Maternal omega-3 rich-diet linked to improved infant problem solving: Study

By Will Chu

03-Jul-2018 - Last updated on 03-Jul-2018 at 15:59 GMT

The benefits of omega-3 fatty acids were highlighted again in a Norwegian study that demonstrates the positive effect a maternal diet rich in the oil can have on a child's problem-solving abilities.

The researcher's findings suggest that a mother's intake of the omega-3 fatty acid docosahexaenoic acid (DHA) in pregnancy was associated with an infant's skill in problem solving at 12 months.

"We see a clear connection between mother's omega-3 status and the children's ability to solve problems, and the same effect we see at the child's level of fatty acids when they are three months," explained study researcher and research scientist at the Institute of Marine Research, Maria Wik Markhus.

Since higher problem-solving scores in infancy are related to higher childhood IQ scores, the study emphasises the importance of adequate DHA intake before the rapid growth of infant brains during the last trimester of pregnancy.

"The level of DHA decreases in pregnancy and after birth," added Markhus. *"It is therefore important for pregnant women to get enough omega-3 fatty acids, either through diet as fat fish or by dietary supplements."*

The findings correlate well with recent work that looks into the beneficial effects of omega-3 fatty acid consumption during pregnancy on child development.

A UK **study** found that maternal seafood intakes of more than 340 grams (g) per week decreased the risk of their children being in the lowest quartile for verbal intelligence quotient (IQ), when compared with mothers who consumed less than 340 g per week.

Indeed, the European Food Safety Authority (EFSA) recommends pregnant and lactating women to take 100-200 milligrams (mg) of DHA per day in addition to general adult requirements.

DHA

Indian J Pediatr. 2005 Mar;72(3):239-42.
Essential fatty acids, DHA and human brain.
Singh M.

Abstract
Essential fatty acids cannot be synthesized in the body but they are required for maintenance of optimal health. There are two classes of polyunsaturated fatty acids (PUFAs)--omega-6 and omega-3. The parent omega-6 fatty acid, linoleic acid (LA) is desaturated in the body to form arachidonic acid while parent omega-3 fatty acid alpha-linolenic acid (ALA) is desaturated by microsomal enzyme system through a series of metabolic steps to form eicosapentaenoic acid (EPA) and decosahexaenoic acid (DHA). But there is a limited metabolic capability during early life to metabolize PUFAs to more active long-chain fatty acids. There is a critical role of EFAs and their metabolic products for maintenance of structural and functional integrity of central nervous system and retina. Most of the brain growth is completed by 5-6 years of age. At birth brain weight is 70% of an adult, 15% brain growth occurs during infancy and remaining brain growth is completed during preschool years. DHA is the predominant structural fatty acid in the central nervous system and retina and its availability is crucial for brain development. It is recommended that the pregnant and nursing woman should take at least 2.6 g of omega-3 fatty acids and 100-300 mg of DHA daily to look after the needs of her fetus and suckling infant. The follow-up studies have shown that infants of mothers supplemented with EFAs and DHA had higher mental processing scores, psychomotor development, eye-hand coordination and stereo acuity at 4 years of age. Intake of EFAs and DHA during preschool years may also have a beneficial role in the prevention of attention deficit hyperactivity disorder (ADHD) and enhancing learning capability and academic performance.

Feb 7, 2019 - A new Cochrane Review published today has found that increasing the intake of omega-3 long-chain polyunsaturated fatty acids (LCPUFA) during pregnancy reduces the risk of premature births.

Premature birth is the leading cause of death for children under 5 years old worldwide, accounting for close to one million deaths annually. Premature babies are at higher risk of a range of long-term conditions including visual impairment, developmental delay and learning difficulties.

'We know premature birth is a critical global health issue, with an estimated 15 million babies born too early each year,' explains Cochrane Pregnancy and Childbirth lead author Associate Professor Philippa Middleton.

'While the length of most pregnancies is between 38 and 42 weeks, premature babies are those born before the 37 week mark – and the earlier a baby is born, the greater the risk of death or poor health.'

The author team took a close look at long-chain omega-3 fats and their role in reducing the risk of premature births – particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) found in fatty fish and fish oil supplements. They looked at 70 randomised trials and found that for pregnant women, increasing the daily intake of long-chain omega-3s:

- lowers the risk of having a premature baby (less than 37 weeks) by 11% (from 134 per 1000 to 119 per 1000 births
- lowers the risk of having an early premature baby (less than 34 weeks) by 42% (from 46 per 1000 to 27 per 1000 births)
- reduces the risk of having a small baby (less than 2500g) by 10%

'There are not many options for preventing premature birth, so these findings are very important for pregnant women, babies and the health professionals who care for them,' Philippa says. 'We don't yet fully understand the causes of premature labour, so predicting and preventing early birth has always been a challenge. This is one of the reasons omega-3 supplementation in pregnancy is of such great interest to researchers around the world.'

The Cochrane review published today was first undertaken back in 2006, and concluded there wasn't enough evidence to support the routine use of omega-3 fatty acid supplements during pregnancy. Over a decade on, this updated review concludes that there's high quality evidence for omega-3 supplementation being an effective strategy for preventing preterm birth.

'Many pregnant women around the world are already taking omega-3 supplements by personal choice rather than as a result of advice from health professionals,' Philippa says. 'It's worth noting though that many supplements currently on the market don't contain the optimal dose or type of omega-3 for preventing premature birth. **Our review found the optimum dose was a daily supplement containing between 500 and 1000 milligrams (mg) of long-chain omega-3 fats (containing at least 500mg of DHA) starting at 12 weeks of pregnancy.'**

Am J Clin Nutr. 2018 Jan 1;107(1):35-42. doi: 10.1093/ajcn/nqx007.

Intrauterine DHA exposure and child body composition at 5 y: exploratory analysis of a randomized controlled trial of prenatal DHA supplementation.

Hidaka BH[1], Thodosoff JM[1], Kerling EH[1], Hull HR[1], Colombo J[2], Carlson SE[1].

Abstract

BACKGROUND:

Observational studies find associations between maternal docosahexaenoic acid (DHA) and greater fat-free mass and lower percentage of body fat, but randomized trials of prenatal DHA supplementation have not found significant intent-to-treat effects on childhood body composition.

OBJECTIVE:

This study sought to explore associations between intrauterine DHA exposure and body composition and size at 5 y in the offspring of women who participated in a randomized trial of prenatal DHA supplementation (corn and soybean oil placebo or 600 mg/d).

DESIGN:

At 5 y, body composition was measured by air displacement plethysmography in 154 offspring of women who had participated in the Kansas University DHA Outcomes Study and who had red blood cell (RBC) phospholipid (PL) fatty acids assessed at enrollment and delivery. We used linear regression models to analyze the relation among 3 indicators of intrauterine DHA exposure-1) intent-to-treat (placebo or DHA), 2) maternal RBC PL DHA status at delivery, and 3) change in maternal DHA (delivery minus enrollment)-and 6 outcomes of interest: 5-y fat mass, fat-free mass, percentage of body fat, height, weight, and body mass index z score.

RESULTS:

Change in maternal RBC PL DHA correlated with higher fat-free mass ($r = 0.21$, $P = 0.0088$); the association was unchanged after adjustment for maternal, perinatal, and childhood dietary factors. Intent-to-treat and DHA status at delivery showed positive trends with fat-free mass that were not statistically significant. There was no evidence relating intrauterine DHA exposure to any other body composition measure.

CONCLUSIONS:

Change in maternal DHA status during pregnancy was related to higher offspring 5-y fat-free mass. The other 2 indicators of intrauterine exposure to DHA suggested a trend for higher offspring 5-y fat-free mass. Our findings agree with an earlier observational study from the United Kingdom.

Polyunsaturated Fatty Acids in Perinatal Depression: A Systematic Review and Meta-analysis

Pao-Yen Lin et al.

Biological Psychiatry .2017.02.1182

Abstract

BACKGROUND

Omega-3 (or n-3) polyunsaturated fatty acids (PUFAs) are promising antidepressant treat-ments for perinatal depression (PND) because of supporting evidence from clinical trials, the advantage in safety, and their anti-inflammatory and neuroplastic effects. Although several observational studies have shown n-3 PUFA deficits in women with PND, the results of indi-vidual PUFAs from different studies were inconsistent.

