BREASTFEEDING MEDICINE
Volume 14, Number 5, 2019

DOI: 10.1089/bfm.2019.0077

High-Dose Vitamins

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Concentrations of most vitamins in breast milk are dependent on maternal diet.[1] Daily vitamin supplementation to achieve adequate dietary intake is thus a recommended intervention for lactating mothers who are undernourished, or for those with dietary restrictions. Even in mothers with no known dietary deficiency risks, the use of prenatal vitamins during lactation is commonplace and is considered safe for the breastfed infant (Table 1).[2,3] Some lactating mothers may elect to consume high-dose or ''megadose'' vitamin therapy, beyond that required for adequate daily intake. Commonly used vitamins taken in megadoses are listed in Table 2. Depending on the vitamin, dosage, and the mother's underlying vitamin status, this practice could potentially lead to vitamin concentrations in milk that are harmful to the infant. This column briefly reviews the available published data and provides recommendations for nursing mothers considering vitamin megadosing.

Vitamin C

Average milk vitamin C concentrations are 50–80 mg/L in well-nourished mothers consuming adequate vitamin C in their diet, and their milk concentrations are not markedly increased with routine daily multivitamin supplementation.

In a study of mothers given high doses between 250 and 1,000 mg daily, average milk concentrations were ~100–120 mg/L after 2 days of supplementation, but were not significantly related to dose. The maximum measured concentration was 158 mg/L in a subject taking only 250 mg/day.[4] In a separate case, a mother taking 4,000 mg vitamin C per day during pregnancy and lactation had a milk concentration of 105 mg/L.[5] Based on the highest milk concentration reported, an exclusively breastfeeding infant would be expected to consume ~25 mg/kg per day, which is similar to the treatment dose for infants with scurvy, and well below infant exposures known to cause harm.[6] A once daily 500 mg vitamin C dose, along with 100 IU of vitamin E, also improves the milk biochemical antioxidant profile.[7] Maternal use of high-dose daily vitamin C (>200 mg/day) is not a reason to discontinue breastfeeding.

Vitamin B_2 (riboflavin)

Average milk concentrations are 300–600 mcg/L in well-nourished mothers consuming adequate riboflavin in their diet. Routine 1.8–2 mg daily supplementation modestly increases milk concentrations by 30–70 mcg/L in both under- and well-nourished lactating mothers.

The highest supplemental dose studied has been 10 mg/day; milk concentrations increased from 200 mcg/L at baseline to 750 mcg/L after several months of supplementation.[8] There have been no reports of milk concentrations or breastfed infant safety during maternal high-dose riboflavin therapy. Intravenous high-dose riboflavin has been safely used in hyperbilirubinemic newborns as an adjunct to phototherapy. Riboflavin is considered to have a wide safety margin in humans and there is no established upper limit of tolerability. A common benign side effect of larger doses is bright yellow urine discoloration.[6,9] Owing to a lack of data, other drugs for migraine prophylaxis with good safety records during breastfeeding (e.g., propranolol, nortriptyline) are preferred over riboflavin. However, considering the wide safety margin of riboflavin, maternal use of 400 mg/day of riboflavin is not a reason to discontinue breastfeeding.

Vitamin B_6

Pyridoxal is the dominant form of vitamin B_6 in human milk rather than pyridoxine or pyridoxamine. All three forms are equally bioactive and interconvertible in the mother's body. Pyridoxine is used medicinally because it is the most chemically stable. Average total vitamin B_6 milk concentrations are 70–180 mcg/L in healthy mothers not taking a supplement. Modest daily maternal supplementation with 6–7.5 mg pyridoxine increases milk concentrations to 200–400 mcg/L, whereas higher daily doses of 10–20 mg increase concentrations to 400–700 mcg/L. At these higher concentrations, the breastfed infant would only be exposed to ~100 mcg/kg per day.

