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Effect of n-3 long-chain polyunsaturated fatty acid intake during pregnancy on maternal, infant, and child health outcomes: a systematic review

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Review published: 2012.

CRD summary

The authors concluded that infants born to women taking omega-3 long-chain polyunsaturated fatty acids were slightly heavier and less likely to be born before 34 weeks gestation, than those born to controls. There were clinical differences between the trials and there was no high-quality evidence, so the reliability of these conclusions is unclear.

Authors' objectives

To investigate the effect of omega-3 long-chain polyunsaturated fatty acid intake, during pregnancy, on mother, infant and child health outcomes.

Searching

PubMed, EMBASE, POPLINE, The Cochrane Library, and Web of Science were searched, in January 2011, for articles published in English. Search terms were reported. The references of relevant studies were handsearched.

Study selection

Randomised controlled trials investigating the effect of omega-3 long-chain polyunsaturated fatty acid supplementation in pregnant women were eligible for inclusion. Where there were co-interventions, both groups had to receive the same co-intervention. Outcomes eligible for inclusion were maternal morbidity or mortality, pre-term (under 37 weeks gestation) or early pre-term (under 34 weeks gestation) birth, low birth weight (less than 2.5kg), intra-uterine growth restriction or small for gestational age, still birth, infant or child growth, infant death, and infant morbidity. Trials of short-chain omega-3 polyunsaturated fatty acids, such as alpha-linolenic acid, were excluded.

The included trials investigated docosahexaenoic acid, eicosapentaenoic acid fish oil, or both in capsules, or docosahexaenoic acid enriched eggs milk supplements, or supplemented cereal bars, compared with placebo in the same form as the intervention (capsules, eggs, milk, or cereal bars). Dosages ranged from 80mg to 2.2g per day. Supplementation began in the second trimester and continued until delivery, in most trials. Most pregnancies were low risk. Some trials focused on high-risk groups, such as women with allergic disease, women with a history of complications in previous pregnancies, or women with current risks. The trials were carried out in the USA, UK, Spain, Norway, Netherlands, Germany, Europe,Denmark, Australia, Angola, Bangladesh or Mexico.

Observational studies of the effects of dietary intake of fish or seafood during pregnancy were included, but these studies were outside the scope of this abstract. The authors did not state how many reviewers selected the studies.

Assessment of study quality

The quality of included trials was assessed according to the Child Health Epidemiology Reference Group's adaptation of GRADE criteria. This covered sequence generation, allocation concealment, blinding, loss to follow-up, relevance to outcome of interest, and selective reporting. The overall quality of the evidence, for each key outcome, was graded according to the quality and consistency of the individual trials, the amount of evidence, and the strength of the effect.

The authors did not state how many reviewers assessed quality.

Data extraction

For dichotomous data, the number of events, in each group, was extracted and used to calculate relative risks, with 95% confidence intervals. The rates of infant death in the first year were calculated using the number of

live births as the denominator (excluding still births). For continuous data, the means and standard deviations were extracted to calculate the mean difference, for each group.

Where statistical data were not available, they were calculated from figures in the text and tables, and where possible, authors were contacted for any missing data. The data were extracted into a standardised data extraction form, and a minimum of 75% of them were entered twice, for accuracy.

Methods of synthesis

For dichotomous outcomes, the relative risks and 95% confidence intervals were pooled. For continuous outcomes, the mean differences, with 95% confidence intervals, were pooled. Statistical heterogeneity was assessed using Cochran's Q and I^2. Where I^2 was less than 50%, a fixed-effect model was used; where it was over 50%, a random-effects model was used.

The subgroup of trials of high-risk pregnancies, and the subgroup excluding trials of high-risk pregnancies, were analysed.

Results of the review

Fifteen randomised controlled trials were included, with over 8,454 pregnant women. Three trials were graded high, three were moderate to high, five were moderate, three were low to moderate, and one was low. The overall quality of the evidence was moderate for the outcomes of gestational duration, risks of pre-term and early pre-term birth, mean difference in birth weight, and risks of low birth weight and small-for-gestational age or intra-uterine growth restriction. It was moderate to low for the risk of maternal high blood pressure, risk of pre-eclampsia, mean difference in birth length, mean difference in head circumference, risk of still birth, and risk of infant death. It was low for the risk of admission to neonatal intensive care unit.

Supplementation with omega-3 long-chain polyunsaturated fatty acids was associated with 26% lower risk of early pre-term birth (RR 0.74, 95% CI 0.58 to 0.94; I^2=0; five trials; 4,343 women), and moderately increased birth weight (MD 42.22, 95% CI 14.76 to 69.68; I^2=27%; nine trials; 6,020 women), compared with placebo. There was no evidence of statistical heterogeneity.

Supplementation did not significantly affect maternal high blood pressure, maternal pre-eclampsia, gestational duration, pre-term birth, risk of low birth weight, birth length, head circumference, risk of small for gestational age, intra-uterine growth restriction, risk of admission to neonatal intensive care, still birth and infant death, compared with placebo. Excluding trials of high-risk pregnancies did not significantly alter the findings.

In the subgroup of trials of high-risk pregnancies, supplementation was not associated with a reduced risk of pre-eclampsia, pre-term birth, low birth weight, small for gestational age, still birth and neonatal death, compared with placebo.

Authors' conclusions

Infants born to women taking omega-3 long-chain polyunsaturated fatty acids were slightly heavier and were less likely to be born before 34 weeks gestation, than those born to controls.

CRD commentary

The review addressed a clear question, with well-defined inclusion criteria. The search was restricted to articles in English, introducing a risk of language bias. Attempts to find unpublished data were not reported, and publication bias was not assessed and cannot be ruled out. It was unclear whether appropriate steps were taken in study selection and quality assessment to minimise the risks of reviewer error and bias. A suitable tool was used to assess the quality of the included trials. Their overall quality was moderate, moderate to low, or low for all outcomes; the absence of high-quality evidence, for all outcomes, undermines the reliability of the findings.

Appropriate methods were used to combine the trial data. Statistical heterogeneity was assessed and was low for most outcomes. Subgroup analyses were conducted to explore the impact of pregnancy risk on the outcomes. There were clinical differences between the trials in the form (capsule, milk, etc.), dosage, and duration of supplementation, which were not explored. Most trials were conducted in high-income countries, and the findings might not be generalisable to countries with lower incomes. The small number of events, for rare occurrences, such as infant death or still birth, made it difficult to determine any differences between groups.

Given the clinical differences between trials, and the absence of high-quality evidence, the reliability of the authors' conclusions is unclear.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that further research was needed to investigate the impact of omega-3 long-

chain polyunsaturated fatty acid intake in pregnant women, in low-income countries, where the dietary intake of marine foods was low, and the rate of adverse maternal and infant health outcomes was high.

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CRD has determined that this article meets the DARE scientific quality criteria for a systematic review.

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