METHODS

This systematic review and meta-analysis aims to compare the levels of PUFA indices, in-cluding eicosapentaenoic acid, docosahexaenoic acid, arachidonic acid, total n-3, total n-6, and the n-6/n-3 ratio between women with PND and healthy control subjects. The meta-a-nalysis included 12 eligible studies available as of December 2016. The effect sizes were synthesized by using a random effects model. In addition, we performed subgroup analysis for the PUFA levels in patients with prenatal and postnatal depression, both of which were compared with healthy control subjects.

RESULTS

There were significantly lower levels of total n-3 PUFAs and docosahexaenoic acid and si-gnificantly increased n-6/n-3 ratios in PND patients. In the subgroup analyses, there were significantly lower levels of n-3 PUFAs, eicosapentaenoic acid, and docosahexaenoic acid in women with prenatal depression. The n-6/n-3 ratio was significantly increased in both pre-natal and postnatal depression subgroups.

CONCLUSIONS

Our meta-analysis consolidates the important role of n-3 PUFAs in PND. Nutritional medi-cine is an important strategy to improve the effectiveness of treatment for depression, and our findings provide the strong rationale to conduct clinical trials to test the therapeutic and prophylactic effects of n-3 PUFAs in PND.

Citation: Translational Psychiatry (2017) 7, e1229; doi:10.1038/tp.2017.182
Published online 5 September 2017

Polyunsaturated fatty acid deficiency during neurodevelopment in mice models the prodromal state of schizophrenia through epigenetic changes in nuclear receptor genes

M Maekawa et al.1
Received 17 April 2017; Revised 26 June 2017; Accepted 6 July 2017
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Abstract
The risk of schizophrenia is increased in offspring whose mothers experience malnutrition during pregnancy. Polyunsaturated fatty acids (PUFAs) are dietary components that are crucial for the structural and functional integrity of neural cells, and PUFA deficiency has been shown to be a risk factor for schizophrenia. Here, we show that gestational and early postnatal dietary deprivation of two PUFAs—arachidonic acid (AA) and docosahexaenoic acid (DHA)—elicited schizophrenia-like phenotypes in mouse offspring at adulthood. In the PUFA-deprived mouse group, we observed lower motivation and higher sensitivity to a hallucinogenic drug resembling the prodromal symptoms in schizophrenia. Furthermore, a working-memory task-evoked hyper-neuronal activity in the medial prefrontal cortex was also observed, along with the downregulation of genes in the prefrontal cortex involved in oligodendrocyte integrity and the gamma-aminobutyric acid (GABA)-ergic system. Regulation of these genes was mediated by the nuclear receptor genes Rxr and Ppar, whose promoters were hyper-methylated by the deprivation of dietary AA and DHA. In addition, the RXR agonist bexarotene upregulated oligodendrocyte- and GABA-related gene expression and suppressed the sensitivity of mice to the hallucinogenic drug. Notably, the expression of these nuclear receptor genes were also downregulated in hair-follicle cells from schizophrenia patients. These results suggest that PUFA deficiency during the early neurodevelopmental period in mice could model the prodromal state of schizophrenia through changes in the epigenetic regulation of nuclear receptor genes.

Am J Clin Nutr. 2016 Oct;104(4):1075-1082. Epub 2016 Sep 7.

Prenatal supplementation with DHA improves attention at 5 y of age: a randomized controlled trial.

Ramakrishnan U et al.

BACKGROUND:
Docosahexanoic acid (DHA) is an important constituent of the brain. Evidence from well-designed intervention trials of the long-term benefits of increasing DHA intake during pregnancy has been sparse.

OBJECTIVE:
We evaluated global cognition, behavior, and attention at age 5 y in the offspring of Mexican women who participated in a randomized controlled trial of prenatal DHA supplementation.

DESIGN:
A total of 1094 women were randomly assigned to receive 400 mg of either DHA or placebo/d from 18 to 22 wk of pregnancy until delivery. We assessed cognitive development and behavioral and executive functioning, including attention, in 797 offspring at age 5 y (82% of 973 live births) with the use of the McCarthy Scales of Children's Abilities (MSCA), the parental scale of the Behavioral Assessment System for Children, Second Edition (BASC-2), and the Conners' Kiddie Continuous Performance Test (K-CPT). We compared the groups on raw scores, T-scores, and standardized scores, as appropriate. We examined heterogeneity by the quality of the home environment, maternal intelligence, and socioeconomic status.

RESULTS:
There were no group differences for MSCA scores ($P > 0.05$), but the positive effect of the home environment at 12 mo on general cognitive abilities was attenuated in the DHA group compared with in the placebo group (P-interaction < 0.05). There were no differences between groups on the BASC-2. On the K-CPT, offspring in the DHA group showed improved mean ± SD T-scores compared with those of the placebo group for omissions (DHA: 47.6 ± 10.3; placebo: 49.6 ± 11.2; $P < 0.01$) with no differences ($P > 0.05$) for the other K-CPT scores or of the proportion who were clinically at risk of attention deficit hyperactivity disorders after Bonferroni correction for multiple comparisons.

CONCLUSION:
Prenatal exposure to DHA may contribute to improved sustained attention in preschool children.

Biochimie. 2011 Jan;93(1):7-12. doi: 10.1016/j.biochi.2010.05.005.
Docosahexaenoic acid (DHA) and the developing central nervous system (CNS) - Implications for dietary recommendations.
Guesnet P, Alessandri JM.

Abstract
The accretion of docosahexaenoic acid (DHA) in membranes of the central nervous system is required for the optimum development of retina and brain functions. DHA status is determined by the dietary intake of n-3 polyunsaturated fatty acids (PUFA), both the metabolic precursor α-linolenic acid (α-LNA) and DHA. Clinical studies have shown that feeding term or premature infants with formula low in total n-3 PUFA may alter the maturation of visual acuity. Moreover, feeding infants over the first 6 mon of life with formula containing adequate α-LNA, but no DHA, did not sustain the same cerebral accretion of DHA as that of breast-fed infants. Whether lower DHA accretion in brain of formula-fed term infants impairs neurophysiological performances is not clearly established. Contradictory data have been published, possibly owing to confounding factors such as maternal intakes and/or genetic variations in PUFA metabolism. Nevertheless, a large corpus of data is in favor of the recommendation of regular dietary intakes of DHA (during at least the first 6 mon of life) and suggest that DHA should be added in formulas at the level generally found in human milk (0.2-0.3 wt% of total fatty acids). The maternal intake of n-3 PUFA during pregnancy and lactation is also crucial, since the n-3 PUFA are provided during perinatal development through placental transfer and maternal milk, which determines the DHA status of the newborn and consequently impacts on post-natal development of brain and visual functions. Whether more clinical studies are needed to control and improve the impact of DHA maternal intakes on the progeny's neurodevelopment, several commissions recommended by precaution that DHA average intake for pregnant and lactating women should be of 200-300 mg/day.

Am J Clin Nutr. 2013 Apr;97(4):808-15. doi: 10.3945/ajcn.112.050021.

DHA supplementation and pregnancy outcomes.

Carlson SE, Colombo J, Gajewski BJ, Gustafson KM, Mundy D, Yeast J, Georgieff MK, Markley LA, Kerling EH, Shaddy DJ.

Abstract

BACKGROUND:

Observational studies associate higher intakes of n-3 (omega-3) long-chain polyunsaturated fatty acids (LCPUFAs) during pregnancy with higher gestation duration and birth size. The results of randomized supplementation trials using various n-3 LCPUFA sources and amounts are mixed.

OBJECTIVE:

We tested the hypothesis that 600 mg/d of the n-3 LCPUFA docosahexaenoic acid (DHA) can increase maternal and newborn DHA status, gestation duration, birth weight, and length. Safety was assessed.

*DESIGN***:**

This phase III, double-blind, randomized controlled trial was conducted between January 2006 and October 2011. Women (n = 350) consumed capsules (placebo, DHA) from <20 wk of gestation to birth. Blood (enrollment, birth, and cord) was analyzed for red blood cell (RBC) phospholipid DHA. The statistical analysis was intent-to-treat.

