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[Intervention Review]

Omega-3 fatty acid addition during pregnancy

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ABSTRACT

Background

Higher intakes of foods containing omega-3 long-chain polyunsaturated fatty acids (LCPUFA), such as fish, during pregnancy have been associated with longer gestations and improved perinatal outcomes. This is an update of a review that was first published in 2006.

Objectives

To assess the effects of omega-3 LCPUFA, as supplements or as dietary additions, during pregnancy on maternal, perinatal, and neonatal outcomes and longer-term outcomes for mother and child.

Search methods

For this update, we searched Cochrane Pregnancy and Childbirth's Trials Register, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) (16 August 2018), and reference lists of retrieved studies.

Selection criteria

Randomised controlled trials (RCTs) comparing omega-3 fatty acids (as supplements or as foods, stand-alone interventions, or with a co-intervention) during pregnancy with placebo or no omega-3, and studies or study arms directly comparing omega-3 LCPUFA doses or types. Trials published in abstract form were eligible for inclusion.

Data collection and analysis

Two review authors independently assessed study eligibility, extracted data, assessed risk of bias in trials and assessed quality of evidence for prespecified birth/infant, maternal, child/adult and health service outcomes using the GRADE approach.

Main results

In this update, we included 70 RCTs (involving 19,927 women at low, mixed or high risk of poor pregnancy outcomes) which compared omega-3 LCPUFA interventions (supplements and food) compared with placebo or no omega-3. Overall study-level risk of bias was mixed, with selection and performance bias mostly at low risk, but there was high risk of attrition bias in some trials. Most trials were conducted in upper-middle or high-income countries; and nearly half the trials included women at increased/high risk for factors which might increase the risk of adverse maternal and birth outcomes.

Preterm birth < 37 weeks (13.4% versus 11.9%; risk ratio (RR) 0.89, 95% confidence interval (CI) 0.81 to 0.97; 26 RCTs, 10,304 participants; high-quality evidence) and **early preterm birth < 34 weeks** (4.6% versus 2.7%; RR 0.58, 95% CI 0.44 to 0.77; 9 RCTs, 5204 participants; high-quality evidence) were both lower in women who received omega-3 LCPUFA compared with no omega-3. **Prolonged gestation > 42 weeks** was probably increased from 1.6% to 2.6% in women who received omega-3 LCPUFA compared with no omega-3 (RR 1.61 95% CI 1.11 to 2.33; 5141 participants; 6 RCTs; *moderate-quality evidence*).

For infants, there was a possibly reduced risk of **perinatal death** (RR 0.75, 95% CI 0.54 to 1.03; 10 RCTs, 7416 participants; moderate-quality evidence: 62/3715 versus 83/3701 infants) and possibly fewer **neonatal care admissions** (RR 0.92, 95% CI 0.83 to 1.03; 9 RCTs, 6920 participants; *moderate-quality evidence* - 483/3475 infants versus 519/3445 infants). There was a reduced risk of **low birthweight** (LBW) babies (15.6% versus 14%; RR 0.90, 95% CI 0.82 to 0.99; 15 trials, 8449 participants; high-quality evidence); but a possible small increase in **large-for-gestational age** (LGA) babies (RR 1.15, 95% CI 0.97 to 1.36; 6 RCTs, 3722 participants; moderate-quality evidence, for omega-3 LCPUFA compared with no omega-3. Little or no difference in **small-for-gestational age or intrauterine growth restriction** (RR 1.01, 95% CI 0.90 to 1.13; 8 RCTs, 6907 participants; moderate-quality evidence) was seen.

For the **maternal outcomes**, there is insufficient evidence to determine the effects of omega-3 on **induction post-term** (average RR 0.82, 95% CI 0.22 to 2.98; 3 trials, 2900 participants; low-quality evidence), **maternal serious adverse events** (RR 1.04, 95% CI 0.40 to 2.72; 2 trials, 2690 participants; low-quality evidence), **maternal admission to intensive care** (RR 0.56, 95% CI 0.12 to 2.63; 2 trials, 2458 participants; low-quality evidence), or **postnatal depression** (average RR 0.99, 95% CI 0.56 to 1.77; 2 trials, 2431 participants; low-quality evidence). Mean **gestational length** was greater in women who received omega-3 LCPUFA (mean difference (MD) 1.67 days, 95% CI 0.95 to 2.39; 41 trials, 12,517 participants; moderate-quality evidence), and **pre-eclampsia** may possibly be reduced with omega-3 LCPUFA (RR 0.84, 95% CI 0.69 to 1.01; 20 trials, 8306 participants; low-quality evidence).

