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Review

Effects of polyunsaturated fatty acid intake and status during pregnancy, lactation, and early childhood on cardiometabolic health: A systematic review

Trudy Voortman [a,*], Edith H. van den Hooven [a], Kim V.E. Braun [a,b], Marion van den Broek [a,b], Wichor M. Bramer [c], Rajiv Chowdhurry [d], Oscar H. Franco [a]

[a] Department of Epidemiology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
[b] Department of Health Sciences, Faculty of Earth and Life Sciences, VU University, Amsterdam, The Netherlands
[c] Medical Library, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
[d] Department of Public Health and Primary Care, University of Cambridge, Cambridge, United Kingdom

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ABSTRACT

The importance of polyunsaturated fatty acid (PUFA) intake in fetal life and infancy has been widely studied in relation to child cognitive and visual development, but whether early life PUFA exposure is related to cardiometabolic risk factors is unclear. The focus of this systematic review was to evaluate the effects of PUFA dietary intake and blood levels during pregnancy, lactation, or early childhood (⩽5 y) on obesity, blood pressure, blood lipids, and insulin sensitivity. We identified 4302 abstracts in the databases Embase, Medline and Cochrane Central (April 2014), of which 56 articles, reporting on 45 unique studies, met all selection criteria. Many of the included studies focused on obesity as an outcome (33 studies), whereas studies on insulin sensitivity were relatively scarce (6 studies). Overall, results for obesity, blood pressure, and blood lipids were inconsistent, with a few studies reporting effects in opposite directions and other studies that did not observe any effects of PUFAs on these outcomes. Four studies suggested beneficial effects of PUFAs on insulin sensitivity. We conclude that there is insufficient evidence to support a beneficial effect of PUFAs in fetal life or early childhood on obesity, blood pressure, or blood lipids. More research is needed to investigate the potential favorable effects of PUFAs on insulin sensitivity, and to examine the role of specific fatty acids in early life on later cardiometabolic health.

Contents

Abbreviations: %E, percentage of total energy; %fat, percentage of total fat; ARA, arachidonic acid; ALA, alpha-linolenic acid; BF, body fat; BMI, body mass index; BP, blood pressure; DBP, diastolic blood pressure; DHA, docosahexaenoic acid; DGLA, dihomo-gamma-linolenic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; FA, fatty acid; HDL-C, high-density lipoprotein cholesterol; HOMA-β, homeostatic model assessment of beta-cell function; HOMA-IR, homeostatic model assessment of insulin resistance; LA, linoleic acid; LCPUFA, long chain polyunsaturated fatty acid; LDL-C, low-density lipoprotein cholesterol; PL, phospholipid; PUFA, polyunsaturated fatty acid; QS, quality score; SBP, systolic blood pressure; TAG, triacylglycerol; y, years; *Z*-score, age- and sex-specific standard deviation score.

* Corresponding author at: Department of Epidemiology, Erasmus MC, Office Na-2909, PO Box 2040, 3000 CA Rotterdam, The Netherlands.
E-mail address: trudy.voortman@erasmusmc.nl (T. Voortman).

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1. Introduction

Obesity and cardiometabolic risk factors can already develop in childhood and predict cardiovascular disease and type 2 diabetes in later life [1,2]. Therefore, it is important to study early determinants of cardiometabolic risk. Nutritional exposures in critical periods in pregnancy or early childhood may have a lasting influence on later cardiometabolic health [3,4]. Lipids, especially polyunsaturated fatty acids (PUFAs), have received considerable interest in this context because of their diverse roles in cell membrane synthesis, gene expression, and eicosanoid metabolism [5].