RESULTS:

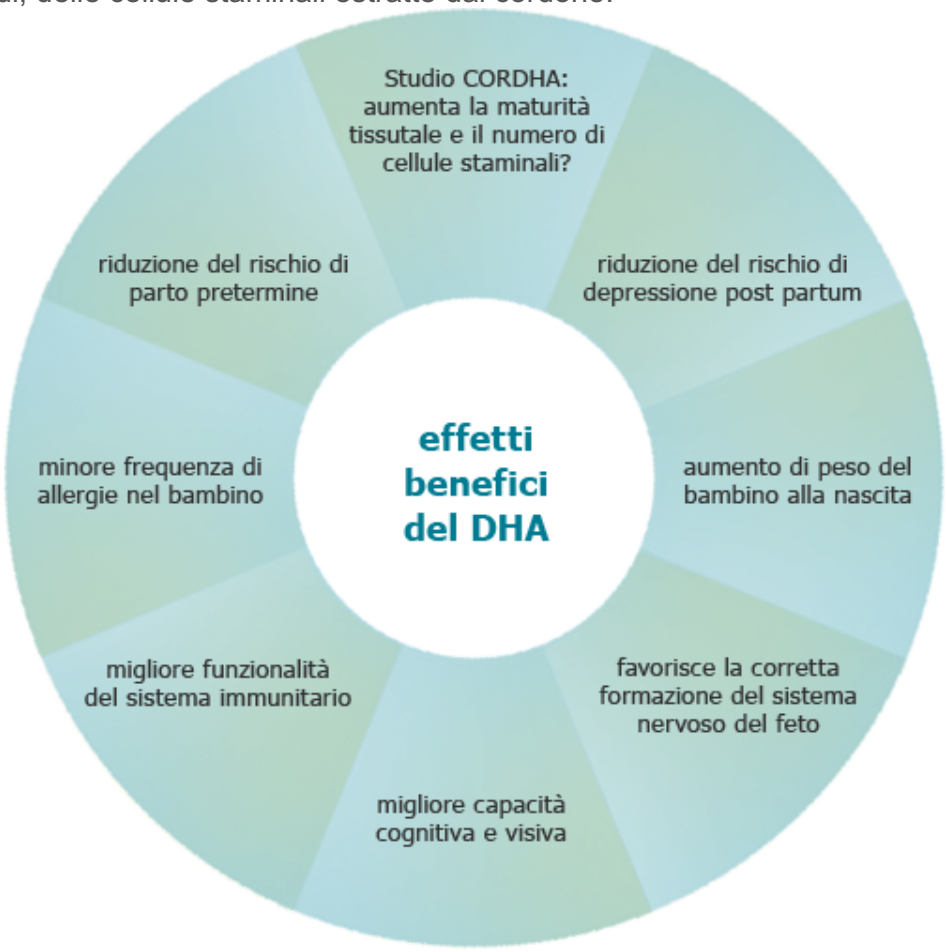
Most of the capsules were consumed (76% placebo; 78% DHA); the mean DHA intake for the treated group was 469 mg/d. In comparison with placebo, DHA supplementation resulted in higher maternal and cord RBC-phospholipid-DHA (2.6%; P < 0.001), longer gestation duration (2.9 d; P = 0.041), and greater birth weight (172 g; P = 0.004), length (0.7 cm; P = 0.022), and head circumference (0.5 cm; P = 0.012). In addition, the DHA group had fewer infants born at <34 wk of gestation (P = 0.025) and shorter hospital stays for infants born preterm (40.8 compared with 8.9 d; P = 0.026) than did the placebo group. No safety concerns were identified.

CONCLUSIONS:

A supplement of 600 mg DHA/d in the last half of gestation resulted in overall greater gestation duration and infant size. A reduction in early preterm and very-low birth weight could be important clinical and public health outcomes of DHA supplementation. This trial was registered at clinicaltrials.gov as NCT00266825.

Studio Clinico CORDHA

Lo studio clinico CORDHA, sulla "*Ottimizzazione della vitalità delle cellule staminali cordonali dopo somministrazione del DHA durante il terzo trimestre di gravidanza*", promosso da SmartBank, attraverso l'attività di SmartBank Foundation, aveva l'obiettivo di dimostrare come il **DHA**, somministrato in gravidanza, determini un incremento della maturità tissutale e della vitalità, quindi, delle cellule staminali estratte dal cordone.



Il **DHA (acido docosaesaenoico)** è un acido grasso essenziale della linea Omega 3, sempre meno presente nella dieta occidentale per il basso consumo di pesce; viene normalmente prescritto alle **donne in gravidanza** come integratore della dieta alimentare per i suoi benefici effetti sulla mamma e sullo sviluppo neurocognitivo, psicomotorio e visivo del feto.

Assieme a proteine, ferro, calcio, magnesio e vitamina B rappresenta un nutriente cruciale durante la seconda parte della gestazione, quando avviene il 90% della crescita fetale. *

Tra gli effetti benefici degli **Omega-3:** la riduzione della pressione sanguigna, la stimolazione della produzione di ormoni e delle fibre nervose,la regolazione della temperatura corporea e delle vie bronchiali.
Ciò è particolarmente importante per la **conservazione delle cellule staminali**, in quanto il limite dell'utilizzo dell'unità cordonale a scopo terapeutico è legato al numero e alla vitalità delle cellule presenti: generalmente le quantità raccolte dal cordone ombelicale sono sufficienti per il trapianto in un bambino di 14 anni, mentre per un adulto potrebbe essere necessario reperire un ulteriore unità di cellule, da un donatore compatibile o mediante l'espansione delle staminali in laboratorio, per un trapianto "combinato".
Più alta sarà la quantità e la vitalità, quindi, delle cellule raccolte al momento del prelievo, maggiore sarà il potenziale per i futuri utilizzi terapeutici.
Oggi, a dimostrare la validità di questo studio clinico, portato avanti con un team di biologi dell'Università " La Sapienza" di Roma, medici e ostetriche del Dipartimento di Ostetrica e Ginecologia dell'Ospedale Fatebenefratelli di Roma e ricercatori ISOF del CNR di Bologna, **sono i risultati** che la d.ssa **Irene Martini**, direttore scientifico di SmartBank, ha **presentato a Montecarlo**, in occasione del quarto **Congresso Mondiale ESH/NetCord/Eurocord sulle** "**Cellule staminali del cordone ombelicale**" organizzato dal 24 al 27 ottobre '13.

VITAMINA B2

Crit Rev Food Sci Nutr. 2016 Mar 30:0.
Riboflavin and health: A review of recent human research.
Thakur K, Tomar SK, Singh AK, Mandal S, Arora S.

Abstract
There has lately been a renewed interest in Riboflavin owing to insight into its recognition as an essential component of cellular biochemistry. The knowledge of the mechanisms and regulation of intestinal absorption of riboflavin and its health implications has significantly been expanded in recent years. The purpose of this review is to provide an overview of the importance of riboflavin, its absorption and metabolism in health and diseased conditions, its deficiency and its association with various health diseases and metabolic disorders. Efforts have been made to review the available information in literature on the relationship between riboflavin and various clinical abnormalities. The role of riboflavin has also been dealt in the prevention of a wide array of health diseases like migraine, anemia, cancer, hyperglycemia, hypertension, diabetes mellitus and oxidative stress directly or indirectly. The riboflavin deficiency has profound effect on iron absorption, metabolism of tryptophan, mitochondrial dysfunction, gastrointestinal tract, brain dysfunction and metabolism of other vitamins as well as is associated with skin disorders. Toxicological and photosensitizing properties of riboflavin make it suitable for biological use such as virus inactivation, excellent photosensitizer and promising adjuvant in chemo radiotherapy in cancer treatment. A number of recent studies have indicated and highlighted the cellular processes and biological effects associated with riboflavin supplementation in metabolic diseases. Overall, a deeper understanding of these emerging roles of riboflavin intake is essential to design better therapies for future.

Asia Pac J Clin Nutr. 2002;11(4):263-7.

Effect of low-dosage vitamin A and riboflavin on iron-folate supplementation in anaemic pregnant women.

Suprapto B, Widardo, Suhanantyo.