For the **child/adult outcomes,** very few differences between antenatal omega-3 LCPUFA supplementation and no omega-3 were observed in **cognition, IQ, vision, other neurodevelopment and growth outcomes, language and behaviour** (mostly low-quality to very low-quality evidence). The effect of omega-3 LCPUFA on **body mass index at 19 years** (MD 0, 95% CI -0.83 to 0.83; 1 trial, 243 participants; very low-quality evidence) was uncertain. No data were reported for development of **diabetes** in the children of study participants.

Authors' conclusions

In the overall analysis, **preterm birth < 37 weeks** and **early preterm birth < 34 weeks** were reduced in women receiving omega-3 LCPUFA compared with no omega-3. There was a possibly reduced risk of **perinatal death** and of **neonatal care admission**, a reduced risk of **LBW** babies; and possibly a small increased risk of **LGA** babies with omega-3 LCPUFA.

For our GRADE quality assessments, we assessed most of the important perinatal outcomes as high-quality (e.g. preterm birth) or moderate-quality evidence (e.g. perinatal death). For the other outcome domains (maternal, child/adult and health service outcomes) GRADE ratings ranged from moderate to very low, with over half rated as low. Reasons for downgrading across the domain were mostly due to design limitations and imprecision.

Omega-3 LCPUFA supplementation during pregnancy is an effective strategy for reducing the incidence of preterm birth, although it probably increases the incidence of post-term pregnancies. More studies comparing omega-3 LCPUFA and placebo (to establish causality in relation to preterm birth) are not needed at this stage. A further 23 ongoing trials are still to report on over 5000 women, so no more RCTs are needed that compare omega-3 LCPUFA against placebo or no intervention. However, further follow-up of completed trials is needed to assess longer-term outcomes for mother and child, to improve understanding of metabolic, growth and neurodevelopment pathways in particular, and to establish if, and how, outcomes vary by different types of omega-3 LCPUFA, timing and doses; or by characteristics of women.

PLAIN LANGUAGE SUMMARY

Omega-3 fatty acid addition during pregnancy

What is the issue?

Do omega-3 long chain polyunsaturated fatty acids (LCPUFA) taken during pregnancy - either as supplements or as dietary additions in food (such as some types of fish) - improve health outcomes for babies and their mothers? This is an update of a Cochrane Review that was first published in 2006.

Why is this important?

Preterm birth (babies born before 37 weeks pregnancy (gestation)) is a leading cause of disability or death in the first five years of life. Fish and fish oil contain omega-3 LCPUFA (particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)) and have been associated with longer pregnancies. So it is suggested that additional omega-3 LCPUFAs in pregnancy may reduce the number of babies born preterm and may improve outcomes for children and mothers. However, many pregnant women do not eat fish very often. Encouraging pregnant women to eat fatty fish (which generally have low toxin levels) or to use omega-3 LCPUFA supplements may improve children's and women's health. This is an update of a Cochrane Review that was first published in 2006.

What evidence did we find?

We searched for evidence in August 2018 and found 70 randomised controlled trials (RCTs; this type of trial provides the most reliable results) (involving 19,927 women). Most trials evaluated a group of women who received omega-3 LCPUFA and compared them with a group of women who received something that looked like omega-3 LCPUFA but did not contain it (placebo) or received no omega-3. The trials were mostly undertaken in upper-middle or high-income countries. Some studies included women at increased risk of preterm birth. The quality of the evidence from the included studies ranged from high to very low; this affected the certainty of the findings for different outcomes.

We found the incidence of preterm birth (before 37 weeks) and very preterm birth (before 34 weeks) was lower in women who received omega-3 LCPUFA compared with no additional omega-3. There were also fewer babies with low birthweight. However, omega-3 LCPUFA probably increased the incidence of pregnancies continuing beyond 42 weeks, although there was no difference identified in induction of labour for post-term pregnancies. The risk of the baby dying or being very sick and going to neonatal intensive care may be lower with omega-3 LCPUFA compared with no omega-3. We did not see any differences between groups for serious adverse events for mothers or in postnatal depression. Very few differences between the omega-3 LCPUFA groups and no omega-3 groups were observed in child development and growth.

Eleven trials reported that they had received industry funding. When we omitted these trials from the main outcomes (such as preterm birth and very preterm birth) it made very little, or no difference, to the results.

What does this mean?

Increasing omega-3 LCPUFA intake during pregnancy, either through supplements or in foods, may reduce the incidence of preterm birth (before 37 weeks and before 34 weeks) and there may be less chance of having a baby with a low birthweight. Women who take omega-3 LCPUFA supplements during pregnancy may also be more likely to have longer pregnancies. More studies are underway and their results will be included in a further update of this review. Future studies could consider if and how outcomes may vary in different populations of women, and could test different ways of increasing omega-3 LCPUFA during pregnancy.