

Nutritional Studies in Childhood

Ph.D. Thesis

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Abbreviations

n-6 fatty acids:

C18:2n-6: linoleic acid (LA)

C18:3n-6: γ -linolenic acid (GLA)

C20:4n-6: arachidonic acid (AA)

n-3 fatty acids:

C18:3n-3: α -linolenic acid (ALA)

C20:5n-3: eicosapentaenoic acid (EPA)

C22:6n-3: docosahexaenoic acid (DHA)

LCPUFA: long-chain polyunsaturated fatty acid

PC: phosphatidylcholine

PE: phosphatidylethanolamine

Fatty acid composition of erythrocyte membrane lipids in healthy subjects from birth to young adulthood

Introduction

Long-chain polyunsaturated fatty acids (LCPUFAs), i.e. products of chain elongation and desaturation of the essential fatty acids, linoleic acid (C18:2n-6) and alpha-linolenic acid (C18:3n-3) are substantial for maintaining various biofunctions in the human organism. N-3 fatty acids are reportedly essential for normal neurodevelopment and may play an important role in the prevention and treatment of coronary artery disease, hypertension, arthritis, other inflammatory and autoimmune disorders, and cancer. Eicosapentaenoic acid (C20:5n-3), dihomo-gamma-linolenic acid (C20:3n-6) and arachidonic acid (C20:4n-6) are precursors of prostaglandins, thromboxanes and leukotrienes, play important roles in the pathophysiology of thrombosis and atherosclerosis as well as immunologic processes and inflammation. Growing children need LCPUFAs not only for eicosanoid biosynthesis and oxidation, but also in relatively large amounts for deposition in growing tissues.

Discovery of the multifaceted roles of LCPUFAs led to application of various LCPUFA metabolites as dietary supplements to pregnant women and as added ingredients to infant formulae. Enhancement of dietary LCPUFA supply has been put forward also in various paediatric diseases. However, LCPUFAs are biologically highly potent compounds requiring close monitoring of any dietary manipulation. Hence, the availability of normal values is a prerequisite of dietary LCPUFA supplementation. Previously we reported fatty acid composition of plasma lipid classes in healthy subjects from birth to young adulthood. The data published have been extensively utilised by the medical community, as indicated by the more than thirty independent citations retrievable via Scientific Citation Index. Recently the importance of the fatty acid composition of erythrocyte membrane lipids increased, because it may better reflect the fatty acid composition of tissues. Therefore, we carried out a cross-sectional study in healthy subjects from birth to young adulthood in order to obtain reference values for erythrocyte membrane phosphatidylcholine and phosphatidylethanolamine lipids.

Subjects and methods

Subjects

One hundred and eighty-eight healthy subjects were enrolled into the study. Cord blood samples were collected in apparently healthy infants born at term after uneventful pregnancies. The infants, children and young adults were investigated in the Department of Paediatrics, University of Pécs, Pécs, Hungary. Because of symptoms presumably unrelated to metabolism or because of minor surgery requiring general anaesthetic. Written informed consents were obtained from the parents of newborns, infants and children as well as from the young adults participating in the study. The study protocol was approved by the ethical committee of the university.

Methods

Venous blood samples of 1 ml volume were drawn into tubes containing EDTA as an anticoagulant. The plasma was removed within 30 min, and the erythrocyte mass was washed three times in isotonic sodium chloride solution. The last sediment was haemolysed in 1 ml volume of distilled water for 20 min at ambient temperature, then 2 ml ice-cold isopropyl alcohol with 0.5% BHT (Butylated hydroxitoluolene, as antioxidant) was added, drop by drop, during continuous shaking. Thereafter, the samples were stored at -80°C until further analysis.

Erythrocyte membrane lipids were separate with the help of thin layer chromatography to phosphatidylcoline (PC) and phosphatidylethanolamine (PE) fractions. During transesterification fatty acid methyl esters were made by a hydrochloric acid methanol. Identification and quantitative determination of fatty acids was made by resolution capillary gas – liquid chromatography, with the use of internal standard.

Fatty acid results were expressed as percentages (weight/weight) of fatty acids detected with a chain length between 12 and 24 carbon atoms.

