Dietary supplements: infant brain development and cognitive enhancement

Introduction

Children nutrition during their first 1000 days is significant to their body development, especially for their brain development. adequate nutrition could be obtained from either breast milk or fortified milk. In further, an improved cognitive function has been observed in both term and preterm infants fed with breast milk when compared with formula. Nevertheless, pregnant women are still susceptible to vitamin B12 deficiency and iodine deficiency in severe areas, and preterm infants are susceptible to docosahexaenoic acid deficiency. Various nutrients requirement might be depended on two parts, postnatal health outcome, and gene expression or molecule mechanisms related to key regions of the cerebral cortex. Traditional maternal diet among poverty areas, or lacking related high-education or ignorance of nutrition needs could influence infant intake of certain nutrients such as zinc and protein. Therefore, within two years old, especially the first year of infant, in order to maintain adequate nutrition, from both breast milk and formula such as fatty acid, vitamin A, B6 and B12, amino acid such as glutamine, iron, iodine, choline and folic acid, dietary supplement might be suggested by their health care professionals [1, 2] . Here, two common questions will be replied in the following part, what kind of DS could/should be taken by pregnant women, what kind of nutrients should be added in fortified formula or breast milk to maintain infant brain development after delivery? Therefore the following 4 dietary supplements would be good implications for pregnant moms and fortified milk manufactures, and future research directions.

Docosahexaenoic acid (DHA)

Docosahexaenoic acid (DHA), a long-chain polyunsaturated fatty acid is one of the membrane composition of brain tissue [3]. DHA is beneficial to improve hippocampal function related to cognitive health in children of school age [4]. Preterm (< 37 weeks) infants have a higher risk of impaired brain development when compared with term infants, almost half of preterm infants (< 28 weeks) have impaired neurodevelopment in 2010 [5] Since preterm infants could not get adequate DHA from maternal utero, Supplementation of DHA might improve brain development among infants [6]. DHA accumulates in the frontal Robes of the fetal brain during the last trimester of pregnancy. Their deficiency might cause aged cerebral by delayed membranes metabolism.

DHA might not have apparent benefits on the infant's brain. A randomized prospective study of DHA given to pregnant women with 400 mg/d from 16 weeks of gestation has shown benefits in infants, including visual acuity at 2 months old and higher receptive and expressive language skills at 18 months old measured by Bayley Scales of Infant Development [7]. Results from a self-questionnaire among 1516 healthy pregnant women who take DHA during their pregnancy have shown that improved brain development and increased height and head circumference among infants [8]. Another meta-analysis study among 34 RCT has shown that crystallized intelligence, improved fluid intelligence with supplemented Long-chain polyunsaturated fatty acids (LCPUFA) [6]. However, a randomized clinical trial among toddlers born preterm infants with 200 mg/d DHA supplementation in their feeding diet has shown that DHA might not improve cognitive development on term

infants [9] . Even a negative effect of DHA taken by pregnant women on childhood neurodevelopment has been reported [10.]

Iodine

Iodine deficiency, combined with a low level of thyroid hormones might cause infant impaired brain development. Besides, severe iodine deficiency may cause cretinism, manifested in impaired speaking ability and etc. Urine Iodine Concentration (UIC)< 150 μg/L has been defined as iodine deficiency in pregnancy by the World Health Organization. Therefore, it is of significance to maintain an adequate level of iodine in the maternal diet and infant [13, 14] . It has also revealed an adverse outcome point-lower expressive language skills of iodine (<100 μg/L measured by UIC) intake up to 18 months pregnancy.

As for the mechanism between iodine and infant neurodevelopment, iodine helps to synthesize thyroid hormones, triiodothyronine T3 and thyroxine T4 in brain development, especially during the first pregnant trimester.

Iodine supplementation during pregnancy might not have a significant advantage to infant cognitive enhancement. A population-based cohort research among 851 Norway mother-infant pairs has shown that mild-to-moderate maternal iodine deficiency (<78 μg/L, most up to 18 months of pregnancy) is measured through UIC, and significantly increased infant neurodevelopment at 5 and 12 months is measured through the Bayley Scales of Infant and Toddler Development (Bayley- III), including increased

receptive and expressive communication, however, with reduced cognitive or motor development.

