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Study confirms the effect of a supplement on the micronutrient content of breast milk

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Even in countries with a high standard of living, the intake of essential nutrients by breast-feeding women is often inadequate – with potentially negative effects on the development of their baby. A randomised, double-blind, placebo-controlled study confirms the evidence in favour of daily supplementation with a combination of several micronutrients plus lutein and docosahexaenoic acid (DHA) during lactation.

Micronutrient intake by lactating mothers often insufficient

A child grows faster in the first weeks of life than in any subsequent phase of development. After six months, both its body weight and brain weight have doubled; at the end of the first year, the child's body weight has tripled and the brain has already reached 70% of its adult weight. Healthy development requires an adequate supply of key nutrients. Breastfeeding is considered the optimum way to feed an infant and is recommended by specialist organisations [1], but the composition of breast milk can vary, depending on the metabolic and nutritional status of the mother. The levels of some micronutrients in breast milk such as calcium, iron, copper and zinc appear not to be influenced by maternal dietary intake, whereas the amounts of others – for example, B vitamins and DHA – are found to vary in the breast milk depending on the mother's diet.

The recommended intake for crucial nutrients, for example iodine, is considerably higher in lactating than in non-lactating women [2, 3]. Even in countries with a high standard of living, multiple micronutrient deficiencies are widespread [3]. A randomised, double-blind, placebo-controlled study was conducted in Germany on the effects of supplementation with a combination of several micronutrients plus DHA and lutein (hereinafter referred to as Multiple Micronutrient Supplementation, MMS) during lactation [3].

Study investigates supplementation with multiple micronutrients, DHA and lutein

70 healthy, breastfeeding women and their infants were randomly assigned to two treatment groups (35 in each group). Among the inclusion criteria were a singleton pregnancy, a haemoglobin level >105 g/L, the desire to breastfeed for at least four months, and an omnivorous diet. Infants with an appropriate birth weight (gestational age >37 weeks/<43 weeks) and no abnormalities were included in the accompanying study.

The investigational product was a soft gel capsule with the following ingredients (Elevit® 3, Bayer): vitamin A (beta-carotene) 3600 IU; vitamin C 60 mg; vitamin D 600 IU; vitamin E 10 IU; vitamin B1 1.4 mg; vitamin B2 1.6 mg; vitamin B3 17 mg; vitamin B5 7 mg; vitamin B6 2 mg; vitamin B12 2.8 mg; folic acid 500 µg; biotin 35 µg; calcium 120 mg; iodine 225 µg; iron 9 mg; selenium 55 µg; zinc 10 mg; DHA 200 mg; lutein 250 µg.

The MMS group (n = 35, of whom 32 completed the study) received the investigational product once daily. Supplementation began four to six weeks after delivery (Visit 2) and lasted about twelve weeks (Visit 4). Over the same period, the placebo group (n = 35, of whom 33 completed the study) received a soft gel capsule that contained no active constituent apart from iodine (225 µg). The dose of iodine in the investigational product and in the placebo was the same and corresponded to the recommendations of the German Maternity Guidelines.

The effects of supplementation on maternal milk and blood biomarkers were investigated. The primary endpoint was the change in percentage DHA content in breast milk, determined in weight percent relative to total fatty acids (wt. % TFA) Secondary endpoints included the status of other micronutrients in breast milk and in maternal blood.

Significant increase in DHA content of breast milk

The long-chain polyunsaturated fatty acid docosahexaenoic

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Tab. 1. Primary and secondary maternal efficacy endpoints with significant changes reported from Visit 2 to Visit 4 (per protocol population, LOCF approach).

Parameters	Placebo (n = 33) Mean ± SD (Range)	MMS (n = 32)	LS Mean Difference (95 % CI)[1]	p Value*
Milk parameters				
DHA [wt. % TFA] (primary)	−0.05 ± 0.11 (−0.32 to 0.22)	0.11 ± 0.12 (−0.23 to 0.32)	0.15 (0.11–0.19)	<0.0001
EPA [%]	−0.01 ± 0.04 (−0.11 to 0.06)	0.01 ± 0.03 (−0.06 to 0.06)	0.0110 (0.0006–0.0214)	0.038
Mead acid [%]	0.019 ± 0.054 (−0.03 to 0.19)	−0.004 ± 0.015 (−0.07 to 0.01)	−0.022 (−0.040 to −0.003)	0.024
Beta carotene [ng/mL]	−5.1 ± 17.2 (−48.0 to 28.0)	22.7 ± 34.5 (−20.0 to 142.0)	28.4 (15.0–41.9)	<0.0001
Blood parameters				
DHA [mg/L]	−9.76 ± 8.98 (−37.0 to 6.9)	7.14 ± 11.40 (−29.0 to 28.1)	15.66 (11.96–19.36)	<0.0001
DHA/TFA	−0.004 ± 0.007 (−0.008 to −0.001)	0.009 ± 0.009 (−0.02 to 0.03)	0.013 (0.010–0.016)	<0.0001
Docosatetraenoic acid [mg/L]	−0.44 ± 1.08 (−3.9 to 1.9)	−0.70 ± 0.87 (−2.2 to 1.8)	−0.46 (−0.86 to −0.05)	0.0270
EPA [mg/L]	−2.84 ± 4.27 (−11.2 to 4.6)	0.59 ± 4.48 (−10.6 to 13.5)	2.21 (0.44–3.98)	0.0155
25-OH-vitamin D [ng/mL]	−1.02 ± 8.18 (−7.5 to 5.50)	5.88 ± 9.98 (−8.4 to 28.9)	7.82 (4.36–11.28)	<0.0001
Folic acid [ng/mL]	−1.73 ± 4.73 (−11.6 to 16.5)	17.82 ± 9.51 (11.70–23.80)	21.20 (17.84–24.56)	<0.0001
Homocysteine [µM]	0.56 ± 1.47 (−3.51 to 3.72)	−1.08 ± 1.24 (−4.24 to 1.71)	−1.63 (−2.27 to −0.99)	<0.0001
Vitamin B12 [pg/mL]	−17.9 ± 97.0 (−313.0 to 342.0)	69.0 ± 135.7 (−190.0 to 510.0)	89.89 (31.45–148.3)	0.0031
Beta carotene [ng/mL]	−49.3 ± 160.3 (−443.0 to 222.0)	223.3 ± 334.2 (−480.0 to 1182.0)	296.35 (183.06–409.64)	<0.0001
Lutein [ng/mL]	−16.8 ± 33.1 (−91.0 to 40.0)	5.8 ± 52.2 (−182.0 to 90.0)	21.13 (4.15–38.31)	0.0157