Statistical analysis

Fatty acid composition was expressed as medians and ranges from the 1st to the 3rd quartile, because skewed distribution were found, particularly for low concentrations of fatty acids. SPSS for Windows, Release 11.0 was used for statistical analysis. Comparisons between fatty acid values in cord blood versus infantile blood were made by using the Mann-Whitney two-

sided rank test. Comparison between fatty acid values in infants, children and young adults were made using the Kruskal-Wallis analysis of non-parametric variance. If this analysis showed statistically significant ($p < 0.05$) variability of the data, the Mann-Whitney two-sided rank test was used for comparisons of fatty acid profiles between groups.

Results

Trans isomeric fatty acids

Both in PC and PE lipids, values of every trans isomeric fatty acids (C16-1n9,t; C18-1n9/7,t and C18-2n6, tt as well as the sum of trans isomers) were significantly higher at birth than in infancy. Values of t16-1n7 significantly decreased between infancy and young adulthood. In contrast, values of t18-1n9/7 and tt18-2n6 were significantly higher in childhood than in infancy. Values of t18-1n9/7 decreased significantly between childhood and young adulthood, whereas values of tt18-2n6 increased significantly further. The values of total trans fatty acids were significantly higher at birth than in infancy; however, no significant differences were seen among infants, children and young adults.

N-6 polyunsaturated fatty acids

The values of C18:2n-6 increased significantly between birth and infancy in both PC and PE lipids, and increased further to young adulthood in PC lipids. Values of C20:4n-6 decreased significantly between infancy and young adulthood in both lipid fractions. Alterations of total n-6 LCPUFA and total n-6 PUFA values mimiced those of C20:4n-6 values.

N-3 polyunsaturated fatty acids

Values of C18:3n-3 increased significantly between birth and infancy in PC lipids. Values of docosahexaenoic acid (C22:6n-3) decreased significantly between birth and infancy, and then significantly increased until young adulthood in PE lipids, whereas no alterations were observed in PC lipids. Values of n-3 LCP and n-3 PUFA exhibited similar alterations as C22:6n-3 values.

Discussion

The fatty acid composition of erythrocyte membrane lipids in children suffering from various diseases has been determined in a number of investigations. Comparison of FA in children and adults and differences between cord blood samples, infants and healthy children were made.

Humans do not synthesize trans-isomeric fatty acids, the trans-isomeric fatty acids which we detected must have originated from the diet. In this present study we found significantly higher trans-isomeric fatty acids values in newborn, than in other groups. In our previous study we reported about a significant inverse association between trans-isomeric and long-chain polyunsaturated fatty acids in cord blood lipids. Long-chain polyunsaturated fatty acids are important for early postnatal visual and cognitive development. Because of trans-isomeric fatty acids inhibit delta6 desaturation of linoleic acid, trans fatty acids reduce the availability of long-chain polyunsaturated fatty acids at birth, which is a serious concern.

There are a lot of investigations concerning with LCPUFA supplementation therefore the publications of normal values are very important.

LIFETIME HEALTH OUTCOMES OF BREAST FEEDING

Introduction

The feeding of infants and young children is an important area of public health policy. Extensive research into the physical, psychological and social implications of breastfeeding (or not breastfeeding) for baby, mother and other family members, has resulted in widespread endorsement of breastfeeding as the gold standard. Many reasons are advanced in favour of breastfeeding, and the impact on the health and wellbeing of the baby is central.

The decisions made by new parents about feeding their infant, particularly the choice between breast and formula milk and the age at which complementary foods are introduced, have significant public health implications. Evidence is accumulating from animal science and human observation studies that early nutrition influences a child's growth, development and lifelong health. Breast milk is a complex natural food containing antibodies, enzymes and hormones. Formula milks have not been able to perfectly replicate the properties of breast milk, and have been associated with a range of short term health problems for babies, particularly increased risks for gastric and respiratory infections. The health consequences of not breastfeeding may also extend into late infancy, childhood, adolescence and beyond, for example, the longer term effects are purported to include elevated risks of obesity, CVD, allergy, type 2 diabetes mellitus and gastro intestinal conditions. In addition, the growing evidence base around the concept of 'programming' suggests that the nutritional environment in the early months of life may 'set' a baby's metabolism with significant lifelong health implications.

Based on an extensive review of the evidence on health outcomes, the World Health Organisation issued a global recommendation in 2001 for six months exclusive breast feeding.

Infant feeding policies are made by various organisations including international agencies, national and regional governments, professional colleges and associations.

Policy documents provide guidance for healthcare professionals who are important intermediaries taking the messages of policy making bodies to consumers. Women, and their partners, have contact with a range of professionals before, during and after the birth of their babies, each of whom have the potential to have a significant influence on how the parents choose to feed their baby.