Contrary to saturated and monounsaturated fatty acids, omega-3 (*n*-3) and omega-6 (*n*-6) PUFAs cannot be synthesized by the human body and are therefore considered essential nutrients in the diet [6]. During pregnancy and lactation, PUFAs are transferred from mother to fetus or infant [7,8]. PUFAs are important for growth and development, as they are incorporated into cell membranes in all tissues of the body [5,6]. The importance of PUFA intake during pregnancy and in infancy has been widely studied in relation to child cognitive and visual development [9–11]. In adults, PUFAs have been associated with improved cardiometabolic health [12–18], but whether early life PUFA exposure affects cardiometabolic health is unclear. The presence of long-chain PUFAs (LCPUFAs) in breast milk has been suggested as a potential mechanism for beneficial effects of breastfeeding on subsequent health outcomes such as a lower blood pressure [19], but randomized controlled trials with PUFA supplementation to infant formula, or to lactating or pregnant women have reported inconsistent effects on blood pressure in later childhood [20–24].

Therefore, our aim was to systematically review the current literature on the effects of PUFA intake and blood levels, during pregnancy, lactation, or in early childhood up to the age of 5 y, on cardiometabolic health. Cardiometabolic outcomes included obesity (body mass index (BMI), weight-for-height, or body fat), blood pressure, blood lipids (triacylglycerol (TAGs), or total, low-density lipoprotein (LDL), or high-density lipoprotein (HDL) cholesterol), and measures of insulin sensitivity (glucose or insulin levels, or homeostatic model assessment (HOMA)).

2. Methods of the systematic review

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [25].

2.1. Search strategy

The literature search was performed in the electronic databases Medline (OvidSP), Embase (embase.com), and Cochrane Central. All databases were searched from their inception until 1 April 2014. The search strategy (provided in Supplementary Appendix A) consisted of four elements: PUFAs (PUFA, fish oil, *n*-3 and *n*-6 FAs); the population of interest (infants, children, pregnant and lactating women); cardiometabolic outcomes (obesity, blood lipids, blood pressure, insulin sensitivity); and observational or interventional study designs. All elements were searched using both controlled vocabulary terms (MeSH and/or Emtree) and free text words in the title or abstract. Limits were applied to include only human studies and exclude letters or editorials. No limits were set on language or year of publication. In addition to the systematic search, we contacted experts in the field and we screened reference lists of studies that were included in our review.

2.2. Selection criteria

Studies were included if they fulfilled the following criteria:

- **Study design**: Intervention, cohort, case-control, or cross-sectional studies.
- **Population**: Exposure measure or intervention in healthy pregnant or lactating women, or in healthy children ⩽5 y; outcome measures in the offspring at any age.
- **Exposure**: Intake and/or blood levels of PUFAs, including total PUFAs; total *n*-3 FAs; total *n*-6 FAs; ratios between *n*-6 and *n*-3 FAs; fish oil; the *n*-3 FAs alpha-linolenic acid (ALA, C18:3 (*n*-3)); eicosapentaenoic acid (EPA, C20:5 (*n*-3)); docosapentaenoic acid (DPA, C22:5 (*n*-3)); or docosahexaenoic acid (DHA, C22:6 (*n*-3)); or the *n*-6 FAs linoleic acid (LA, C18:2 (*n*-6)); gamma-linolenic acid (GLA, C18:3 (*n*-6)); dihomo-gamma-linolenic acid (DGLA, C20:3 (*n*-6); or arachidonic acid (ARA, C20:4 (*n*-6)).
- **Outcomes**: Cardiovascular and metabolic outcomes, including obesity (BMI, weight-for-height, body fat), blood pressure (BP), blood lipids (TAG and total, HDL and LDL cholesterol), or measures of insulin sensitivity (glucose or insulin levels, HOMA, type 2 diabetes mellitus).

2.3. Study selection

Working in pairs, two authors independently reviewed each title and abstract to determine whether the study fulfilled the selection criteria. Full text articles were retrieved for the selected titles after initial appraisal and assessed once more by two independent authors to ensure that they satisfied the inclusion criteria. Disagreement with article selection was resolved through discussion or with help of a third independent author.

2.4. Data extraction

Data were extracted using a structured data extraction form created prior to the literature search. Detailed study-level characteristics were extracted including study design, study size, study

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