FOOD-CT-2005-007036

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 1.2.2

Title of activity: Follow-up studies in the EU Childhood Obesity Programme cohorts in Poland, Belgium, Germany, Spain and Italy

Period covered from 15.04.2005 to 14.10.2010

Start date of project: 15.04.2005 Duration: 5,5 Years

Organisation Name of Lead Contractor for this report: LMU Muenchen

Background

Higher protein intake during the first year of life was proposed to increase the secretion of insulin-like growth factor I and consecutively cell proliferation, which leads to accelerated growth and increased adipose tissue. Since rapid weight gain in early life is an identified risk factor for later obesity, this could provide a promising starting point for obesity prevention.

Introduction

Rapid weight gain in infancy is associated with an increased risk of later obesity (1). Formula fed infants have a more rapid weight gain than breastfed infants which was suggested to be caused by the higher protein content of formula milk compared to human milk (2). The Childhood Obesity Project, a multicenter, randomized double blind intervention trial, was designed to study whether higher protein intake during the first year of life leads to more rapid length and weight gain up to the age of 24 months.

The study was carried out in five European countries (Belgium, Italy, Germany, Poland and Spain), where 1138 formula fed infants were randomly assigned to receive a formula with higher or lower protein content. Additionally a reference group of 619 exclusively breastfed infants were recruited.

Besides anthropometry data for exploring several secondary hypotheses have been collected, including detailed data on diet, lifestyle and behaviour, biochemical and endocrine markers, genetics, clinical data like blood pressure, bio electrical impedance, markers on renal function and intima media thickness to explore underlying mechanisms and to test for possible untoward effects of the study formulas.

Following those children up until the age of 6 years and actually in the NUTRIMENTHE project until the age of 8 years enables to study also long term effects of the early nutritional intervention. Since data on the follow up period from the age of 30 months to 72 months are not fully analyzed yet, the summarized results are mainly from the first period of the CHOP study.

Results

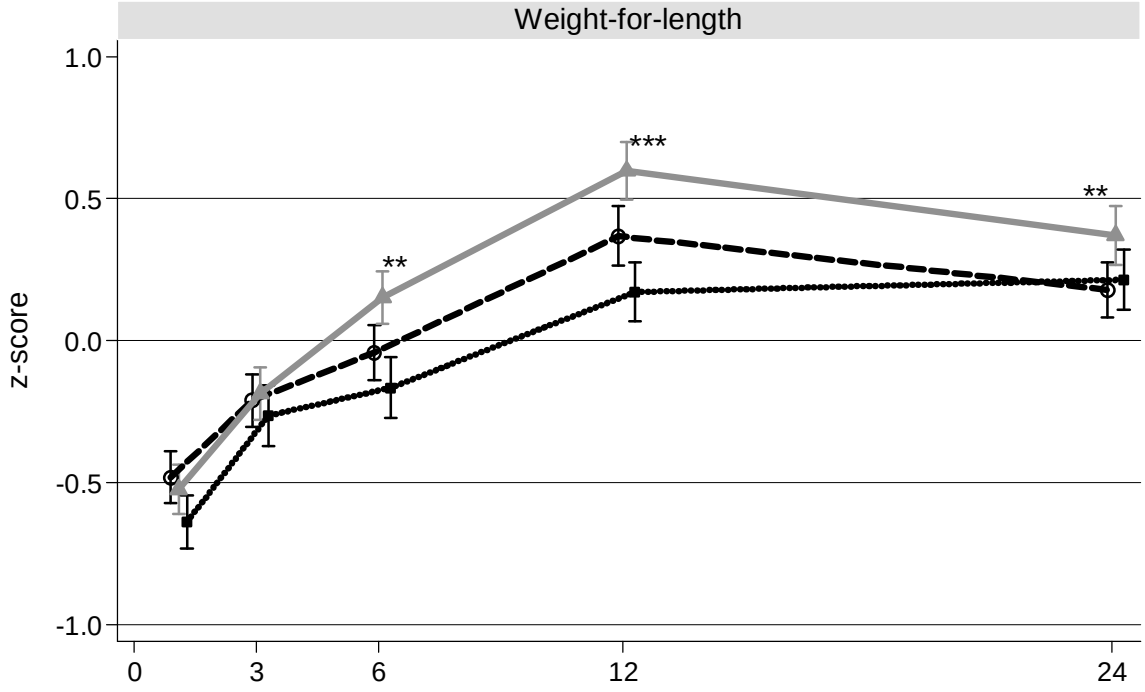
1. Anthropometrical evaluation

Six hundred thirty-six children in the lower (n=313) and higher (n=323) protein formula groups and 298 children in the breastfed group were followed until 24 months.