Abstract

A double-blind, placebo, controlled trial was conducted in Banyudono subdistrict, Boyolali regency, Central Java province, Indonesia. The aim of the study was to determine whether adding low-dosage vitamin A and riboflavin can enhance the effect of iron-folate supplementation in anaemic pregnant women. From July to November 2000, 202 pregnant women were screened for anaemia (haemoglobin < 11.0 g/dL). One hundred and three pregnant women (51%) were found to be anaemic and were then allocated alternately into four groups. Over a period of 60 days, group IF (n = 29) received iron-folate tablets (200 mg FeSO4 and 250 microg folic acid) + 5 mg glucose: group IFR (n = 22) received iron-folate tablets + 5 mg riboflavin; group IFA (n = 29) received iron-folate tablets + 2.75 mg retinyl palmitate (equal to 5000 IU vitamin A); and group IFRA (n = 23) received iron-folate tablets + 5 mg riboflavin + 2.75 mg retinyl palmitate. At the end of the study 19 pregnant women (18.4%) were excluded from the analysis because of various reasons. Statistical analysis was based on 84 women (81.5%): group IF, n = 25; group IFR, n = 22; group IFA, n = 18; and group IFRA, n = 19. Haemoglobin measurements were carried out using the Technicon H1* (cyanmethaemoglobin method). All groups showed a significant increase in haemoglobin concentration ($P < 0.05$), except group IFA ($P > 0.05$), with the highest increment being in group FR. Multiple comparisons only showed significant differences between group IFR and group IFA ($P < 0.05$). It can be concluded that iron-folate supplementation can increase haemoglobin concentrations in anaemic pregnant women. Adding riboflavin tends to enhance the effect of iron-folate supplementation, but this is not the case with adding vitamin A.

LATTOFERRINA

Dev Period Med. 2016 Apr-Jun;20(2):118-25.
[Lactoferrin - a glycoprotein of great therapeutic potentials].
Lauterbach R, Kamińska E, Michalski P, Lauterbach JP.

Abstract
Lactoferrin is an iron-binding glycoprotein, which is present in most biological fluids with particularly high levels in colostrum and in mammalian milk. Bovine lactoferrin is more than 70% homologous with human lactoferrin. Most of the clinical trials have used bovine lactoferrin for supplementation. This review summarizes the recent advances in explaining the mechanisms, which are responsible for the multifunctional roles of lactoferrin, and presents its potential prophylactic and therapeutic applications. On the ground of the results of preliminary clinical observations, authors suggest beneficial effect of lactoferrin supplementation on the prevalence of necrotizing enterocolitis in infants with birth weight below 1250 grams.

Acta Pharmacol Sin. 2014 May;35(5):557-66. doi: 10.1038/aps.2013.200.
Immunomodulatory effects of lactoferrin.
Siqueiros-Cendón T, Arévalo-Gallegos S, Iglesias-Figueroa BF, García-Montoya IA, Salazar-Martínez J, Rascón-Cruz Q.

Abstract
Lactoferrin (Lf) is an iron-binding glycoprotein of the transferrin family, which is expressed in most biological fluids with particularly high levels in mammalian milk. Its multiple activities lie in its capacity to bind iron and to interact with the molecular and cellular components of hosts and pathogens. Lf can bind and sequester lipopolysaccharides, thus preventing pro-inflammatory pathway activation, sepsis and tissue damages. Lf is also considered a cell-secreted mediator that bridges the innate and adaptive immune responses. In the recent years much has been learned about the mechanisms by which Lf exerts its activities. This review summarizes the recent advances in understanding the mechanisms underlying the multifunctional roles of Lf, and provides a future perspective on its potential prophylactic and therapeutic applications.

Biochem Cell Biol. 2012 Jun;90(3):245-51. doi: 10.1139/o2012-018.
Lactoferrin--50 years on.
Brock JH.

Abstract
It is now some 50 years since iron-binding lactoferrin was first isolated and purified, an event that opened the way to subsequent extensive research on lactoferrin structure and function. The initial recognition that lactoferrin closely resembled the plasma iron-transport protein transferrin meant that lactoferrin was first thought to mediate intestinal iron absorption or to act as an antimicrobial agent. It was also suggested that it could mediate the hyposideraemia of inflammation. This paper will assess to what extent early proposals have stood the test of time and also suggest possible mechanisms by which lactoferrin can mediate the large number of potential functions that have subsequently been proposed. It will also review the ability of lactoferrin to resist digestion in the gastrointestinal tract and identify areas for future research.

ACIDO FOLICO

Ann Intern Med. 2009 May 5;150(9):626-31.
Folic acid for the prevention of neural tube defects: U.S. Preventive Services Task Force recommendation statement.
U.S. Preventive Services Task Force.

Abstract
DESCRIPTION:
In 1996, the U.S. Preventive Services Task Force (USPSTF) recommended that all women planning or capable of pregnancy take a multivitamin supplement containing folic acid for the prevention of neural tube defects. This recommendation is an update of the 1996 USPSTF recommendation.

METHODS:
The USPSTF reviewed the evidence on folic acid supplementation in women of childbearing age published since the 1996 USPSTF recommendation. The USPSTF did not review the evidence on folic acid food fortification, counseling to increase dietary intake, or screening for neural tube defects.

RECOMMENDATION:
The USPSTF recommends that all women planning or capable of pregnancy take a daily supplement containing 0.4 to 0.8 mg (400 to 800 microg) of folic acid. (Grade A recommendation).

Rev Obstet Gynecol. 2011 Summer; 4(2): 52–59.
PMCID: PMC3218540

Folic Acid Supplementation and Pregnancy: More Than Just Neural Tube Defect Prevention

James A Greenberg, MD, Stacey J Bell, DSc, RD, Yong Guan, MD, and Yan-hong Yu, MD, PhD

Abstract

Folate (vitamin B_9) is an essential nutrient that is required for DNA replication and as a substrate for a range of enzymatic reactions involved in amino acid synthesis and vitamin metabolism. Demands for folate increase during pregnancy because it is also required for growth and development of the fetus. Folate deficiency has been associated with abnormalities in both mothers (anemia, peripheral neuropathy) and fetuses (congenital abnormalities). This article reviews the metabolism of folic acid, the appropriate use of folic acid supplementation in pregnancy, and the potential benefits of folic acid, as well as the possible supplementation of l-methylfolate for the prevention of pregnancy-related complications other than neural tube defects.

Biol Reprod. 2011 Jun;84(6):1148-53. doi: 10.1095/biolreprod.110.088351.

Possible roles for folic acid in the regulation of trophoblast invasion and placental development in normal early human pregnancy.

Williams PJ, Bulmer JN, Innes BA, Broughton Pipkin F.

Abstract

In addition to its role in the prevention of neural tube defects, folic acid has many other physiological functions, including cell proliferation, DNA replication, and antioxidant protection. The aim of this study was to determine the role that folic acid has in regulating placental trophoblast development. Placental explants from placentae at gestational age 7 wk (n = 3) were cultured in folic acid at concentrations of 10(-6) M, 10(-8) M, and 10(-10) M. Extravillous trophoblast (EVT) invasion was assessed following 6-day culture, and explants were used for immunohistochemical evaluation of proliferation (MKI67) and apoptosis (active caspase 3). In addition, an array was performed on cell culture supernatants to examine a range of matrix metalloproteinases (MMPs) and tissue inhibitors of MMPs (TIMPs). Folic acid increased the invasion of EVT cells in this explant model by between 83% and 19% (P = 0.005), and this was associated with increased MKI67 positivity and decreased active caspase 3 positivity; this effect was concentration dependent and showed a biphasic response. In addition, culture in folic acid increased vascular density, as determined by anti-CD31 immunostaining (P = 0.05). The increase in EVT invasion correlated with increased placental explant secretion of MMP2 (P = 0.01), MMP3 (P = 0.01), and MMP9 (P = 0.02). This study demonstrates that folic acid is potentially important in a number of crucial early stages of placental development, including EVT invasion, angiogenesis, and secretion of MMPs, and highlights the need for further studies to address the benefit of longer-term folic acid supplementation throughout pregnancy to prevent pregnancy disorders associated with deficient placental development, including preeclampsia.

Am J Obstet Gynecol. 2008 Jan;198(1):45.e1-7. doi: 10.1016/j.ajog.2007.06.067.
Folic acid supplementation in early second trimester and the risk of preeclampsia.
Wen SW, Chen XK, Rodger M, White RR, Yang Q, Smith GN, Sigal RJ, Perkins SL, Walker MC.