Parents use various sources to inform their infant feeding decisions. They take advice from family members, friends, and health professionals, consult a range of media sources such as books, leaflets, or the internet, and are exposed opportunistically to information from public health messages, advertisements or programmes on the television. Their decisions may be influenced by a range of considerations, of which the possible implication for the health of the baby is one.

Aims

My thesis reports the findings from three parallel studies undertaken in five European countries (England, Finland, Germany, Hungary and Spain), and conducted within a larger body of work on early nutrition programming. The first study investigated how the lifetime health implications (for the baby) of the choice between breast and formula milk feeding are represented in policy documents in a sample of European countries. The overall aim of the study was to compare the citing of health outcomes in policy documents within and between geographically dispersed European countries with diverse public health nutrition traditions, and to consider the findings in the context of the policy making in Europe. The specific objectives of the study were to: (1) identify and describe the prevailing infant feeding policy documents in five diverse European countries; (2) analyse the types of health outcomes for the infant that are associated with breast rather than formula milk feeding in the documents of different countries; (3) assess the extent to which documents reflect the WHO global recommendation for six months exclusive breast feeding; (4) consider coverage of the emerging concept of early nutritional programming, and the issues associated with bringing new scientific evidence in the policy arena.

In the second and third studies the purpose of the work was to explore what parents can learn from available leaflets and magazine articles about the health implications of the choices they make about feeding their infant in its first year of life. The aims were to (1) investigate the relative importance of written information as an influence on early feeding decisions of first time mothers; (2) explore the characteristics of mothers who stated their infant feeding decisions were influenced by written materials; (3) map the availability of written information for parents in the form of leaflets and articles in parenting magazines; (4) analyse the content of the leaflets and magazines articles with particular reference to statements about the association between feeding behaviours and health outcomes for the baby.

Methods

Policy documents

A search for current policy documents on infant feeding was conducted in five European countries: England, Finland, Germany, Hungary and Spain. We followed established principles of documentary analysis. A standard operating procedure and coding frame was agreed at the outset to ensure that the study was conducted in the same way in each country, and regular meetings were held and attended by all partners.

Documents were located in each country through an open search, including the internet, and by targeting the websites of relevant organisations, using key words: nutrition, diet, breastfeeding, bottle feeding, formula feeding, weaning, complementary feeding, infant feeding and baby (in local languages). Policy documents were retrieved if they contained recommendations or guidelines for healthcare professionals about the feeding of healthy infants in the first year of life, and originated from a government body or a professional association. Documents on websites that were not in PDF or HTML format were excluded. Titles of documents were translated into English if necessary, and bibliographic information and a brief description of content were stored in a central database.

Statements were entered verbatim into a database using the SPSS statistical software package, with an English translation, where necessary. Each statement was coded by the type of feeding behaviour to which it referred (exclusive breastfeeding for unspecified time or less 6 months / 6 months or more; breastfeeding in general of unspecified duration; formula feeding), and by health outcome (22 health benefits associated with breast (rather than formula) feeding, which were grouped into four main categories: health in general; infections; allergy; long term conditions). Use of SPSS facilitated manipulation of the data for the analysis of statements by country, document, type of milk feeding behaviour and health outcome. Following principles of documentary analysis, and the number of statements per health outcome, document and country were calculated to allow comparisons.

Influences on infant feeding choices

Data on sources of information on infant feeding by parents were collected by means of two questionnaires distributed to cohorts of mothers in the five countries shortly after the birth of their baby, and eight months later. The study focussed on first time mothers because they were more likely than multiparous mothers to have recently collected information on feeding methods. Following discussion amongst all partners, the survey instruments were initially produced and piloted in England, and then translated into Finnish, German, Hungarian and

Spanish. Minor cultural adaptations were made to accommodate national differences, for example, the role of General Practitioners (GPs) in England and Finland rather than specialist doctors in Germany, Hungary and Spain.

Ethical approval was obtained locally in each country. Mothers were recruited through local maternity hospitals. Recruitment continued in each country until 400 mothers had returned a completed questionnaire. The questionnaire was in three sections: (A) About the baby: gestation, weight at birth, gender; (B) About feeding the baby: milk vs formula intentions prior to weaning (exclusive breast, exclusive formula, breast and formula), views about how infant feeding affects lifelong health, sources of information on infant feeding; (C) Background socio- economic and demographic characteristics of the mother: age, country of birth, language spoken at home, family income, living arrangements, education, health related behaviours (smoking, diet, healthy eating, physical activity), pre-pregnancy BMI, employment, health history.