Primary endpoints were length and weight at 24 months of age, expressed as length and weight-for-length z scores based on the 2006 WHO growth standards. These measures were compared using linear regression with adjustment for the corresponding baseline values.

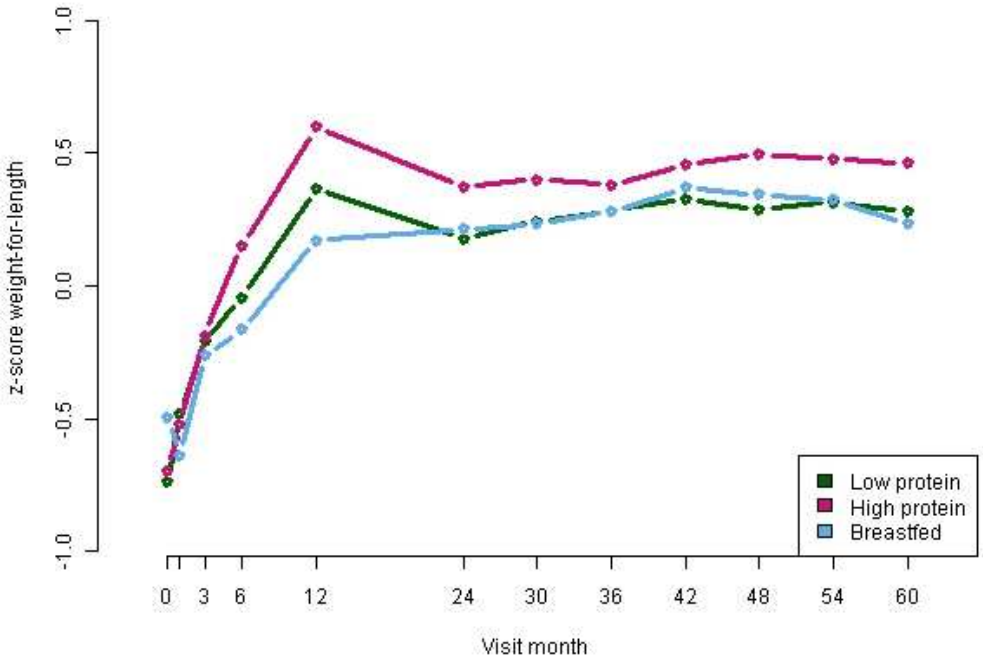
Length z-score was not different between the higher and lower protein group at any time. But at 24 months weight-for-length z scores of infants in the lower protein formula group were 0.2 lower than those of the higher protein group and did not differ from that of the breastfed reference group (Figure 1). Since energy intake was equal between the two intervention groups one can assume that this difference in weight-for-length at the age of 2 years is induced by the different protein intake. According to Monteiro et al (4) an increase of 0.2 SD in weight-for-length during the first 2 years of life is associated with a 13% higher risk for obesity at the age of 14-16 years (3).

Figure 1: Mean z scores (with 95% CIs) for weight-for-length in the lower protein (n=540) and higher-protein (n=550) group and in the breastfed (n=588) children at baseline (0-8 wk of age) and at 3, 6, 12, 24 months of age. *, **, *** Significantly different from the lower protein group (ANOVA adjusted for baseline value)



Anthropometrical data has been collected biannually since the age of 30 months and is reviewed and available now. Since analyses have not been carried out completely only a graphical representation of the weight-for-length z scores are presented (Figure 2). Differences between the higher and lower protein group seem to keep stable over time.

Figure 2: weight for length z-scores trajectories for the age of 0 to 60 months



Publication of this data with complete analyses is planned for the first half of 2011.