Abstract
OBJECTIVE:
The objective of the study was to evaluate the association between folic acid supplementation in early second trimester and the risk of developing preeclampsia.

STUDY DESIGN:
We carried out a prospective cohort study between October 2002-December 2005. We recruited women who had their prenatal care visit (12-20 weeks' gestation) at the Ottawa Hospital and Kingston General Hospital. All charts for participants with a diagnosis of preeclampsia were audited and blindly adjudicated by 4 study investigators to validate the diagnosis.

RESULTS:
A total of 2951 pregnant women were included in the final analysis. Supplementation of multivitamins containing folic acid was associated with increased serum folate (on average 10.51 micromol/L), decreased plasma homocysteine (on average 0.39 micromol/L), and reduced risk of preeclampsia (adjusted odds ratio, 0.37; 95% confidence interval, 0.18-0.75).

CONCLUSION:
Supplementation of multivitamins containing folic acid in the second trimester is associated with reduced risk of preeclampsia.

Am J Clin Nutr. 2005 May;81(5):1213S-1217S.

Folic acid supplementation and the occurrence of congenital heart defects, orofacial clefts, multiple births, and miscarriage.

Bailey LB, Berry RJ.

Abstract

Key research findings relative to the question of whether maternal use of folic acid before and during pregnancy reduces the chance that offspring will be born with a congenital heart defect or an orofacial cleft are reviewed in this paper. Observational studies in general support an association between maternal use of multivitamins containing folic acid and a reduction in the occurrence of congenital heart defects and orofacial clefts. Results from one randomized controlled trial (RCT) provide the strongest evidence that multivitamins prevent congenital heart defects, but this RCT did not provide evidence that multivitamins prevent orofacial clefts. In addition, most observational and interventional studies are not designed to detect an independent effect from folic acid. Early studies suggested that periconceptional multivitamin use was associated with an increased occurrence of both miscarriages and multiple births, which has resulted in a great deal of controversy about the safety of folic acid use during pregnancy. We also review reports that were designed to answer these questions with more definitive data. When more substantial evidence about the effect of periconceptional folic acid on the occurrence of congenital heart defects and orofacial clefts is reported, we will have additional support for promoting folic acid intervention programs. All women capable of becoming pregnant should continue to consume 400 mug/d of folic acid in addition to a healthy diet as advised.

PLoS Med. 2009 May 5;6(5):e1000061. doi: 10.1371/journal.pmed.1000061.

Preconceptional folate supplementation and the risk of spontaneous preterm birth: a cohort study.

Bukowski R, Malone FD, Porter FT, Nyberg DA, Comstock CH, Hankins GD, Eddleman K, Gross SJ, Dugoff L, Craigo SD, Timor-Tritsch IE, Carr SR, Wolfe HM, D'Alton ME.

Abstract

BACKGROUND:

Low plasma folate concentrations in pregnancy are associated with preterm birth. Here we show an association between preconceptional folate supplementation and the risk of spontaneous preterm birth.

METHODS AND FINDINGS:

In a cohort of 34,480 low-risk singleton pregnancies enrolled in a study of aneuploidy risk, preconceptional folate supplementation was prospectively recorded in the first trimester of pregnancy. Duration of pregnancy was estimated based on first trimester ultrasound examination. Natural length of pregnancy was defined as gestational age at delivery in pregnancies with no medical or obstetrical complications that may have constituted an indication for delivery. Spontaneous preterm birth was defined as duration of pregnancy between 20 and 37 wk without those complications. The association between preconceptional folate supplementation and the risk of spontaneous preterm birth was evaluated using survival analysis. Comparing to no supplementation, preconceptional folate supplementation for 1 y or longer was associated with a 70% decrease in the risk of spontaneous preterm delivery between 20 and 28 wk (41 [0.27%] versus 4 [0.04%] spontaneous preterm births, respectively; HR 0.22, 95% confidence interval [CI] 0.08-0.61, p = 0.004) and a 50% decrease in the risk of spontaneous preterm delivery between 28 and 32 wk (58 [0.38%] versus 12 [0.18%] preterm birth, respectively; HR 0.45, 95% CI 0.24-0.83, p = 0.010). Adjustment for maternal characteristics age, race, body mass index, education, marital status, smoking, parity, and history of prior preterm birth did not have a material effect on the association between folate supplementation for 1 y or longer and spontaneous preterm birth between 20 and 28, and 28 to 32 wk (adjusted HR 0.31, 95% CI 0.11-0.90, p = 0.031 and 0.53, 0.28-0.99, p = 0.046, respectively). Preconceptional folate supplementation was not significantly associated with the risk of spontaneous preterm birth beyond 32 wk. The association between shorter duration (<1 y) of preconceptional folate supplementation and the risk of spontaneous preterm birth was not significant after adjustment for maternal characteristics. However, the risk of spontaneous preterm birth decreased with the duration of preconceptional folate supplementation (test for trend of survivor functions, p = 0.01) and was the lowest in women who used folate supplementation for 1 y or longer. There was also no significant association with other complications of pregnancy studied after adjustment for maternal characteristics.

CONCLUSIONS:

Preconceptional folate supplementation is associated with a 50%-70% reduction in the incidence of early spontaneous preterm birth. The risk of early spontaneous preterm birth is inversely proportional to the duration of preconceptional folate supplementation. Preconceptional folate supplementation was specifically related to early spontaneous preterm birth and not associated with other complications of pregnancy.

VITAMINA B12

Adv Nutr. 2016 Sep 15;7(5):879-88. doi: 10.3945/an.115.012021. Print 2016 Sep.
Vitamin B-12 and Cognition in Children.
Venkatramanan S, Armata IE, Strupp BJ, Finkelstein JL.

Abstract
Vitamin B-12 is essential for brain development, neural myelination, and cognitive function. Inadequate vitamin B-12 status during pregnancy and early childhood has been associated with adverse child health outcomes, including impaired cognitive development. However, the underlying mechanisms have not been elucidated. This review was conducted to examine the evidence that links vitamin B-12 and cognition in children. The search strategy resulted in 17 studies: 3 cross-sectional, 1 case-control, and 12 cohort studies, and 1 randomized trial. Cognitive processes assessed included attention, memory, and perception. Developmental outcomes, academic performance, and intelligence quotient were also considered. Despite the high prevalence of vitamin B-12 insufficiency and associated risk of adverse cognitive outcomes in children, to our knowledge, no studies to date have been conducted to examine the effects of vitamin B-12 supplementation on cognition in children. The role of vitamin B-12 in the etiology of child cognitive outcomes needs to be elucidated to inform public health interventions.

Am J Epidemiol. 2017 Jan 20. doi: 10.1093/aje/kww212.

Associations of Maternal Vitamin B12 Concentration in Pregnancy With the Risks of Preterm Birth and Low Birth Weight: A Systematic Review and Meta-Analysis of Individual Participant Data.

Rogne T, Tielemans MJ, Chong MF, Yajnik CS, Krishnaveni GV, Poston L, Jaddoe VW, Steegers EA, Joshi S, Chong YS, Godfrey KM, Yap F, Yahyaoui R, Thomas T, Hay G, Hogeveen M, Demir A, Saravanan P, Skovlund E, Martinussen MP, Jacobsen GW, Franco OH, Bracken MB, Risnes KR.

Abstract

Vitamin B12 (hereafter referred to as B12) deficiency in pregnancy is prevalent and has been associated with both lower birth weight (birth weight <2,500 g) and preterm birth (length of gestation <37 weeks). Nevertheless, current evidence is contradictory. We performed a systematic review and a meta-analysis of individual participant data to evaluate the associations of maternal serum or plasma B12 concentrations in pregnancy with offspring birth weight and length of gestation. Twenty-two eligible studies were identified (11,993 observations). Eighteen studies were included in the meta-analysis (11,216 observations). No linear association was observed between maternal B12 levels in pregnancy and birth weight, but B12 deficiency (<148 pmol/L) was associated with a higher risk of low birth weight in newborns (adjusted risk ratio = 1.15, 95% confidence interval (CI): 1.01, 1.31). There was a linear association between maternal levels of B12 and preterm birth (per each 1-standard-deviation increase in B12, adjusted risk ratio = 0.89, 95% CI: 0.82, 0.97). Accordingly, B12 deficiency was associated with a higher risk of preterm birth (adjusted risk ratio = 1.21, 95% CI: 0.99, 1.49). This finding supports the need for randomized controlled trials of vitamin B12 supplementation in pregnancy.