The question on sources of infant feeding information asked the extent to which each of 17 possible sources influenced mothers' decisions about how to feed their baby (not at all, slightly, moderately, very much, extremely). The 17 sources were grouped into three categories: family and friends (partner, parents, other relatives, friends); health care professionals (General Practitioner / doctor, antenatal midwife, staff in hospital, other health care professionals, private antenatal class); media (leaflets, advertisements, TV programmes, radio programmes, internet, books, magazines, videos / DVDs).

All mothers who provided data at baseline were mailed a follow up questionnaire when their baby was eight months old. This questionnaire asked them to self report their milk feeding and weaning behaviours and probed further their views on how infant nutrition affected healthy growth and development. The baseline question on sources of information on infant feeding was repeated so that changes could be assessed.

Responses to both questionnaires were entered into SPSS version 15 database and descriptive statistics were calculated. Forward stepwise regression modelling was used to explore, for each country separately, the characteristics of mothers who reported that written materials influenced their infant feeding decisions. The dependent variable was whether or not mothers reported that their infant feeding choices were moderately, very much or extremely influenced by leaflets / magazines / books (separate models), at the time of the birth of their baby, and eight months later. Data relating to the baby, feeding intentions and background characteristics of the mother were entered into the model as potential explanatory variables.

Consumer information

A search for leaflets (defined to include small booklets and information sheets) was conducted in each country through an open internet search and by targeting the websites of relevant organisations (national and regional government agencies, professional associations, interest groups, retail and manufacturing industries) using the key words: nutrition, diet, breast feeding, bottle feeding, formula feeding, weaning, complementary feeding, infant feeding and baby (in local languages). Leaflets were collected if they referred to the feeding or nutrition of healthy infants aged 0 – 12 months. Materials targeting pregnancy, older children, health professionals or focussing on legal or practical aspects were excluded. Titles of leaflets were translated into English (if necessary), and bibliographic information and a brief description of the content were stored in a central database. Coding frames for statements were the same than in policy documents.

In order to assess information on infant feeding in magazines, the most popular monthly parenting magazine for each country (defined on the basis of annual average circulation figures) was identified. All 12 issues were screened for articles (including notes or comments) on the feeding or nutrition of healthy infants aged 0 -12 months. Articles on nutrition in pregnancy or for toddlers, and advertisements or promotional text were excluded. Statements that related a feeding behaviour to a health outcome for the baby were identified in each article and processed in the same way as the statements from leaflets.

Results

Twenty six policy documents were included in the analysis: England (4), Finland (2), Germany (9), Hungary (6), Spain (5).

National governments dominated the policy arena in England and Finland. In these countries the search identified substantial expert reports providing the background and evidence – based recommendations for health care professionals. In England, two summary documents in support of the WHO global recommendation for six month exclusive breast feeding were also available. In Germany, Hungary and Spain, most guidance for front line health care staff is provided by professional associations. Documents in Hungary tended to be shorter, and not to cite references in support of recommendations. All documents except two in Hungary and one in England had been published in the five years prior to the study.

A total of 203 statements about the health implications for the baby of the choice between breast and formula feeding were extracted from the policy documents that were included in the most statements referred to protection afforded by breast feeding against infections (32.5% of all statements) and longer term conditions (31.5%). About a quarter of statements

referred to the health benefits of breast feeding in general, and about one eighth to protection against allergy. Considering only the documents containing any health outcome statements, those from Germany and Finland had the highest number of statements per document, and Hungary had the lowest.

Generic statements about the health benefits of breast feeding, compared to formula (n=49) were most common in Finnish documents (2.3 statements per document vs mean of 4.0 for the other four countries), and positive effects on neurological and mental development were the most frequently cited advantages in this group (n=19; 38.8%) vs n=10 (20.4%) for each of the other outcomes). Statements that referred to reduced risk of infection (n=66) mainly concerned the protection provided by breast feeding against gastro-intestinal (n=16; 24.2%) and respiratory / chest infections (n=15; 22.7%) of 66 statements respectively). All documents in England and Finland mentioned gastric infections, but this was not the case in the other three countries. Infection was mentioned less in documents from Hungary (1.3 statements per document) than in those of other countries (mean of 4.3). The benefit of breast feeding for protection against allergy was mostly presented in general terms (14 (58.3%) of 24 statements).