Due to missing rescue time of vital stage in brain development, none apparent changes in brain development in infants with iodine supplementation among pregnant women has been detected, even if a lower gross motor development in infants has been detected with low iodine supplementation (150 µg to 200 µg) among a small proportion of pregnant women (18%) [13] . The same conclusion of a study among 6-18 months old infants has been got in mild-to-moderate iodine deficiency area-Spanish. [15] Instead of huge low-income moms in this study, a population with adjusted socioeconomic bias should be selected as future main subjects aimed for accurate relations between iodine intake and outcome. A similar outcome has also been proved in Chinese children of 18 months and 2 years old, with 187. 8 µg/L colostrum iodine level measured among 150 women [16] . However, a recent meta-analysis has shown an association between maternal of mild-to-moderate iodine deficiency and impaired child brain development [17] . Besides, hypothyroidism might be induced by iodine deficiency (<70 µg/d)

Glutamine

Since it is during infant stage that the vital process of gut colonization and brain development will occur, and thus relations between the intestinal microbiome and infant brain development have been focused on [19] . Impaired cognitive development of preterm infants is related to a low level of

glutamine [20] . As for the mechanism between glutamine and brain development, gut-immune-brain axis might be a potential theory. Glutamine has been proved to protect brain health by preventing neonatal infection induced by pathogens, achieved through maintaining gut health [21] .

Parental or enteral glutamine supplementation might be beneficial to very low birth weight (VLBW) infants on increased morbidity and improved growth outcome. A long-term outcome study has shown that taking enteral glutamine supplementation during Day 3 to day 30 (0. 3 g/kg per day) has no apparent beneficial or adverse effects on cognitive improvement for pre-term (< 32 weeks) and/ or very low birth weight (VLBW, <1500 g) 64 children at around 7 years old (their school age), indicating its safety at least for around 7 years [22] . However, there is still not enough research about the efficacy of glutamine supplementation on infant brain development, this might be caused by several reasons, such as varying doses and injected time, duration time and cognitive measurement. Studies on neurodevelopment follow-up could be conducted to obtain the safety report of glutamine intake.

Bovine Milk Fat Globule Membrane(BFGM)

Formula supplemented with Bovine milk fat globule membrane (BFGM) might be beneficial to cognitive improvement. sphingomyelin (SM), one of the brain cell membrane, is composed of BFGM. SM-supplemented breast milk (20% of phospholipids) has been found to improve neurodevelopmental in 24 VLBW infants, showing an increased SMs level and a better score of Visual evoked

potentials (VEPs)- increased neurotransmitter without any side effects on preterm infants [23.]

Besides, a double-blinded randomized study on 160 infants using 6 months supplemented formula might show some benefits of BFGM with infant cognitive enhancement when compared with standard formulas [24] . Results have revealed a significant change in infant plasma lipidomes, such as an increased level of phosphatidylcholines(PC) and altered content of SMs, indicating the positive effect of BFGM on cognitive development. Although lipid metabolism and further outcome on infant cognitive enhancement are needed to be investigated, SMs has been proved to have none side effects on preterm infants [23] .

The formula contained Sphingomyelin, iron, choline and DHA [11]

Choline might support infant myelination, there’s a formula patent added with choline (30-300 mg/100g). Besides, folic acid added here has an amount of at least 50 -500 mcg/100g. The effect of this formula (SMs, iron, choline, DHA) on myelination has been observed similar to the effect of the first month breastfed infants. High myelin content has been detected by Magnetic Resonance Imaging (MRI) brain scans for 7 days among infants, and their elevated cognitive abilities including gross motor, visual reception, and language (expressive and receptive and learning abilities have been tested through Mullen Scales of Early Learning.

Conclusion

Although it might be effective on improved infant visual acuity with maternal intake of DHA, enhanced cognitive development has only been found in older ages-children, the reason might be inefficient infant cognitive tests. For pregnant women, Nordic Naturals ProOmega for 180 Soft gels is my suggested fish oil brand. After delivery, it’s better to add adequate DHA in formula or breast milk. Here are two examples for the term and preterm infants, especially for pre-term ones, the amount of DHA in an infant formula patent is between 30-300mg/100g [11] . DHA of 9 mg/100 mL has been added in formula supplemented with milk fat globule mMFGM [12] .

Since outcomes of severe deficient iodine have been solved in most of the area, so people start to concentrate on mild-to-moderate areas. Recommended Dietary Allowance for infants is 110 mcg (0-6 months) and 130mcg (6-12months) [6] . Recommended doses of iodine added in the formula for infants between 2-5 months old is 70 μg/d [18] . Since iodized salt is a better source of iodine than a dietary supplement, I would not recommend dietary supplement contained iodine. Besides, in order to improve the efficacy of iodine on the neurodevelopment of infants, certain intake doses and duration of iodine sources are also needed.

I think glutamine supplementation such as L-Glutamine powder from Pure Encapsulations, could be used because it is basically safe. Glutamine could be added L-glutamine < 9g/d of a mother or breast milk or formula to ensure gut microbiome balance and possible brain development.

Since SMs (200mg-2g /kg) has been added in infant formula as a patent [11] . BFGM (4%(wt/wt) of the total protein) has been added in experimental formula [24] (Arla Foods ingredients, Viby, Denmark). Therefore it is possible to add milk polar lipid supplementation in infant diet.

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