BJOG. 2016 Feb;123(3):384-92. doi: 10.1111/1471-0528.13574.
Vitamin B12 and folate status in early pregnancy and cardiometabolic risk factors in the offspring at age 5-6 years: findings from the ABCD multi-ethnic birth cohort.
Krikke GG, Grooten IJ, Vrijkotte TG, van Eijsden M, Roseboom TJ, Painter RC.

Abstract
OBJECTIVE:
To explore whether maternal vitamin B12 and folate status during early pregnancy are associated with cardiometabolic risk factors in the offspring at age 5-6.

DESIGN:
Prospective multi-ethnic birth cohort, the Amsterdam Born Children and their Development study (ABCD).

SETTING:
12,373 pregnant women living in Amsterdam were approached between 2003 and 2004 for participation in the study.

POPULATION:
Mother-child pairs for whom information on maternal vitamin B12 or folate status in early gestation and health at age 5-6 years was available (n = 1950).

METHODS:
Vitamin B12 and folate concentrations were determined in maternal serum at intake in early pregnancy (median 13 weeks' gestation). Anthropometric measurements, blood pressure and fasting blood samples were collected during a health check of children aged 5-6 years. Multiple linear regression was performed to investigate the association between maternal serum concentrations and children's outcomes, corrected for confounders. *MAIN*

OUTCOME MEASURES:
Gestational age at birth, birthweight, body mass index (BMI), glucose levels, triglyceride levels, blood pressure and heart rate of the offspring at age 5-6.

RESULTS:
Low maternal folate levels during early pregnancy were associated with slightly higher BMI in the offspring [decrease per 10 units: β 0.07 kg/m(2), 95% confidence interval (CI) 0.01, 0.13]. Low maternal vitamin B12 concentrations were associated with higher heart rates (decrease per 100 units: β 0.49 beats/min, 95% CI 0.11, 0.87).

CONCLUSION:
This study provides further evidence that maternal nutrition in early pregnancy may possibly program cardiometabolic health of the offspring.

TWEETABLE ABSTRACT:
Low folate and vitamin B12 levels during pregnancy are associated with higher BMI and heart rate in offspring.

Adv Nutr. 2015 Sep 15;6(5):552-63. doi: 10.3945/an.115.008201. Print 2015 Sep.
Vitamin B-12 and Perinatal Health.
Finkelstein JL, Layden AJ, Stover PJ.

Abstract
Vitamin B-12 deficiency (<148 pmol/L) is associated with adverse maternal and neonatal outcomes, including developmental anomalies, spontaneous abortions, preeclampsia, and low birth weight (<2500 g). The importance of adequate vitamin B-12 status periconceptionally and during pregnancy cannot be overemphasized, given its fundamental role in neural myelination, brain development, and growth. Infants born to vitamin B-12-deficient women may be at increased risk of neural tube closure defects, and maternal vitamin B-12 insufficiency (<200 pmol/L) can impair infant growth, psychomotor function, and brain development, which may be irreversible. However, the underlying causal mechanisms are unknown. This review was conducted to examine the evidence that links maternal vitamin B-12 status and perinatal outcomes. Despite the high prevalence of vitamin B-12 deficiency and associated risk of pregnancy complications, few prospective studies and, to our knowledge, only 1 randomized trial have examined the effects of vitamin B-12 supplementation during pregnancy. The role of vitamin B-12 in the etiology of adverse perinatal outcomes needs to be elucidated to inform public health interventions.

FERRO

Glob Health Action. 2016 Jan;9(1):29621. doi: 10.3402/gha.v9.29621.
Iron/folic acid supplementation during pregnancy prevents neonatal and under-five mortality in Pakistan: propensity score matched sample from two Pakistan Demographic and Health Surveys.
Nisar YB, Dibley MJ.

Abstract
Background Several epidemiological studies from low- and middle-income countries have reported a protective effect of maternal antenatal iron/folic acid (IFA) on childhood mortality. Objective The current study aimed to evaluate the effect of maternal antenatal IFA supplementation on childhood mortality in Pakistan. Design A propensity score-matched sample of 8,512 infants live-born within the 5 years prior to interview was selected from the pooled data of two Pakistan Demographic and Health Surveys (2006/07 and 2012/13). The primary outcomes were childhood mortality indicators and the main exposure variable was maternal antenatal IFA supplementation. Post-matched analyses used Cox proportional hazards regression and adjusted for 16 potential confounders. Results Maternal antenatal IFA supplementation significantly reduced the adjusted risk of death on day 0 by 33% [adjusted hazard ratio (aHR)=0.67, 95% confidence interval (95% CI) 0.48-0.94], during the neonatal period by 29% (aHR=0.71, 95% CI 0.57-0.88), and for under-fives by 27% (aHR=0.73, 95% CI 0.60-0.89). When IFA was initiated in the first 4 months of pregnancy, the adjusted risk of neonatal and under-five deaths was significantly reduced by 35 and 33%, respectively. Twenty percent of under-five deaths were attributable to non-initiation of IFA in the first 4 months of pregnancy. With universal initiation of IFA in the first 4 months of pregnancy, 80,300 under-five deaths could be prevented annually in Pakistan. Conclusions Maternal antenatal IFA supplementation significantly reduced neonatal and under-five deaths in Pakistan. Earlier initiation of supplements in pregnancy was associated with a greater prevention of neonatal and under-five deaths.

J Nutr Sci Vitaminol (Tokyo). 2016;62(6):397-401. doi: 10.3177/jnsv.62.397.

The Relationship between Iron Deficiency and Thyroid Function in Chinese Women during Early Pregnancy.

Li S, Gao X, Wei Y, Zhu G, Yang C.

Abstract

Previous studies have identified an association between iron deficiency and thyroid function. We aimed to determine if there is a relationship between iron deficiency and thyroid function during the first trimester of pregnancy. Two thousand five hundred eighty-one pregnant women who presented for the first prenatal care were enrolled and divided into three groups, the mild iron deficiency (MID) group, iron deficiency anemia (IDA) group and normal control (NC) group, according to serum ferritin and hemoglobin levels. The former two groups can be merged into one iron deficiency (ID) group. Thyroid function parameters were compared among the three groups, including free thyroxine (FT4), thyroid stimulating hormone (TSH), total thyroxine (TT4) and thyroid peroxidase antibodies (TPOAb). Moreover, the rates of thyroid dysfunction were also compared. Our results show that pregnant women in the MID and IDA groups have higher TSH and lower FT4 status than those in the NC group ($p<0.01$), and the difference between the IDA group and MID group is significant ($p<0.05$). TPOAb in the IDA group is higher than in the MID group and NC group. Meanwhile, the rate of hypothyroidism or subclinical hypothyroidism in the IDA group was significantly higher than in the MID group and NC group ($p<0.01$). And the positive rate of TPOAb is also higher in the IDA group than MID group and NC group ($p<0.05$). Iron deficiency is related to thyroid function and could lead to hypothyroidism during early pregnancy, which could be explained by thyroid autoimmunity.

Biol Trace Elem Res. 2016 Nov 19.
Anemia and Dental Caries in Pregnant Women: a Prospective Cohort Study.
Costa EM, Azevedo JA, Martins RF, Alves CM, Ribeiro CC, Thomaz EB.

Abstract
The objective was to evaluate the effect of anemia during pregnancy on the risk of dental caries development in pregnant women. A prospective cohort including a sample of pregnant women in a prenatal care unit of São Luís, Brazil, was done. The incidence of dental caries during pregnancy, according to Nyvad's criteria, was the outcome. The main independent variables were serum iron, ferritin, hemoglobin, erythrocyte, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW). Pregnant women (n = 121) were evaluated at two moments: up to 16th week of gestational age (T1) and in the last trimester of pregnancy (T2). Crude and adjusted associations were estimated by the incidence ratio risk (IRR) and respective 95% confidence intervals (95%CI). After adjustment, higher serum concentrations of ferritin (IRR = 0.97, 95%CI 0.95-0.99) in T1, and Fe (IRR = 0.99, 95%CI 0.98-0.99), ferritin (IRR = 0.99, 95%CI 0.98-0.99), erythrocyte (IRR = 0.71, 95%CI 0.50-0.99), hemoglobin (IRR = 0.84, 95%CI 0.73-0.96), hematocrit (IRR = 0.93, 95%CI 0.88-0.98), MCV (IRR = 0.91, 95%CI 0.86-0.96), and MCH (IRR = 0.83, 95%CI 0.74-0.93) in T2, were associated with fewer incidence of dental caries in pregnant women. Iron deficiency anemia during pregnancy is a risk factor for the incidence of dental caries in these women.

