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EARNest

EARly Nutrition programming- long term follow up of Efficacy and Safety Trials and integrated epidemiological, genetic, animal, consumer and economic research

Instrument: Integrated Project

Thematic Priority 5.4.3.1: Food Quality and Safety

Final public report on activity 2.3.1

Title of activity: Prenatal and postnatal dietary factors in relation to markers of chronic diseases within the first years of life

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Duration: 5,5 Years

Organisation Name of Lead Contractor for this report: Danish Epidemiology Science Centre, Statens Serum Institut (now: Centre for Fetal Programming, Statens Serum Institut)

This activity was based on follow up from the Danish National Birth Cohort (DNBC), which is a large prospective birth cohort holding extensive information on maternal and infant diet. During 1996-2002, 101,046 Danish pregnant women were recruited into this cohort for long-term follow up of themselves and their subsequent children. Information on a broad range of lifestyle and other factors was collected through 1) the recruitment form completed in weeks 6-10 of gestation, 2) telephone interviews of the women in gestation weeks 12 and 30 (prenatal interviews) and when the children were 6 and 18 (postnatal interviews) months old, and 3) through a comprehensive dietary questionnaire sent by postal mail to the women around gestation week 25. Three blood samples were collected, two from the mother (around weeks 6-10 and 25 of gestation) and one from the umbilical cord. The database can be linked to Danish registries containing information on socio-economic and health related variables: this includes the medical birth registry, which records information on birth weight and other variables recorded by health personnel around the time of birth. Information on maternal diet was recorded in the interviews and in the mid-pregnancy 300-item food frequency questionnaire, whereas information on infant diet was recorded in the postnatal interviews.

Objectives

The objectives of this activity were to study associations between maternal and infant dietary exposures on the one hand and early markers of chronic diseases occurring within the first years of life on the other.

Tasks

Developing outcome variables: A laborious task of this activity was to define and ascertain the outcomes to be studied. Cryptorchidism was ascertained from mothers' reports in the postpartum telephone interviews at 6 and 18 months, combined with information obtained from linkages to the mandatory National Patient Registry. Early psychomotor development was ascertained from mothers' responses to specific questions regarding child development asked in postpartum telephone interviews at 6 and 18 months. Atopic diseases were ascertained on the basis of specific questions regarding wheezing, asthma and allergies asked in postpartum telephone interviews at 6 and 18 months and in the postal questionnaire completed when the child was 7 years, combined with information obtained from linkages to the mandatory National Patient Registry. Growth was ascertained on the basis of specific questions regarding growth asked in postpartum telephone interviews at 18 months and in the postal questionnaire completed when the child was 7 years.

Developing dietary exposures variables: Since the full dietary database was needed for the exploratory analyses, this activity implied cleaning and validation procedures of the comprehensive set of dietary variables that was available. Likewise, the infant dietary variables also required substantial development and elaboration.

Developing analytical strategy: In addition to applying conventional statistical methods to examine associations between early dietary variables and health outcomes, such as logistic and linear regression, an important element was to undertake exploratory analyses by means of split sample techniques, where the overall principle was to generate hypotheses on a random sample of the dataset which were then tested in remaining dataset as a priori hypotheses. Furthermore, for some of the outcomes, techniques such as Principal Component Analyses were employed to indentify underlying dietary patterns and latent variables which in turn led to the definition of variables (named 'western type diet', 'prudent diet' etc.) that could depict such patterns and be related to the outcome.

Results

Cryptorchidism: No association was found between risk of cryptorchidism and intake of milk and fish as hypothesised due to the potential hormonal substances. The following food groups remained in the model after backward selection: Vegetables, vegetable juice, soy products, poultry, low fat dairy and fruit syrup and marmalade. Risk of cryptorchidism was directly associated with intake of vegetables and vegetable juice and inversely associated with intake of soy products, when comparing the lowest quintiles/groups with the highest. No clear association was found regarding intake of any of the other food groups, or of intakes of any of the macronutrients.

Growth: In comparison to children whose mothers did not drink milk during pregnancy, children whose mothers consumed >4 glasses of milk/day have higher adjusted z-scores for birth weight 0.17, (95%CI: 0.06, 0.27) and birth length 0.13 (95%CI: 0.02, 0.24). At 12 months of age, the corresponding z-scores are 0.14 (95%CI: -0.00, 0.28) and 0.12 (95%CI: -0.03, 0.27) for weight and length respectively. At the age of 7 the corresponding difference is 0.10, (95%CI: 0.002, 0.21) for weight and 0.12, (95%CI: 0.02, 0.22) for length, while no differences were observed in the offspring's body mass index z-scores: 0.05 (95%CI: -0.06, 0.018). At 7 years of age adjustment for concurrent milk intake does not change our effect estimates.

