain.[3,4] Unlicensed supplements are also available with varying amounts of fatty acids.

A systematic review and meta-analysis, published in late 2012, included data on cardiovascular outcomes in 63,030 patients.[5] Omega-3 fatty acids had no effect on the primary outcome (a composite endpoint of MI, stroke or cardiovascular death). Omega-3 fatty acids also had no statistically significant effect on total mortality, coronary events, arrhythmias or cerebrovascular events. A borderline statistically significantly beneficial effect on vascular death was seen.

A further meta-analysis published in 2012 also found no effect of omega-3 fatty acids on the secondary prevention of cardiovascular events.[6] The meta-analysis included 14 randomized, double-blind, placebo-controlled trials involving 20,485 patients with a history of cardiovascular disease. Supplementation with omega-3 fatty acids did not reduce the risk of overall cardiovascular events, all-cause mortality, sudden cardiac death, myocardial infarction, congestive heart failure, or transient ischemic attack and stroke.

A Cochrane systematic review looking at the evidence for prevention and treatment of cardiovascular disease, included 48 randomised controlled trials (36,913 participants) and 41 cohort analyses.[7] Pooled trial results did not show a reduction in the risk of total mortality or combined cardiovascular events in those taking omega-3 fatty acids. Trials varied in the doses used and trial design.

Hypertriglyceridaemia

A systematic review looking at the treatment of hypertriglyceridaemia with omega-3 fatty acids in 2005 looked at ten studies which reported long-chain omega-3 fatty acids to be effective in the treatment of hypertriglyceridaemia. The average decrease in triglycerides was 29% and total cholesterol 11.6%. The review stated that many of the RCTs had serious shortcomings including a short duration, no intention to treat analysis and lack of dietary control. The studies all looked at the secondary prevention of hypertriglyceridaemia.[8]

Lifestyle modification advice should be given to all individuals with raised triglycerides. However, appropriate dietary management of hypertriglyceridemia differs between mild-to-moderate and severe hypertriglyceridemia.

The risk of acute pancreatitis increases when serum triglycerides are approximately 1000 mg/dL or greater (11.3 mmol/L) although some patients have developed acute pancreatitis at lower levels. Lifestyle modification alone is not sufficient treatment in patients with severe hypertriglyceridaemia. When levels are severely raised, the risk of acute pancreatitis outweighs the risk of MI. Fibrates are the first line treatment choice for patients with hypertriglyceridaemia. Niacin is also an option to reduce triglycerides however treatment is associated with significant side effects.[9]

For patients with significantly raised levels, two portions of fish per week would not provide the same level of triglyceride reduction as a daily dose of omega-3 fatty acids. Omega 3 fatty acids are very effective at reducing serum triglycerides although they are also subject to significant side effects which may limit their use. Licensed products should be reserved to treat or those with severe hypertriglyceridaemia (10-20 mmol/litre) rather than as routine treatment.[9] It may be appropriate for the treatment of severe hypertriglyceridaemia to be managed by a specialist.

Schizophrenia

The Maudsley Prescribing Guidelines in psychiatry suggest a possible role for omega-3 fatty acids as an adjunct in patients with schizophrenia, particularly in patients responding poorly to clozapine.[10] One study in adolescents and young adults at high risk of psychosis showed omega-3 fatty acids reduced the emergence of psychotic symptoms compared with placebo. The guidelines recommend that if omega-3 fatty acids are used, response should be monitored carefully and their use should be withdrawn if no effect is observed.

Osteoarthritis

For osteoarthritis (OA), results of human clinical trials have not been consistently significant. Well-designed clinical trials are needed to substantiate or refute the potential benefit of fish oils in OA treatment. Long-term studies are needed to assess the possibility of prevention. In addition, standardisation of the fish oil industry is needed for consistency of therapy.[11]

Other indications

For all other potential therapeutic uses, no conclusions can be drawn as to whether omega-3 or other fish oils are helpful for these conditions, based on the currently available evidence.

National guidance

NICE guidance recommends against prescribing omega-3 fatty acids for the primary or secondary prevention of cardiovascular disease, alone or in combination with a statin, including in people with chronic kidney disease (CKD) or type 1 or type 2 diabetes. Moreover, the clinical guideline recommends that healthcare professionals should tell people that there is no evidence that omega-3 fatty acid compounds help to prevent cardiovascular disease.[12]

NICE also has the following 'do not do' recommendations:

- **NICE CG172 states**: "Do not offer or advise people to use omega-3 fatty acid capsules or omega-3 fatty acid supplemented foods to prevent another MI. Advise people to eat a Mediterranean-style diet (more bread, fruit, vegetables and fish; less meat; and replace butter and cheese with products based on plant oils). If people choose to purchase omega-3 fatty acid capsules or eat omega-3 fatty acid supplemented foods, there is no evidence of harm."[13]
- **NICE CG170 states:** "Do not use omega-3 fatty acids to manage sleep problems in children and young people with autism."[14]
- **NICE CG107 states:** "Do not recommend fish or algal oils solely with the aim of preventing hypertensive disorders in pregnancy."[15]
- **NICE CG71 states:** "Do not recommend omega-3 fatty acid supplements for familial hypercholesterolaemia."[16]
- **NICE CG186 states:** "Do not offer omega-3 or omega-6 fatty acid compounds to treat multiple sclerosis (MS). Explain that there is no evidence that they affect relapse frequency or progression of MS."[17]

Furthermore, the guideline development group for NICE CG155 for 'Psychosis and schizophrenia in children and young people: recognition and management' referenced a moderate-sized randomised controlled trial of omega-3 fatty acids, which showed a reduction in the rates of transition from 'high risk' states to a sustained psychosis.[18] However, this was a single trial, which was underpowered, undertaken in one centre and lacked any health economic analysis. Consequently, additional research is necessary using an adequately powered, multicentre, randomised controlled design, to assess the likely benefits and costs of using omega-3 fatty acids for children and young people at high risk of developing psychosis. The outcomes considered should include transition to psychosis, quality of life, symptomatic and functional improvements, treatment acceptability, side effects and self-harm. There should be follow-up at three years and the trial should also estimate the cost effectiveness of intervening.

Costs

The table below shows the annual cost of the licensed omega-3 fatty acid preparation currently listed in the Department of Health Drug Tariff.[19]

Drug	Drug cost per month
Eicosapentaenoic acid 460mg / Docosahexaenoic acid 380mg (Omacor®) One to four capsules daily.	£14.24 to £56.96

In England and Wales, over £4.6 million is spent on omega-3 fatty acid compounds and fish oils. Reducing this prescribing to nil will produce savings in the region of £8,012 per 100,000 patients.

Further data is available in the data pack: https://pdata.uk/#/views/B210_Omega-3/Bulletindata?:iid=32

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