Pyridoxine 25 mg/day is recommended in mothers taking isoniazid and is not a reason to discontinue breastfeeding according to CDC and WHO tuberculosis management guidelines. Very high dosages of 300 mg/day can be used to treat neuritis caused by certain drugs, and 200–600 mg/day has been studied for postpartum lactation suppression by decreasing prolactin production, although it is often not effective.[10] With usual dosages found in vitamin supplements, pyridoxine has no effect on prolactin or lactation. There have been no reports of milk concentrations or breastfed infant safety with the very high doses of pyridoxine, although the clinical situations in which such dosages might be used typically preclude breastfeeding. Considering the robust

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Table 1. Vitamin Reference Values

Vitamin	*RDA*[a]	*PNV*[b]	*UL*[c]	*Infant AI*[d]
B_2	1.6 mg	2 mg	NE	0.3 mg
B_6	2 mg	2 mg	100 mg	100 mcg
B_{12}	2.8 mcg	4 mcg	NE	0.4 mcg
Biotin	35 mcg	30 mcg	NE	5 mcg
C	120	100 mg	2,000 mg	40
D	600 IU	400 IU	4,000 IU	400 IU
K	90 mcg	—	NE	2 mcg

[a]Recommended dietary allowance (RDA) per day for lactating women >18 years of age.[9]
[b]Typical prenatal vitamin (PNV) content may vary slightly among different products.
[c]Upper limit (UL) of daily tolerability for lactating adult women, from NIH.[9]
[d]Adequate daily intake (AI) for infants 0–6 months of age.[9]

response of milk vitamin B_6 concentrations to maternal supplementation, maternal megadosing (200–600 mg/day) is very likely to expose the breastfed infant to well above their daily requirement. However, such exposures are unlikely to be greater than the 1 mg/kg per day infant pyridoxine dose routinely used to prevent isoniazid-induced neuritis.

Vitamin B_{12} (cobalamin)

Average milk concentrations are 400–900 ng/L in well-nourished mothers with adequate vitamin B_{12} status. A daily 250 mcg maternal dose in B_{12} deficient mothers increased milk concentrations by ~90 ng/L, providing exclusively breastfed infants an extra 0.013 mcg/kg per day of vitamin B_{12}.[11]

Vegan mothers in the United States taking high-dose daily B_{12} supplements (range 100–5,000 mcg/day) had a median milk vitamin B_{12} level of 830 ng/L at 2 weeks postpartum, and 15% had milk concentrations at or more than the assay limit of 1,670 ng/L.[12] Even at such a high milk concentration, a breastfed infant would only be exposed to 0.25 mcg/kg per day, which is about two to three times the adequate daily intake. Vitamin B_{12} is considered to have a wide safety margin in humans and there is no established upper limit of tolerability. Neonates with methylmalonic acidemia are given 1,000 mcg hydroxo- or cyanocobalamin intravenously.[6,9]

Table 2. High-Dose Oral Vitamin Uses

Vitamin	*Use*[a]	*Daily high dose*[b]
B_2	Migraine	400 mg
B_6	Neuritis	200–600 mg
B_{12}	Anemia, CV health, vegetarianism	250–5,000 mcg
Biotin	Skin and hair health	2.5 mg
C	Common cold	250–1,000 mg
D	Bone health, cancer prevention	2,000–6,000 IU
K	Bone health, CV health	1–5 mg

[a]Purported benefits in the mother, not necessarily endorsed by the author. See NIH[9] for more information.
[b]Typical doses likely to be encountered, see text and NIH.[9]
CV, cardiovascular.

For women with known or suspected B_{12} deficiency, megadosing vitamin B_{12} would be expected to normalize breast milk concentrations and is not a reason to discontinue breastfeeding. Megadosing vitamin B_{12} has not been studied in women with normal B_{12} status; however, the expected increase in milk B_{12} concentration from taking B_{12} 400–1,000 mcg/day for cardiovascular health should be clinically unimportant and not a reason to discontinue breastfeeding.