MAGNESIO

BBA Clin. 2015 Apr 22;3:289-98. doi: 10.1016/j.bbacli.2015.04.002. eCollection 2015.
Multifactorial determinants of cognition - Thyroid function is not the only one.
Moncayo R, Ortner K.

Abstract
BACKGROUND:
Since the 1960s hypothyroidism together with iodine deficiency have been considered to be a principal determinant of cognition development. Following iodine supplementation programs and improved treatment options for hypothyroidism this relation might not be valid in 2015. On the other hand neurosciences have added different inputs also related to cognition.

SCOPE OF REVIEW:
We will examine the characteristics of the original and current publications on thyroid function and cognition and also add some general determinants of intelligence and cognition. One central issue for us is the relation of stress to cognition knowing that both physical and psychological stress, are frequent elements in subjects with thyroid dysfunction. We have considered a special type of stress called pre-natal stress which can influence cognitive functions. Fear and anxiety can be intermingled requiring mechanisms of fear extinction.

MAJOR CONCLUSIONS:
Recent studies have failed to show an influence of thyroid medication during pregnancy on intellectual development. Neuroscience offers a better explanation of cognition than hypothyroidism and iodine deficiency. Additional factors relevant to cognition are nutrition, infection, prenatal stress, and early life stress. In turn stress is related to low magnesium levels. Magnesium supplementation can correct both latent hypothyroidism and acquired mild cognitive deficits.

GENERAL SIGNIFICANCE:
Cognition is a complex process that depends on many determinants and not only on thyroid function. Magnesium deficiency appears to be a basic mechanism for changes in thyroid function as well as of cognition.

Nutr Rev. 2016 Sep;74(9):549-57. doi: 10.1093/nutrit/nuw018.
Magnesium in pregnancy.
Dalton LM, Ní Fhloinn DM, Gaydadzhieva GT, Mazurkiewicz OM, Leeson H, Wright CP.

Abstract
Magnesium deficiency is prevalent in women of childbearing age in both developing and developed countries. The need for magnesium increases during pregnancy, and the majority of pregnant women likely do not meet this increased need. Magnesium deficiency or insufficiency during pregnancy may pose a health risk for both the mother and the newborn, with implications that may extend into adulthood of the offspring. The measurement of serum magnesium is the most widely used method for determining magnesium levels, but it has significant limitations that have both hindered the assessment of deficiency and affected the reliability of studies in pregnant women. Thus far, limited studies have suggested links between magnesium inadequacy and certain conditions in pregnancy associated with high mortality and morbidity, such as gestational diabetes, preterm labor, preeclampsia, and small for gestational age or intrauterine growth restriction. This review provides recommendations for further study and improved testing using measurement of red cell magnesium. Pregnant women should be counseled to increase their intake of magnesium-rich foods such as nuts, seeds, beans, and leafy greens and/or to supplement with magnesium at a safe level.

Am J Clin Nutr. 2015 Jul;102(1):222-9. doi: 10.3945/ajcn.114.098616.

Magnesium supplementation affects metabolic status and pregnancy outcomes in gestational diabetes: a randomized, double-blind, placebo-controlled trial.

Asemi Z, Karamali M, Jamilian M, Foroozanfard F, Bahmani F, Heidarzadeh Z, Benisi-Kohansal S, Surkan PJ, Esmaillzadeh A.

Abstract

BACKGROUND:

To our knowledge, prior research has not examined the effects of magnesium supplementation on metabolic status and pregnancy outcomes in maternal-child dyads affected by gestational diabetes (GDM).

OBJECTIVE:

This study was designed to assess the effects of magnesium supplementation on metabolic status and pregnancy outcomes in magnesium-deficient pregnant women with GDM.

DESIGN:

A randomized, double-blind, placebo-controlled clinical trial was performed in 70 women with GDM. Patients were randomly assigned to receive either 250 mg magnesium oxide (n = 35) or a placebo (n = 35) for 6 wk. Fasting blood samples were taken at baseline and after a 6-wk intervention.

RESULTS:

The change in serum magnesium concentration was greater in women consuming magnesium than in the placebo group (+0.06 ± 0.3 vs. -0.1 ± 0.3 mg/dL, P = 0.02). However, after controlling for baseline magnesium concentrations, the changes in serum magnesium concentrations were not significantly different between the groups. Changes in fasting plasma glucose (-9.7 ± 10.1 vs. +1.8 ± 8.1 mg/dL, P < 0.001), serum insulin concentration (-2.1 ± 6.5 vs. +5.7 ± 10.7 μIU/mL, P = 0.001), homeostasis model of assessment-estimated insulin resistance (-0.5 ± 1.3 vs. +1.4 ± 2.3, P < 0.001), homeostasis model of assessment-estimated β-cell function (-4.0 ± 28.7 vs. +22.0 ± 43.8, P = 0.006), and the quantitative insulin sensitivity check index (+0.004 ± 0.021 vs. -0.012 ± 0.015, P = 0.005) in supplemented women were significantly different from those in women in the placebo group. Changes in serum triglycerides (+2.1 ± 63.0 vs. +38.9 ± 37.5 mg/dL, P = 0.005), high sensitivity C-reactive protein (-432.8 ± 2521.0 vs. +783.2 ± 2470.1 ng/mL, P = 0.03), and plasma malondialdehyde concentrations (-0.5 ± 1.6 vs. +0.3 ± 1.2 μmol/L, P = 0.01) were significantly different between the supplemented women and placebo group. Magnesium supplementation resulted in a lower incidence of newborn hyperbilirubinemia (8.8% vs. 29.4%, P = 0.03) and newborn hospitalization (5.9% vs. 26.5%, P = 0.02).

CONCLUSION:

Magnesium supplementation among women with GDM had beneficial effects on metabolic status and pregnancy outcomes. This trial was registered at www.irct.ir as IRCT201503055623N39.

VITAMINA D

Int J Womens Health. 2016 Sep 23;8:529-535. eCollection 2016.
Prevalence and risk factors for low vitamin D status among breastfeeding mother-infant dyads in an environment with abundant sunshine.
Salameh K, Al-Janahi NS, Reedy AM, Dawodu A.

Abstract
PURPOSE:
Evaluation of vitamin D (vD) status and risk factors for low vD among breastfeeding mother-infant dyads in a population at high risk for vD deficiency.

SUBJECTS AND METHODS:
We measured serum 25-hydroxyvitamin D (25(OH)D) and parathyroid hormone at 1 month postpartum in 60 consecutive exclusively breastfeeding Arab mother-infant dyads enrolled in a high dose vD supplementation study to prevent vD deficiency in Doha, Qatar, (latitude 25°N) during summer months. Data were collected on demography, sun exposure, and vD supplementation. Comparison with a US cohort was evaluated. vD deficiency was defined as serum 25(OH)D <50 nmol/L and severe deficiency categorized as 25(OH)D <25 nmol/L in mothers and infants.

RESULTS:
Mean maternal age was 29 years and 77% had college or university education. Maternal median 25(OH)D was 32.5 nmol/L and 78% were vD-deficient and 20% had 25(OH)D <25 nmol/L. Only 42% of mothers had reportedly taken vD supplements postpartum and median dietary vD intake (119 IU/day) and calcium (490 mg/day) were low. Maternal median sun index score (sun exposure [hours/week] × body surface area exposed while outdoors) was 0. Maternal 25(OH)D correlated with percent body surface area exposure while outdoors (r_s=0.37, *P*=0.004). Infant median 25(OH)D was 20 nmol/L and 83% were deficient, while 58% had 25(OH)D <25 nmol/L. Infant 25(OH)D correlated with maternal levels (r_s=0.41, *P*=0.001). None of the infants received vD supplement at 1 month of age and median sun index score was 0. Infant's parathyroid hormone showed negative correlations with 25(OH)D (r_s=-0.28, *P*=0.03). Sun exposure, vD supplementation rate, and vD status were lower in Doha than Cincinnati, US cohort.

