

Can omega-3-rich fish oil supplements reduce allergy risk in infants?

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Results from a meta-analysis show that a mother's fish oil supplementation during pregnancy may reduce allergy in her children, but the exact benefits of this supplement – and many others – are yet to be determined.



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A human foetus is subject to its mother's nutrients, microbes, environmental exposures and medications — all of which can have lifelong effects on the child. These factors are also known as the exposome^[1]. A foetal exposome merits careful scrutiny during a life stage at which many organ systems are in a state of developmental plasticity. An intervention during this crucial window could reduce the rates or severity of long-term diseases^[2], and diet is one component of the exposome that a mother can, to some extent, control. But in a world where nutritional information is increasingly detailed, what advice, based on sound data, might be given to a mother visiting a community pharmacy?

In February 2018, a group of researchers from Imperial College London, the University of Oxford and the University of Nottingham published a number of inferences based on published trials and observational studies between 1946 and 2017^[3]. They concluded that a mother's diet during

pregnancy influences immune-mediated diseases in her children. Specifically, their findings suggest that maternal supplementation with fish oil may reduce children's sensitisation to food allergens.

Allergies in childhood

Over the past 30 years, there has been an increase in reported immune-mediated disease in children. And today, in resource-rich countries, and in some developing countries too, asthma is the most common chronic disease in children^[4]. The early development and persistence of atopic dermatitis is a significant risk factor for childhood asthma. Food allergies and anaphylaxis account for a considerable amount of consultation time in the community pharmacy; the prospect of preventing or reducing atopic sensitisation, and reducing the burden on children, their families and healthcare services, is attractive.

It may be simplistic to group childhood immune-mediated diseases together in one category. Allergies cause pathologies in several organ systems, develop from a range of genetic backgrounds, and present and progress at different times of a child's life (the 'atopic march'). However, two international genome-wide association studies, comprising a total of 62,330 subjects, demonstrated shared susceptibility loci in the pathways for both allergies and autoimmune diseases^[5]. These genetic commonalities could mean that one could predict similar responses to the exposome in these conditions.

Constituents of fish oil and action in the body

Fish oils are rich in omega-3 polyunsaturated fatty acids (PUFAs), such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are known for their anti-inflammatory properties.

In this mechanism, omega-3 PUFAs act as a source of lipid mediators, named specialised pro-resolving mediators (SPMs), which include the E-series — derived from EPA (resolvins) — and the D series (including resolvins, protectins and maresins) — from DHA. These metabolites can limit leucocyte recruitment in inflammation, induce the apoptosis of granulocytes and enhance efferocytosis by macrophages (the removal of dead cells). They can alter cell trafficking by influencing cytokines and chemokines, reduce inflammation, and can help to initiate tissue repair and healing^[6].

SPMs are involved in the resolution of inflammatory processes in all tissues, and they have been found to increase in those taking diets supplemented with fish oils. Dietary fish oils have been identified as helpful therapies in a wide range of human pathologies, including those affecting the coronary arteries, the brain, the liver and skeletal muscle. In pregnant animal models, supplementation with fish oils or omega-3 PUFAs influences the immune responses of mothers' offspring. In humans, such supplementation increases SPMs in both mother and infant, although in one study these effects were not sustained at 12 years of age^[7].

Fish oil supplements and preventing allergic outcomes

The children of women supplementing with fish oil during their third trimester of pregnancy have been found to have a reduced risk of asthma^[8]. Protection against allergic outcomes was found in infants with higher levels of omega-3 PUFA. In this study, the most significant effect of fish oil supplementation was shown in the children of the mothers with the lowest baseline EPA and DHA levels during pregnancy^[8]. These children had a lower risk of persistent wheeze or asthma aged three to five years. A secondary finding was a reduction in lower respiratory tract infection. However, not all studies concur the benefits from fish oil supplements during pregnancy^[9].

Making recommendations to mothers in the pharmacy

A pharmacist may, rightly, challenge the prophylactic power and value of an omega-3 PUFA supplement; not all studies and meta-analyses of these supplements are in agreement on their benefits, although none have shown harm^{[3],[9]}. As yet, no formal dose-response curve for this supplementation strategy exists. Furthermore, the supplements have not been tested in pregnancies that run an especially increased (genetic) risk of passing on allergic or autoimmune disorders to the infant, and there are also challenges relating to the drop out rates from trials involving supplements.

After birth, supplementation of omega-3 PUFAs has not been found to be an effective strategy^[10]. Health professionals recommending omega-3 PUFAs must be careful of which type of supplement is being used; the doses employed have differed in these various studies. There is little information on the relative bioavailability of DHA, EPA and α -linolenic acid, for example, from the various preparations available for pregnant mothers. Although safe for the mother and foetus, large amounts of fish oil are expensive, difficult to take, and have been found to result in problems with palatability and gastrointestinal discomfort in some adult studies^[11].

Other questions will be raised by mothers attending community pharmacy — should I also use probiotics? What about breastfeeding? Could these strategies work in concert? Garcia-Larsen *et al.*'s meta-analysis showed that probiotics reduce the risk of eczema and sensitisation to cow's milk, and a weaker protection was afforded against eczema and type 1 diabetes by prolonged breastfeeding^[3]. No risk reduction was observed from prebiotic supplements, allergenic food avoidance, or vitamin, mineral, fruit or vegetable intake.

Application to the UK population

It is not practical to employ a meta-analysis, however convincing, to develop a public health intervention^[12]. Population-based interventions must be evaluated to establish their level of evidence, cost-effectiveness, applicability and feasibility. Such datasets based on the highest level of evidence are scarce. And trials reviewed in meta-analyses tend to be limited to the racial and ethnic diversity of their candidate populations. Garcia-Larsen *et al.*'s recent meta-analysis is therefore a valuable but early step. Pharmacists might safely recommend fish oils to pregnant mothers, but the supplement's exact benefits cannot yet be predicted.

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