2. Effect of protein intake on the metabolic-endocrine response

The investigation of metabolic and endocrine markers in relation to higher protein intake was an additional aim in the CHOP study. Blood parameters including IGF-axis-parameters, serum amino acids, and insulin levels were analysed in respect to protein intake.
Essential and especially branched chain amino acids were significantly higher in the higher protein formula group compared to lower protein. Total and free IGF-1 increased significantly with the higher protein diet as suggested before (2). IGF-BP2 levels were lower in the higher protein group and no association between protein intake and IGF-BP 3 could be detected. Urinary C-peptide/creatinine ratio showed significantly lower values in the lower protein group indicating that higher protein intake enhances insulin secretion. The breastfed group was more similar to the lower protein group.
In summary, higher protein intake stimulates the IGF axis and insulin release in infancy, which may be important for modulating later body size and adiposity risk (5).

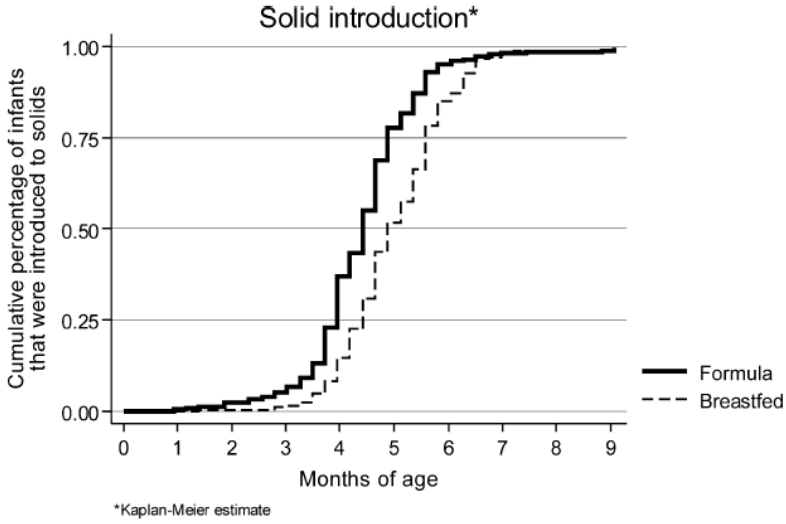
3. Dietary intake

To assess dietary intake in the CHOP study population for the months one to nine (monthly) and for the months 12, 18 and 24 and afterwards annually, a 3-day weighed food protocol was obtained. This data provides the possibility to not only have good estimations for the energy intake of the children but also to give an overview of feeding practices during the first year of life in five European countries and of differences between formula and breast fed infants.

Introduction of complementary feeding in 5 European countries

Although according to the recommendation of the World Health Organization for all countries, complementary food should be introduced from the seventh month of life onwards, advisory boards in industrialized countries continue to recommend and age range from 4 to 6 months of age for the introduction of complementary foods.
Definition of complementary foods and the assessment methods were published previously (6, 7). Summarizing the results, solids were introduced earlier in formula fed (median 19 weeks) than in breastfed (median 21 weeks) infants (Figure 3). Earlier introduction of solids (at 3 and 4 completed months) is associated with maternal age, low education level and maternal smoking. Significant differences were detected between countries for both, formula fed and breastfed infants, with infants in Belgium receiving solids earliest.
Although recommendations are similar across countries and are the same for formula and breastfed infants, there are differences in the time point of introducing complementary foods.