Most of the health outcome statements (n=152; 74.9%) referred to breastfeeding in general and did not specify whether the health effect was dependent on the duration of breast feeding or exclusivity. Eleven of the 26 policy documents that were included in the analysis were published after the release of the WHO global recommendation, but only the English infant feeding recommendations from the Department of Health referred in any detail to this evidence (in five statements).

The term 'programming' was mentioned by name in three documents, twice in the context of long term metabolic effects and once for the 'anti- inflammatory and immune modulating factors which programme the child's defence system so the child has less risk of immune disease later in life.

Information sources used by new mothers

A total of 2071 first time mothers completed baseline questionnaires in the five countries. The response rates to the eight month follow up questionnaire were: England, 80.8%; Finland, 91.1%; Germany, 86.2%; Hungary, 85.2%; Spain, 47.3%.

The proportions of mothers rating the influence of each of the possible sources of information on how to feed their baby as moderately, very much or extremely important at birth and eight month follow up are higher at follow up than baseline, except for 'staff in hospital' and 'private antenatal class'. There were some changes in ranking between baseline and follow

up: antenatal midwife dropped down, and parents, partners, GPs/ doctors, other health professionals and internet were all reported to be relatively more important. For many types of information, the overall ranking reflects an averaging across large inter-country differences.

Influence of written information

Written sources of information are important to larger numbers of mothers than audio- visual approaches.

Availability of written information: leaflets and magazines

The search for leaflets revealed 127 separate publications. At least half of the leaflets in Finland and Hungary were produced by special interest groups (e.g. breast feeding support groups), and in Germany were produced by manufacturers or retailers of formula milk or infant foods. Government sources were important in England and Spain.

Statements about health outcomes for baby in leaflets and magazine articles that covered milk feeding

A total of 516 statements about the implications for the baby of the choice between breast and formula feeding were extracted from consumer information materials across the five countries (395 from 105 leaflets, 121 from magazine articles). Some leaflets (n=24, 22.9%) contained no statements about the health implications of breast vs formula feeding (12 of 35, 34.3% in Hungary). The leaflets with health explanations to guide consumer choices contained an average of 4.9 statements (range 3.0 Finland to 6.5 Germany). About one third of the statements referred to protection afforded by breastfeeding against infections, and a further one third to a range of general health benefits from breast feeding.

The analysis of the content of the magazines revealed little attention to milk feeding issues (56 articles in a total of 60 issues, of which 44 articles mention health outcomes). Statements on the health implications for the baby of the choice between breast and formula feeding averaged about two per issue (range 0.25 Finland to 7.2 England). Protection against infection was the most frequently cited advantage of breastfeeding.

Of the 395 statements in leaflets, 19 (4.8%) were explicitly related to the six month exclusive breastfeeding recommendation of the WHO. The equivalent figure for the magazine statements was 21 / 121 (17.4%).

Statements about health outcomes for baby in leaflets and magazine articles that covered complementary feeding

A total of 193 statements on the health implications for the baby of CF behaviours were extracted across the five countries (117 from 69 leaflets, 76 from magazines). None of the leaflets in Finland or Hungary contained statements that met the study inclusion criteria on the health implications for infants of introducing CF. Overall, only 25 (of 69, 36%) of leaflets had eligible statements.

The leaflets with statements that related the introduction of complementary foods and beverages to infant's health contained an average of 4.7 statements. Most statements (48/117, 41.0%) related to possible allergy reactions from specific foods (mainly eggs, nuts, wheat / gluten). Nearly one in five statements related various foods to long term health conditions. A small proportion of statements (14/117, 12%) referred to the establishment of good eating habits, and the rest gave advice on potential health risks associated with particular foods or feeding behaviours. Magazines contained an average of 1.3 statements per issue. There were no health outcome statements in any issue of the Finnish or Spanish magazines. Again, allergy was the main health issue raised (46.1% of statements).

Discussion

Systematic assessments of the evidence base show differences in interpretation. Whilst some reviewers endorse the evidence about the protective effect of breast feeding for diseases like lymphoma, insulin dependent diabetes mellitus and Crohns, others adopt a more cautious position. Although increased susceptibility of non breastfed infants to respiratory tract infection and otitis media, other evidence suggests that prolonged breastfeeding does not protect against these illnesses. Similar debates exist regarding allergy. Recent studies conclude that breastfeeding does not reduce the risk of allergy or asthma, or that the evidence is equivocal, but others suggest an association between increased risk of atopic disease and feeding formula milk.