* p value < 0.05 considered statistically significant. [1] Difference = supplementation − placebo.
CI: confidence interval; DHA: docosahexaenoic acid; EPA: eicosapentaenoic acid; LOCF: last observation carried forward; LS mean: least squares mean; Mead acid: eicosa-5,8,11-trienoic acid; MMS: multiple micronutrients, lutein, and DHA supplementation; SD: standard deviation; TFA: total fatty acids; wt.: weight.

acid (DHA) is a constituent of membrane phospholipids, especially of nerve cells. Particularly high concentrations are found in the brain, central nervous system and retina. The intake of DHA by the mother can contribute to normal brain development and to normal development of vision in the infant [4]. The concentration of DHA in breast milk is determined by the maternal dietary intake of DHA.

Supplementation over the 12-week study period significantly increased the DHA content of breast milk, compared to a reduction in the placebo group ($p < 0.0001$) (see **Tab. 1**). The DHA content in the milk rose with MMS during the study from a mean of 0.25% ± 0.09% (range 0.12–0.57%) to 0.35% ± 0.08% (range 0.18–0.49%) after twelve weeks. In contrast, the DHA content in the placebo group fell from 0.26% ± 0.12% (range 0.12–0.64%) to 0.21% ± 0.08% (range 0.10–0.47%) over the study period. The decrease in the placebo group might be caused by the fact that during pregnancy, all participants were allowed to take dietary supplements, which could have contained DHA. In addition, the study authors point out that the DHA levels in breast milk are known to decrease with increasing duration of lactation.

The LS mean difference in milk DHA levels (wt. % TFA) between MMS and placebo over the 12 weeks was 0.15 (95% CI 0.11–0.19) ($p < 0.0001$ in favour of MMS). (Continuous data are summarised in the study as mean ± SD or LS means [least squares means] of the change compared to Visit 2 [95 % confidence interval, CI], as appropriate.)

Significant increase of other micronutrients in maternal milk and blood

In agreement with the observed changes in breast milk, a significant increase in DHA levels was also observed in maternal blood in the MMS group, compared to a decrease in the placebo group. There was likewise a significant rise in blood and milk levels of the omega-3 fatty acid eicosapentaenoic acid (EPA) in the MMS group, whereas they fell in the placebo group.

Vitamin concentrations differed significantly between the active treatment and placebo groups (see **Tab. 1**). A significant increase in the blood levels of 25-OH vitamin D, folic acid, vitamin B12 and lutein was measured in the MMS group as compared with a decrease in the placebo group. Levels of beta-carotene rose in both blood and milk in the MMS group, but fell in the placebo group.

Blood levels of homocysteine showed the opposite effect, with a decrease in the MMS group and an increase in the placebo group. High levels of homocysteine are a risk factor for the development of thrombotic or cardiovascular events in adults. Also, blood levels of the omega-6 fatty acid docosatetraenoic acid fell in both groups, significantly more in the MMS group than under placebo. Although long-chain omega-6 fatty acids such as docosatetraenoic acid play an important role in the regulation of inflammation, the eicosanoids derived from them exhibit pro-inflammatory action.

Apart from these parameters, there were no significant differences in other maternal blood biomarkers or in the composition of milk nutrients.

Safe and well-tolerated

One mother in each treatment group experienced an adverse event that the investigators considered was causally related to the investigational product: in the placebo group this was of mild intensity (flatulence) and in the MMS group of moderate intensity (peripartal bleeding).

The investigators did not consider any of the adverse events reported in the infants to be causally related to the investigational product.

Summary

The study results showed that the ingestion of a micronutrient supplement with DHA and lutein during lactation was associated, among other things, with a significant increase in DHA levels in breast milk and significantly increased concentrations of selected nutrients in maternal blood and breast milk compared with the placebo. Although the study was performed in a country with a high standard of living, the dietary intake of macro- and micronutrients was often inadequate. The study authors emphasise that supplementation preserves DHA levels in breast milk and state that this may lead to clinical benefits for the infant [3]. However, the present study did not investigate such possible clinical benefits.

The supplement was well tolerated, with no significant difference in terms of the number of adverse events between the study and control groups.

Literature

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