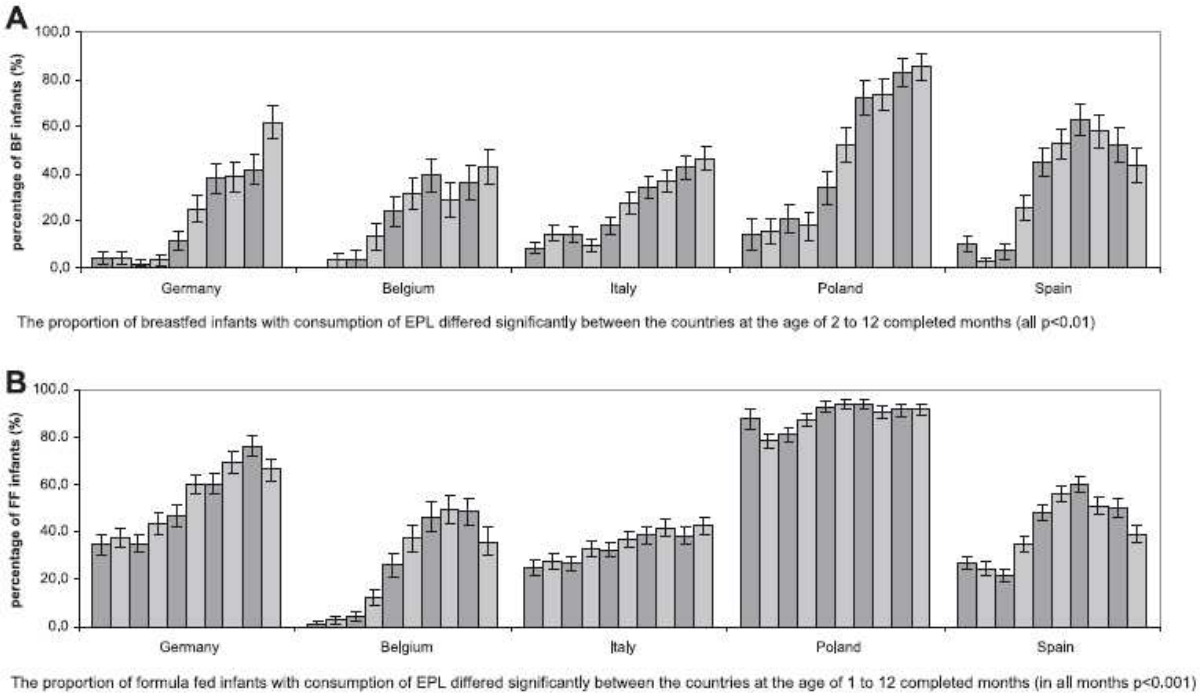
Figure 3: Cumulative percentage of formula and breastfed infants with introduction of solids, per month.



Intake of energy providing liquids during the first year of life in five European countries

The intake of energy providing liquids (EPL) other than breast milk or formula is not recommended for healthy infants during the first year of life. EPL may displace breast milk or formula intake and may adversely affect nutrient supply.
Energy providing liquids were defined as sugared instant tea, fruit juices (100% fruit juice, fruit drinks), vegetable juices provided as drinks and other sugared beverages.
Thirteen percent of breastfed and 43% of formula fed infants received EPL at the age of 4 months with formula fed infants starting earlier (median 17 weeks in formula fed infants and 30 weeks in breastfed infants). Significance differences were also observed between countries (Figure 4). Intake of EPL was associated with a lower intake of formula milk and solids in the first year of life.

Figure 4: Percentage (%) and standard error (SE) of breastfed (A) and formula fed infants (B) with intake of energy providing liquid (EPL) by country, at the age of 1. to 9 and 12 completed months



Since regular intake of EPL not only reduces the intake of formula or breast milk but also increases the risk for later development of dental caries or obesity a better counselling regarding this topic should be given to the caregivers.

4. Effects of maternal postnatal depression

Maternal postnatal depression was assessed in the CHOP cohort using the Edinburgh postnatal depression scale (EPDS) at an infant's age of 2 and 6 months. Postpartum depression has a prevalence of about 10%. Infantile colic and prolonged crying are known risk factors for maternal postnatal depression. This association was also studied in the CHOP population where data of 1015 mothers and infants at the age of 2 and 6 years were available. Excessive crying (crying for at least 3h per day on at least 3 days per week) was defined as infantile colic if recorded 2 months after birth and as prolonged crying if it was present 6 months after birth. Mothers with a score higher than 12 were identified at risk of depression. Infant crying was associated with high EPDS scores at 2 months (OR: 4.4) and 6 months (OR: 10.8) postpartum. Even if crying had resolved mothers of infants with infantile colic still had a higher risk of depression (OR: 3.7) at 6 months postpartum (9).

Maternal postnatal depression was suggested to be associated with positive and negative effects on early infant growth. Therefore in the CHOP cohort weight, length and skinfold thickness at two years of age were explored to differ between children of mothers with high or low EPDS scores. Anthropometrical measures were transformed to z scores according to the 2006 WHO growth standards. Different cut off values for the definition of high risk for postnatal depression were used (<=9, >=13, and categories <9, 10-12, 13-15, >15 for estimation of a linear trend) to look for a potential dose response relationship.

No effects of postnatal maternal depression on anthropometric indices in the first two years of life could be found. A high postnatal maternal depression score is not a risk factor for under- or overweight in childhood in affluent societies.

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