

LETTER TO THE EDITOR

Choline: The forgotten essential nutrient, playing a crucial role in fetal development

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Why are we interested in the nutrient choline in the mother during pregnancy and lactation?

A sufficient intake of choline in the mother during this life stage ensures that the fetus/infant is getting sufficient choline that contributes to normal function of the liver and the brain of the newborns and breastfed infants.

What is choline?

Choline is a vitamin-like molecule with unique roles in cell functions. It is an essential nutrient for humans (1). This means that humans cannot produce a sufficient amount of choline in the liver to cover the daily requirements. If choline intake through the diet is insufficient, fatty liver will develop within three weeks. When 500 mg/day choline was provided to the depleted persons, the liver function was normalized. Therefore, a sufficient choline intake is needed for a normal liver function in humans (2,3).

What is the adequate intake level of choline in pregnant and lactating women? Is this intake achievable on a population level?

The requirements of choline increase during pregnancy and lactation due to the active transport of choline to the fetus or excretion of high amount of choline in human milk. This has led official authorities (e.g. the US Institute of Medicine (IOM) and the European food and safety authority (EFSA)) to set higher adequate intake of choline for pregnant (EFSA: 480 mg/day) and lactating women (EFSA: 520 mg/day) versus 400 mg/day (EFSA) in non-pregnant adults (1,4). Population based epidemiological studies on women in reproductive age have shown that on average women do not consume sufficient choline through the diet and that the gap in choline intake is approx. 100-150 mg/day (5). Pregnant and lactating women should aim to achieve choline requirements by supplementing this nutrient as part of prenatal supplements.

Mechanisms that may explain the consequences of choline deficiency on health

Choline is involved in three key biochemical reactions that are strictly needed in all body cells.

First, choline is a methyl donor, which is a role similar to that of folate. Choline is oxidized to betaine, the direct methyl donor for homocysteine. Homocysteine is a toxic amino acid that is converted to methionine using the methyl groups of betaine. Sufficient methyl groups in the cell play a key role in numerous enzymatic reactions and regulation of DNA-methylation and expression (1).

Second, choline is a precursor of the neurotransmitter, acetylcholine. Acetylcholine has a role in neuronal function and brain development (1).

Third, choline is used to produce phosphatidylcholine or contribute with its methyl group to synthesizing phosphatidylcholine from phosphatidylethanolamine. Phosphatidylcholine is a structural component of cell membranes, it plays a role in cellular signaling, cell expansion and differentiation (1).

With this in mind, it is important to recognize that when isotope labelled choline is added to the diet of pregnant rats, it was detected in the liver and the brain of the foetus, thereby showing the two fetal organs with most reliance on choline coming from the maternal diet (6). Separate studies have also shown that dietary choline (labelled choline) was taken up and caused an increase in brain acetylcholine (7).

When choline was supplemented to pregnant women, it influenced placental DNA-methylation (8).

What are the consequences of choline insufficiency during pregnancy or lactation?

It has been shown in animal studies that the liver of pregnant and lactating animals become depleted of choline, while choline accumulates in the same time in the placenta, the fetus or breastmilk. Thus, pregnancy and lactation enhance choline depletion in the mother and predispose the mother to develop choline

deficiency related symptoms. For example, a series of animal studies have shown that cutting choline from the diet during late gestation depleted maternal liver choline and caused triglycerides to accumulate in mother's liver compared to animals fed on a choline-sufficient diet (6,9).

What are the health effects of insufficient maternal choline intake on the offspring?

The foetus and the breastfed infants cannot produce sufficient choline to cover their own requirements. They drain choline from the mother through transplacental transport and human milk (1,6).

Liver: Fatty liver is a universal outcome of insufficient choline intake in humans and animals. Thus, sufficient intake of choline in the mother is necessary to ensure normal liver function in the fetus and breastfed infants. This has been shown by depletion studies in pregnant animals, where choline deficient diet during pregnancy caused fatty liver in the mothers and the newborns. This role is obviously analogue to the role of choline as an essential nutrient in human adults. However, it appears that *early life is a very critical time window where infants are sensitive to deficiency of choline and other methyl donors such as folate* (3).

Brain: Insufficient maternal choline can cause a delay in neuronal cell development and thereby negatively influence brain development. This is due to its role in phospholipid metabolism and acetylcholine synthesis, insufficient choline can cause a delay in neuronal cell development and thereby negatively influence brain development. Studies on genetic defects of choline

transport to the brain have shown that infants have microcephaly and retarded brain growth (8,10,11). In addition, epidemiological studies have shown that lower choline intake or plasma concentrations of the mother are associated with 36% higher risk of having a newborn suffering from severe brain/neural tube defects such as spina bifida. This association was independent on supplementing folic acid during pregnancy, suggesting that adding choline to prenatal supplements may have potential to further reduce the risk of brain defects compared to when folate alone is used. Randomized controlled trials to test the effect of choline compared to folic acid are not ethical. However, support to the unique role of choline in early development of the brain comes from experimental choline deficiency in mice embryo and other genetic models, where choline, but not folic acid was able to rescue the neural tube defects (12).

Take home messages

Choline is definitely needed during early life as a methyl donor, to form cell membrane and acetylcholine. Choline requirements increase considerable during pregnancy and even more during lactation compared to outside these life periods. However, young women are not achieving the requirements through the natural diet. Therefore, choline should be included in prenatal supplements (to give roughly 150 mg/d additional intake) to ensure reaching the intake recommendations during this life stage. Adequate choline intake in the mother is necessary for normal function of the liver and the brain of the fetus and breastfed infants.

Literature

1. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). Dietary reference values for choline. EFSA J. 2016;14:e04484
2. Zeisel SH, da Costa KA, Franklin PD, Alexander EA, Lamont JT, Sheard NF, et al. Choline, an essential nutrient for humans. FASEB J. 1991;5:2093-2098
3. EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA). Choline and contribution to normal liver function of the foetus and exclusively breastfed infants: evaluation of a health claim pursuant to Article 14 of Regulation (EC) No 1924/2006. EFSA J. 2023;21:e08115
4. Institute of Medicine. Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. Washington, DC: National Academies Press; 1998. Chapter 12, p. 293
5. Derbyshire E, Obeid R, et al. Habitual Choline Intakes across the Childbearing Years: A Review. Nutrients. 2021;13:4390
6. Zeisel SH, Mar MH, Zhou Z, da Costa KA. Pregnancy and lactation are associated with diminished concentrations of choline and its metabolites in rat liver. J Nutr. 1995;125:3049-3054
7. Cohen EL, Wurtman RJ. Brain acetylcholine: control by dietary choline. Science. 1976;191:561-562
8. Garner SC, Mar MH, Zeisel SH. Choline distribution and metabolism in pregnant rats and fetuses are influenced by the choline content of the maternal diet. J Nutr. 1995;125:2851-2858
9. Gwee MCE, Sim MK. Free choline concentration and cephalin-N-methyltransferase activity in the maternal and foetal liver and placenta of pregnant rats. Clin Exp Pharmacol Physiol. 1978;5:649-653
10. Zeisel SH. Nutritional importance of choline for brain development. J Am Coll Nutr. 2004;23(6 Suppl):621S-626S
11. Derbyshire E, Obeid R. Choline, neurologic development and brain function: a systematic review focusing on the first 1000 days. Nutrients. 2020;12(6):1731
12. Obeid R, et al. Association between Maternal Choline, Fetal Brain Development, and Child Neurocognition: Systematic Review and Meta-Analysis of Human Studies. Adv Nutr. 2022;13:2445-2457