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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 1.1.3

Title of activity: Follow-up of LCPUFA trial in Aarhus, Denmark

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Start date of project: 15.04.2005 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 a population-based trial that we had undertaken in Aarhus, Denmark, in 1990, where 533 pregnant women were randomised to receive either capsules with fish oil or to a control group receiving either capsules with olive oil; a second control group received no oil capsules. In our earlier work based on this trial we had shown that fish oil supplementation is associated with prolonged pregnancies and correspondingly increased birth weights.

Objectives

The objectives of this activity were to examine the relationship between intake of n-3 fatty acids in pregnancy on the one hand and markers of cardiovascular disease and metabolic syndrome risk 18 years later on the other. Later additions to these objectives were to also examine the relationship between intake of n-3 fatty acids in pregnancy and markers of atopic diseases and of cognitive functions during the first 18 years of the offspring's life.

Tasks

First, through registry linkage, we identified all offspring in the Danish central personal registries by means of the unique ID number of every citizen in Denmark; we were very successful in doing so as, among the 533 singleton foetuses that had been randomised in gestation week 30 in the trial in 1990, 527 persons were identified as live persons with a postal address in Denmark in 2006. The 5 drop outs could be explained by either still birth or emigration to another country. Further, from the mandatory National Patient Registry, we made extraction of all asthma related diagnoses given during hospital contacts up to the age of 16.

Second, in 2008, we sent out letters to the young people at their postal addresses inviting them to complete a web-based questionnaire asking them about height, weight and abdominal circumference (a tape measure was sent with the letter), asthma and allergies, and many other issues. 75% completed the questionnaire.

Third, in 2008-2009, we invited those who had completed the questionnaire to participate in a physical-clinical examination which included: measurements of height, weight and waist circumference and, following 10 minutes lying rest, measurement of heart rate variability measured using a hand held device (HealthMate, Medicus Engineering, Aarhus, Denmark); measurements of blood pressure three times with a fully automatic blood pressure device (an average of the last two recordings was used in the analysis); drawing of fasting (10 h) venous blood samples that were stored at -20° and later assessed for total cholesterol, HDL-cholesterol, LDL-cholesterol, triglyceride, glucose, Insulin, HgA1c, leptin, adiponectin and high-sensitivity C reactive protein (hs-CRP). 50% of the originally randomised group participated in these physical-clinical examinations.

Results

As regards markers of cardiovascular diseases and metabolic syndrome quantified at 18 years, we could detect no statistically significant differences between the fish oil and olive oil groups in BMI, waist circumference, systolic or diastolic blood pressures, resting pulse rate,

heart rate variability, HgA1c fraction, insulin, blood glucose, total-, LDL- or HDL-cholesterol, triglycerides, leptin or adiponectin. As regards markers of atopic diseases appearing during the first 16 years after childbirth, 19 children from the fish oil and olive oil groups had received an asthma-related diagnosis, of whom 10 had received the diagnosis allergic asthma. The hazard rate of asthma was reduced by 63% (95% CI: 8%, 85%; *P* 0.03), whereas the hazard rate of allergic asthma was reduced by 87% (95% CI: 40%, 97%; *P* 0.01) in the fish oil compared with the olive oil group. Inspection of the Kaplan-Meier curve indicated that the 'survival' curves of the fish oil and olive oil groups only started to diverge at around year four.

[Insert a figure here showing the asthma results]

Conclusions

Two important conclusions derived from this research:

Conclusion 1

A fish oil supplement taken during third trimester – providing a daily amount of 2.7 grams long chain marine n-3 fatty acids – seemed to have no effect on markers of cardiovascular diseases and metabolic syndrome quantified 18 years later in the offspring.

Conclusion 2

Children whose mothers had taken a fish oil supplement during third trimester – providing a daily amount of 2.7 grams long chain marine n-3 fatty acids – seemed to experience reduced risk of receiving an asthma-related diagnosis from the hospital system during ages 4 to 16 years.

Next step

To follow up on the asthma findings, we are now analysing data from spirometry examinations that were undertaken simultaneously with assessment of markers for metabolic syndrome and cardiovascular diseases. We have linked our data to the Danish school registry, which will enable us to examine impact of fish oil supplementation in third trimester of pregnancy on academic performance in the school as a measure of cognitive capability.