Long-term effects of breastfeeding

A SYSTEMATIC REVIEW

Bernardo L. Horta, MD, PhD
Universidade Federal de Pelotas, Pelotas, Brazil

Cesar G. Victora, MD, PhD
Universidade Federal de Pelotas, Pelotas, Brazil

World Health Organization

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Contents

··· CHAPTER 1 ···

Introduction

Breastfeeding has well-established short-term benefits, particularly the reduction of morbidity and mortality due to infectious diseases in childhood. A pooled analysis of studies carried out in middle/low income countries showed that breastfeeding substantially lowers the risk of death from infectious diseases in the first two years of life (*1*).

Based on data from the United Kingdom Millennium Cohort, Quigley et al (*2*) estimated that optimal breastfeeding practices could prevent a substantial proportion of hospital admissions due to diarrhea and lower respiratory tract infection. A systematic review by Kramer et al (*3*) confirmed that exclusive breastfeeding in the first 6 months decreases morbidity from gastrointestinal and allergic diseases, without any negative effects on growth. Given such evidence, it has been recommended that in the first six months of life, every child should be exclusively breastfed, with partial breastfeeding continued until two years of age (*4*).

Building upon the strong evidence on the short-term effects of breastfeeding, the present review addresses its long-term consequences. Current evidence, mostly from high income countries, suggests that occurrence of non-communicable diseases may be programmed by exposures occurring during gestation or in the first years of life (*5–7*). Early diets, including the type of milk received, is one of the key exposures that may influence the development of adult diseases.

In 2007, we carried out a systematic review and meta-analysis on the long-term consequences of breastfeeding. The Department of Maternal, Newborn, Child and Adolescent Health of the World Health Organization has now commissioned an update of this review. The following long-term outcomes were reviewed: blood pressure, type-2 diabetes, serum cholesterol, overweight and obesity, and intellectual performance. These outcomes are of great interest to researchers, as made evident by the number of publications identified: 60 new publications were identified since 2006. This report describes the methods, results and conclusions of this updated review.

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··· CHAPTER 2 ···

Methodological issues

Randomized controlled trials, if properly designed and conducted, provide the best evidence on a causal association between an exposure – such as breastfeeding – and a health or developmental outcome. Randomization increases the likelihood that results will not be affected by confounding (*1*). Additionally, existing guidelines propose standards for conducting, analyzing and reporting clinical trials, which helps increase the validity of the evidence (*2*).

On the other hand, the recognition of the short-term benefits of breastfeeding, briefly described in **Chapter 1**, constitutes an ethical challenge to the design of randomized trials aimed at assessing its long-term consequences. Currently, it would be considered unethical to randomly allocate subjects not to receive breastmilk. In contrast, in the early 1980s the evidence on the short-term benefits of breastfeeding was not so clear-cut. At that time, preterm infants admitted to neonatal units could be ethically allocated at random to receive banked breastmilk or formula. Follow-up of these subjects in adolescence has provided experimental evidence on the long-term effects of breastfeeding (*3–5*).

An alternative to individual randomization to breastfeeding is to allocate groups of mothers to receive – or not to receive – breastfeeding counseling. In Belarus, the Promotion of Breastfeeding Trial (*6*) randomly assigned maternity hospitals and their affiliated polyclinics to the Baby-Friendly Hospital Initiative. The proportion of infants exclusively breastfed at 3 and 6 months was substantially higher among infants from the intervention group. This trial is ethically sound because mothers were randomly assigned to receive intense breastfeeding promotion, compared to usual care in the hospitals. The follow-up of this study has provided invaluable evidence on the long-term consequence of breastfeeding (*7–8*). On the other hand, compliance to the intervention was far from universal, only 43.3% of the infants in the intervention group were exclusively breastfed at 3 months compared to 6.4% in the comparison arm, and therefore both groups represent a mixture of breastfeeding practices. As a consequence, the effect of breastfeeding itself on outcomes is underestimated, and statistical power is reduced.

Because of the small number of randomized controlled trials with sufficient follow-up time, most of the evidence on the long-term effects of breastfeeding is derived from observational studies. Prospective birth cohort studies are the next-best design in terms of strength of evidence.

Below, we discuss the strengths and weaknesses of observational studies, as well as approaches that may help overcome their main shortcomings.

Factors affecting internal validity

Losses to follow-up

If losses to follow-up are high, selection bias may be introduced. This may affect both randomized and observational studies. In order to assess the study susceptibility to selection bias, baseline data,

such as breastfeeding duration, should be compared between those subjects who were followed up and those who were not. If attrition rates are not related to breastfeeding duration or other baseline characteristics, selection bias is unlikely (*9*). However, not every study provides such information.

Misclassification

When assessment of exposure or the outcomes is inaccurate, misclassification may occur. Misclassification may be differential or non-differential.

Retrospective studies are more susceptible to recall bias and direction of bias may change. For example, Huttly et al (*10*) observed that Brazilian mothers of high socioeconomic status tended to overestimate the breastfeeding duration, whereas among poor mothers this was not the case. This differential recall of breastfeeding duration would tend to overestimate the benefits of breastfeeding because high socioeconomic status is associated with a lower risk of chronic non transmissible diseases.

On the other hand, if the measurement error is not related to exposure or outcome, non-differential misclassification occurs. Such bias underestimates the measure of association, and, therefore, reduces the likelihood of reporting a significant association. Indeed, in a meta-analysis on the relationship between maternal smoking in pregnancy and breastfeeding duration, the odds ratio for weaning at 3 months was inversely related to the length of recall for exposure and outcome (*11*).

Unfortunately, very few of the studies included in this review address these issues. We attempted to address it by stratifying studies according to the length of recall of breastfeeding information, but admittedly this is only a proxy for misclassification.

Confounding

Confounding is one of the challenges in interpreting the evidence of observational studies. Even large studies that managed to measure the possible confounders may still be affected by residual confounding, if the confounder variables were not properly measured or adjusted for. Some methods have been suggested to improve causal inference. These include comparison of siblings in within-family analyses, which allow controlling for unmeasured maternal and family variables (socioeconomic status, maternal variables) as well as for self-selection bias, because these characteristics are shared among siblings. Usually, sibling studies assess the effect of discordance on breastfeeding duration or complementary feeding on the outcome. Gillman et al (*12*) used this design to investigate the association between breastfeeding and overweight (see **Chapter 5**). A limitation of these studies, is that heterogeneity in breastfeeding duration is smaller among siblings than that observed among