Early psychomotor development: *Fish intake and breastfeeding:* Maternal fish intake and greater duration of breastfeeding were associated with higher child developmental scores at 18 mo [odds ratio: 1.29 (95% CI: 1.20, 1.38) for the highest versus the lowest quintile of fish intake, and 1.28 (1.18, 1.38) for breastfeeding for ≥ 10 mo compared with breastfeeding for ≤ 1 mo]. Associations were similar for development at 6 mo. Associations of fish intake with child development did not differ by breastfeeding duration.

Folate: Total dietary folate intake was associated with a higher development score (unadjusted OR: 0.75 [95% CI: 0.71 to 0.79]) for the lowest vs. the highest quintile of folate. Adjustment for fish intake (OR: 0.77 [95% CI: 0.73 to 0.82]) as well as adjustment for breastfeeding duration (OR: 0.79 [95% CI: 0.74 to 0.83]) gave a similar estimate. After adjustment for non-dietary covariates, the estimate still remained similar (OR: 0.77 [95% CI: 0.73 to 0.82]). Estimates increased across all quintiles in the unadjusted as well as in all the adjusted analyses. Folic acid intake from supplements was not associated with a higher development score (fully adjusted OR: 0.97 [95% CI: 0.88 to 1.07] for the lowest vs. the highest quintile of folic acid). When we examined the association between intake of dietary folate partitioned into nine different sources and child development scores, only associations with folate from onions, tomatoes and green vegetables persisted, whereas folate from such foods as grains, dairy or eggs were unassociated with developmental scores.

Asthma and allergies: *Fish and essential fatty acids intake:* Maternal intake of total n-3 fatty acids during pregnancy was not associated with either ever wheeze (Q5 vs. Q1: 0.96, 95% CI: 0.88, 1.05) or recurrent wheeze (Q5 vs. Q1: 1.03, 95% CI: 0.86, 1.24). Fish intake was inversely associated with questionnaire diagnosed asthma (low vs. high intake: 1.53, 95% CI: 1.02, 2.31). Fish intake was positively, but non-significantly, related to allergies when defined using the registry (low vs. high intake: 1.43, 95% CI: 0.42, 4.86), but was inversely associated when using the questionnaire-based data (low vs. high intake: 0.80, 95% CI: 0.48, 1.35).

Folates: Total folate intake was marginally associated with a registry based diagnosis of asthma (Q5 vs. Q1: 1.16, 95% CI: 0.95, 1.42). Folic acid from supplements was generally not associated with asthma or allergies.

Peanut and nut intake: Compared to mothers who consumed no nuts during the pregnancy, those whose intake of nuts was ≥ 1 times/week were only 0.81 (95% CI: 0.73, 0.89) as likely to report wheeze in their children during the first 18 month of life. Children whose mothers consumed peanuts at least 1 time/week were only 0.68 as likely to have an asthma diagnosis in the DNPR (95% CI: 0.47, 0.98).

Exploratory analyses relating maternal diet to psychomotor development and asthma: We ran extensive analyses based on a random 40% sample (n=24309 mother child pairs) of the total sample, and some results are summarised here. Positive associations were identified between early psychomotor development and the vitamins B6, vitamin C, folate (B9), and the mineral selenium. As one noteworthy result for asthma dark bread and total dietary fibre were found to correlate with and be protective for asthma. More time is needed to explore these results before we open up analyses of the remaining parts of the data.

Conclusions

Cryptorchidism: Our analyses could not convincingly point out specific foods or nutrients in the maternal diet which were associated with risk of cryptorchidism.

Growth: Maternal milk intake in pregnancy seems to have stimulating effect on fetal growth which tracks beyond the prenatal period, at least up to the age of 7 years. This effect is more dominant for length compared to weight for length.

Early psychomotor development: Maternal fish intake during pregnancy and the duration of breastfeeding are independently associated with better early child development. The strong direct associations observed with total folate intake may not be due to folate itself, but may instead be attributed to other nutrients which coexist with folate in specific food sources; our data point to green vegetables, onion and tomatoes.

Asthma and allergies: As regards asthma a protective association seems to exist for higher intake of fish, whereas results for allergies were less clear. No association was found for folate from either supplements or diet with wheeze and asthma in childhood. Higher consumption of both peanut, nut, and total nut in mid-pregnancy was inversely associated with wheeze at 18 months and a DNPR diagnosis of asthma at 7 years, which is contrary to the current hypotheses and some recommendations which advise lower intakes of peanuts during pregnancy.

Exploratory analyses: Our preliminary results suggest that vitamin B6, vitamin C, folate (B9), and the mineral selenium in pregnancy may be beneficial for early psychomotor development and bread dark and total dietary fibre may be protective against asthma.

Next step

Results found and hypotheses generated by our exploratory approached will undergo further refinement and testing on the remaining parts of the dataset.