Biotin

Milk biotin concentrations are 5–10 mcg/L in well-nourished mothers not taking a supplement. In poorly nourished mothers given a supplemental dose of 250 mcg/day of biotin, milk concentrations were 5 mcg/L compared with 1.6 mcg/L in those not given a supplement.[8]

Higher biotin doses have not been studied in lactating women. Biotin has a wide safety margin in humans and there is no established upper limit of tolerability. Maternal use of high-dose (2.5 mg/day) biotin is not a reason to discontinue breastfeeding.

Vitamin D

Milk vitamin D concentrations are highly variable between individual mothers due to the positive effect of sunlight exposure. Those taking daily supplements with 400–2,000 IU have average milk concentrations of 50–80 IU/L. These concentrations are slightly higher than those in non-supplemented well-nourished mothers living in higher latitudes during winter months, but not necessarily in summer. In small studies, mothers with normal or borderline deficiency vitamin D given daily supplemental doses in the 4,000–6,400 IU range, or a one-time 150,000 IU dose, had their breastfed infants' vitamin D status improve, *on average*, to more than the minimum cutoff for deficiency during the study period without any direct infant supplementation.[13,14] Since not all infants studied achieved this outcome, infant serum 25-OH-vitamin D monitoring would be prudent to confirm efficacy if a mother chooses to megadose in this range without directly supplementing her infant. Average milk concentrations in these studies were 130–370 IU/L after 1–3 months of treatment, which would not be expected to expose the breastfed infant to excessive vitamin D if the infant were to be also directly supplemented at the recommended 400 IU/day dosage. However, average milk concentrations of ~900 IU/L were reported in mothers after 7 months of 6,400 IU/day supplementation plus increased seasonal maternal sun exposure. Thus, the combination of maternal megadosing 6,400 IU/day plus copious summertime sun exposure plus infant supplementation could potentially expose the exclusively breastfed infant to excessive (>1,000 IU) daily doses of vitamin D and should be avoided or closely monitored.

Vitamin K

Concentrations of vitamin K_1 (phylloquinone, phytonadione) in breast milk are 1–3 mcg/L in most studies of well-nourished women not taking a supplement. Single large oral vitamin K_1 doses of 20 mg can transiently increase milk K_1 concentrations to ~130 mcg/L within 12–24 hours after dosing, but concentrations return to baseline after 1 week. Daily administration of 2.5 or 5 mg K_1 increases milk

concentrations to 60–80 mcg/L. Such concentrations would provide the exclusively breastfed infant with ~10 mcg/kg per day of K_1, which is more than the adequate intake, but very similar to the intake of formula-fed infants. One study found that a 5 mg daily oral maternal K_1 supplement improved the infant biochemical vitamin K status and lowered the infant risk of K_1 deficiency compared with no maternal supplementation, in exclusively breastfed infants who *also received* a standard birth intramuscular 1 mg dose.[15] High-dose maternal vitamin K (1–5 mg) is, therefore, safe for the breastfed infant, but available data do not support maternal supplementation as a substitute for direct administration of vitamin K for the prevention of vitamin K deficiency bleeding.

Although K_1 is the dominant form of vitamin K in the diet and in human milk, vitamin K_2 is also naturally present in milk, predominantly as the K_2 subtype menaquninone-4, also called MK-4. Very high MK-4 doses of 15–45 mg/day are commonly promoted for bone health based on studies conducted in *postmenopausal women* to lower the risk of osteoporosis. No published information regarding vitamin K milk levels in mothers taking any dose of MK-4 supplements could be located. MK-4 has a higher reported milk–plasma ratio than K_1, which is consistent with its known wider distribution throughout the body. There are also multiple forms of K_2 besides MK-4 that may be contained within products marketed or labeled as ''vitamin K_2.'' Lactating mothers should be discouraged from taking very high dose K_2 or MK-4 until better data are available. Low maternal vitamin K_2 doses (<1,000 mcg) taken as a daily supplement to maintain normal dietary intake would not be a reason to discontinue breastfeeding.

Summary

Although megadosing of vitamins is usually unnecessary for the mother or infant, there is little evidence of infant harm from this practice. Extremely high doses of pyridoxine might suppress milk production.

Disclosure Statement

No competing financial interests exist.

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