Differences between the portfolios of policy documents of individual countries may reflect variations in the structure of health services, resources, history and culture. More substantive policy documents on infant feeding are available in England and Finland, where health care is financed and delivered through public sector arrangements. The greater diversity of agencies producing policy documents on infant feeding in Hungary, Germany and Spain may reflect the more pluralistic nature of their health care systems. Moreover, professional associations are more important in the policy arena in these countries because maternity and infant

services are routinely provided by specialist obstetricians and pediatricians, rather than by general practitioners and primary care teams, as occurs in England and Finland.

Several recent studies have found low rates of breastfeeding, poor weaning practices and variability within and between nations, and as a result there have been calls for a consistent approach across Europe. Accordingly, public health policy in the EU is currently seeking to increase the number of mothers who chose to breastfeed their babies. In this context, the policy and information environment facing healthcare professionals and the general public plays a strategic role, and the findings of this study are timely. Cross national comparisons are important because they offer scope for public policy learning.

The WHO global recommendation for six months exclusive breast feeding provides another example of how experts can disagree. Based on a systematic review of more than 2000 papers, the WHO report concluded that there was no evidence that six months exclusive breast feeding (compared to 4 – 6 months exclusive breast feeding) had an adverse effect on growth and development, but that it did have a protective effect against gastrointestinal (but not respiratory) infections. This is a landmark in infant feeding policy, but only two of the policy documents (both from England) in the five countries in this study referred to it.

There were approximately five statements per leaflet in the ones which contained information on health effects, and these mostly focussed on generic health benefits and immediate short term implications such as protection against infections (in the case of milk feeding) and protection against allergy (for complementary feeding). There was less mention of possible long term effects of feeding choices.

This study has shown that about 50% of first time mothers across five European countries report that leaflets (small booklets and information sheets) and articles (or notes) in magazines influenced their decisions about how to feed their eight month old infant moderately, very much or extremely. Sources of information which were important to larger proportions of mothers were books, their antenatal midwife, partner, staff in hospital (at birth only), and the GP / doctor and parents (during the eight months following birth). In line with previous research, the survey of mothers revealed that multiple and concurrent sources of information are accessed to inform infant feeding choices, and that the relative importance of these varied influences can change over time.

Data show that larger proportions of mothers state their feeding choices were influenced by leaflets in countries where smaller numbers of leaflets were identified (Finland and Germany). In contrast, the influence of leaflets was reported as less in countries where more were available (especially Hungary).

Future developments in the area of infant feeding policy are likely to be influenced by output from ongoing research on metabolic programming, and the effect of the early nutrition environment on lifelong health. The concept of programming is rarely represented in policy in the countries in this study. As the flow of research findings on this issue intensifies, it is important that policy makers are able to evaluate the scientific evidence and provide a clear account for health care professionals about what is known about the lifelong health implications, and the associated areas of uncertainty. In this way, consumers will receive full and balanced information on which to make choices about feeding their infant, and public health considerations will be properly addressed.

New results

1. We provided reference values for erythrocyte membrane lipid composition in healthy subjects for birth to young adulthood.
2. Our results regarding essential fatty acids (LA, ALA) and their long-chain polyunsaturated metabolites (AA, DHA) may be used for further scientific research as well as for composing special diet for children suffering from disturbed fatty acid metabolism.
3. Significantly higher trans fatty acid values found in erythrocyte membrane of newborns attract the attention of the potentially harmful effects of trans fatty acid exposure of pregnant women.
4. We found that although the importance of nutritional programming is formulated in publications for parents published in five European countries; however these statements mainly deal with short-term effects of infant nutrition. Further efforts are needed to inform the society about the long term effect of infant feeding.
5. Comparing the options of the included mothers in different European countries, it can be concluded that there are substantial differences in the knowledge about nutritional programming. The option of the Spanish mothers is more likely (44%), while the option of Hungarian mothers is less likely (20%) that the method of infant nutrition may have long-term effect on the health of children.
6. There are significant differences in the acceptance of nutritional programming regarding its role in the later development of some disease. 50% of the mothers think that the quality of infant feeding has effect on development of allergies but only 18% of them think that it can have effect on the formation of malignant tumours.

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