CONCLUSION:
vD deficiency is common in breastfeeding mother-infant dyads in this sunny environment and is associated with sun avoidance and low vD intake. We suggest corrective vD supplement of breastfeeding mothers and their infants, which should preferably start during pregnancy.

BMJ Open 2016;6:e009733 doi:10.1136/bmjopen-2015-009733

Maternal vitamin D deficiency and fetal distress/birth asphyxia: a population-based nested case–control study

Pelle G Lindqvist, Aldo T Silva, Sven A Gustafsson, Sebastian Gidlöf

Abstract

Objective Vitamin D deficiency causes not only skeletal problems but also muscle weakness, including heart muscle. If the fetal heart is also affected, it might be more susceptible to fetal distress and birth asphyxia. In this pilot study, we hypothesised that low maternal vitamin D levels are over-represented in pregnancies with fetal distress/birth asphyxia.

Design and setting A population-based nested case–control study.

Patients Banked sera of 2496 women from the 12th week of pregnancy.

Outcome measures Vitamin D levels were analysed using a direct competitive chemiluminescence immunoassay. Vitamin D levels in early gestation in women delivered by emergency caesarean section due to suspected fetal distress were compared to those in controls. Birth asphyxia was defined as Apgar <7 at 5 min and/or umbilical cord pH≤7.15.

Results Vitamin D levels were significantly lower in mothers delivered by emergency caesarean section due to suspected fetal distress (n=53, 43.6±18 nmol/L) compared to controls (n=120, 48.6±19 nmol/L, p=0.04). Birth asphyxia was more common in women with vitamin D deficiency (n=95) in early pregnancy (OR 2.4, 95% CI 1.1 to 5.7).

Conclusions Low vitamin D levels in early pregnancy may be associated with emergency caesarean section due to suspected fetal distress and birth asphyxia. If our findings are supported by further studies, preferably on severe birth asphyxia, vitamin D supplementation/sun exposure in pregnancy may lower the risk of subsequent birth asphyxia.

PLoS One. 2016 Oct 20;11(10):e0164999. doi: 10.1371/journal.pone.0164999. eCollection 2016.

Vitamin D Deficiency Increases the Risk of Adverse Neonatal Outcomes in Gestational Diabetes.

Weinert LS, Reichelt AJ, Schmitt LR, Boff R, Oppermann ML, Camargo JL, Silveiro SP.

Abstract

BACKGROUND:

Gestational diabetes mellitus (GDM) and vitamin D deficiency have been associated with increased risk of adverse perinatal outcomes but the consequences of both conditions simultaneously present in pregnancy have not yet been evaluated. Our objective was to study the influence of vitamin D deficiency in neonatal outcomes of pregnancies with GDM.

METHODS:

184 pregnant women with GDM referred to specialized prenatal monitoring were included in this cohort and had blood sampled for 25-hydroxyvitamin D measurement. Vitamin D was measured by chemiluminescence and deficiency was defined as < 20 ng/mL. Participants were followed until puerperium and adverse neonatal outcomes were evaluated.

RESULTS:

Newborns of women with vitamin D deficiency had higher incidences of hospitalization in intensive care units (ICU) (32 vs 19%, P = 0.048), of hypoglycemia (any, 17.3 vs 7.1%, P = 0.039requiring ICU, 15.3 vs 3.6%, P = 0.008), and were more frequently small for gestational age (SGA) (17.3 vs 5.9%, P = 0.017). After adjustment, relative risk (RR) for hypoglycemia requiring ICU was 3.63 (95%CI 1.09-12.11) and for SGA was 4.32 (95%CI 1.75-10.66). The incidence of prematurity, jaundice and shoulder dystocia was no statistically different between groups.

CONCLUSIONS:

In this cohort of pregnant women with GDM, vitamin D deficiency was associated with a major increase in the incidence of adverse neonatal outcomes such as SGA newborns and neonatal hypoglycemia.

CALCIO

Am J Obstet Gynecol. 2006 Apr;194(4):937-45.
Calcium supplementation during pregnancy and lactation: effects on the mother and the fetus.
Thomas M, Weisman SM.

Abstract
Calcium consumption is essential for bone development and maintenance throughout life, yet more than one half of the female population in the United States does not consume the recommended amount of calcium. Calcium intake is especially crucial during pregnancy and lactation because of the potential adverse effect on maternal bone health if maternal calcium stores are depleted. There is often a transient lowered bone mineral density and increased rate of bone resorption, with the greatest consequence during the third trimester and throughout lactation. Studies indicate that calcium consumption should be encouraged, especially during pregnancy and lactation, to replace maternal skeletal calcium stores that are depleted during these periods. Because the fetus in utero and the neonate through breast-feeding are dependent on maternal sources for the total calcium load, adequate maternal calcium intake also can affect fetal bone health positively. Proper calcium consumption can be attained through the diet by the consumption of dairy products or leafy greens (such as kale), the consumption of fortified foods, or by supplementation with widely available calcium-containing supplement products. Because many women experience heartburn during pregnancy, calcium-based antacids are ideal for providing heartburn relief, and they offer a calcium supplement to ensure maternal and fetal bone health, without the danger of adverse effects on the neonate.

ZINCO

Pediatr Int. 2016 Oct 3. doi: 10.1111/ped.13176.
Maternal Zinc Deficiency and Congenital Anomalies in Newborns.
Moghimi M, Ashrafzadeh S, Rassi S, Naseh A.

Abstract
BACKGROUND:
Zinc deficiency in pregnant women is common, especially in the third trimester of pregnancy. However, the available data are insufficient regarding the association between zinc deficiency and congenital malformations in Iranian population. We aimed to evaluate if the maternal serum zinc deficiency is associated with development of major congenital malformations in the newborns.

METHODS:
This descriptive, case-control study was performed in mothers of 80 neonates with congenital anomalies (Case group) who were admitted to the Mofid Children's Hospital, Tehran, Iran. During the same period of time (years of 2014 and 2015), the serum level of zinc was measured in 80 mothers who delivered normal newborns without congenital malformations (Control group).

RESULTS:
For mothers with serum zinc deficiency, the Odds of delivering a baby who had developed malformation was 7.013 (Odds Ratio) times larger compared to a mother with normal serum zinc level. Newborn Cases weighting equal or less than 2500 grams had lower maternal serum zinc level compared to the Control group (p value = 0.006).

CONCLUSIONS:
The data from this study indicate there is association between congenital malformations of newborns and maternal zinc deficiency.

Food Nutr Bull. 2009 Mar;30(1 Suppl):S60-78.
Effects of maternal zinc supplementation on pregnancy and lactation outcomes.
Hess SY, King JC.

Abstract
Observational studies in human populations suggest that maternal zinc deficiency during pregnancy may cause adverse pregnancy outcomes for the mother and fetus. Therefore, we reviewed the current evidence from studies of zinc supplementation, with or without other micronutrients, during pregnancy and lactation to assess its impact on maternal, fetal, and infant health. A meta-analysis of supplementation trials indicates a 14% reduction in premature delivery among zinc-supplemented women. Most studies found no significant impact of maternal zinc supplementation on infant birthweight, but a subset of studies conducted in underweight or zinc-deficient women suggests that there may be a positive effect of zinc supplementation in such women. However, the number of relevant studies is limited, and more information is needed to confirm these observations. The results for other pregnancy outcomes are inconsistent, and the number of available studies is small. Likewise, the impact of maternal zinc supplementation during pregnancy on infant postnatal growth and risk of infection is variable, and few studies are available. Thus, more research will be needed to allow definitive conclusions to be drawn, especially for the second half of infancy and later childhood. Studies found no adverse effects of maternal zinc supplementation on iron status during pregnancy. More information is required on other potential adverse effects, particularly with regard to a possible modifying effect of preexisting maternal zinc status. In view of the possible benefits of zinc supplementation for reducing the risk of premature delivery, the possible positive impact of zinc supplementation on infant birthweight among undernourished women, and the lack of reported adverse effects, zinc should be included in maternal supplements given during pregnancy in populations at risk for zinc deficiency.