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Vitamin D

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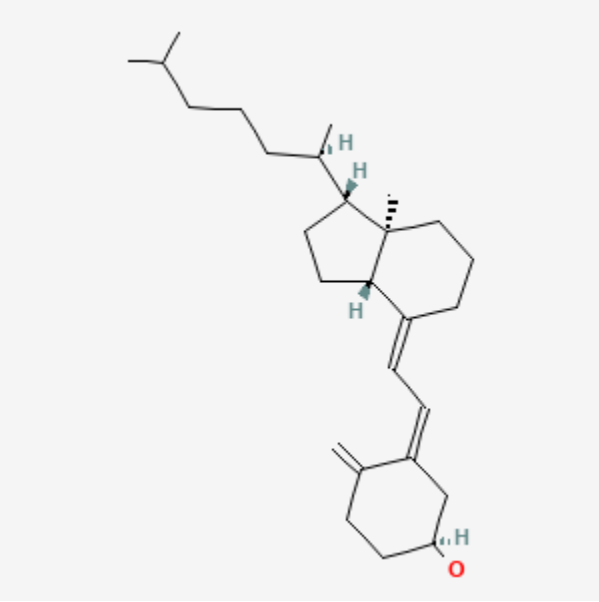

Drug Levels and Effects

Summary of Use during Lactation

Vitamin D is a normal component of human milk. Daily maternal vitamin D_2 or D_3 supplementation in the 10 to 50 mcg (400 to 2,000 IU) range produces milk concentrations that are inadequate to deliver the daily requirement to an exclusively breastfed infant, and inadequate to correct pre-existing infant vitamin D deficiency through breastfeeding alone. Breastfeeding mothers who take vitamin D supplements in this range should give their infants a daily vitamin D supplement of at least 10 mcg (400 IU) to meet pediatric nutritional guidelines.[1-3] Daily maternal vitamin D dosages at or above 100 mcg (4,000 IU) achieve milk levels can potentially meet the 10 mcg daily infant goal intake, depending on the mother's underlying vitamin D status and daily infant milk intake. Obese mothers may have higher requirements.

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Drug Levels

The major forms of vitamin D present in breastmilk are cholecalciferol (vitamin D_3), ergocalciferol (vitamin D_2), and their respective 25-hydroxylates (25-OH) also known as calcidiols. Dihydroxylated metabolites are also present in milk, but in such low quantities that their contribution to total milk vitamin D activity is not routinely accounted for. The low potency C-3 stereoisomer of 25-OH-vitamin D_3 is also present in milk. Analytical techniques that do not detect this isomer can potentially overestimate the true 25-OH-vitamin D_3 level. Vitamin D partitions extensively into the fat fraction of whole milk after 1 to 2 days when stored under refrigeration.[4]

Human vitamin D deficiency is defined as a 25-OH-vitamin D serum level <20 mcg/L (<50 nmol/L), and vitamin D insufficiency as 20 to 30 mcg/L (50 to 75 nmol/L). The goal of vitamin D supplementation is to achieve a serum 25-OH-vitamin D level of 30 to 100 mcg/L (75 to 250 nmol/L).[5] Darker skin pigmentation is a risk factor for vitamin D deficiency due to decreased UVB-mediated cutaneous vitamin D_3 synthesis.[6] U.S. infants and children with darker skin pigmentation do not achieve optimal synthesis, even during summer months, from everyday outdoor sun exposures.[7]

Milk levels of vitamin D and 25-OH-vitamin D are 10 to 20% and 1 to 2% of maternal blood levels, respectively.[8-11] As a mother's vitamin D blood levels increase due to increasing light exposure or dietary intake, milk vitamin D content also increases.[10,12-15] Maternal serum and milk levels and breastfed infant serum levels can be higher during summer and at lower latitudes due to increased sunlight availability and skin ultraviolet B light (UVB) exposure.[11,12,16-21] Levels are 1.5 to 2 times higher in hindmilk than in foremilk.[10]

United States Food and Drug Administration standards for dietary supplement labeling recommend mcg rather than the traditional "international units" (IU) when describing vitamin D doses. One mcg of D_2 or D_3 is equivalent to 40 IU. Many of the studies cited in this monograph were conducted prior to this standard being widely adopted. They also report level measurement results in IU/L to standardize and convert all measured vitamin D forms to total antirachitic activity since the 25-OH-vitamin D forms are 5 times as potent as their parent calciferol forms. Therefore, the original IU provided by the study authors are used when describing these studies throughout this monograph. Conversion to mcg are provided when describing infant exposures or maternal dosage recommendations.

Maternal Levels. Lactating women with nondeficient vitamin D status (serum 25-OH-vitamin D >20 mcg/L or >50 nmol/L) taking 400 to 2000 IU daily have an average or median reported total vitamin D antirachitic activity in their milk of 50 to 80 IU/L.[1,8,10,14,15,22-28] Based on these reported milk levels, an exclusively breastfed infant will ingest only 8 to 12 IU/kg (0.2 to 0.3 mcg/kg) daily of vitamin D, which is well below the 10 mcg daily requirement

In a study of eighteen breastfeeding mothers with nondeficient vitamin D status given 4000 IU daily of vitamin D, average milk levels were approximately 130 IU/L after 3 months of supplementation. Based on this reported average milk level, an exclusively breastfed infant would receive 20 IU/kg (0.5 mcg/kg) daily of vitamin D.[26]

Nineteen fully breastfeeding women were given either 400 or 6,400 IU daily of vitamin D_3 beginning at 1 month postpartum. Dietary intake and skin pigmentation changes did not differ between the two groups. Average maternal baseline vitamin D serum levels were >30 mcg/L. Over 7 consecutive monthly measurements, average milk vitamin D levels increased from 59.6 IU/L at baseline to 76.3 IU/L at 7 months in the 400 IU daily group, and steadily increased in the 6,400 IU daily group from 82.4 IU/L at baseline, to 374.4 IU/L after 4 months, 555.2 IU/L after 5 months, 624.5 IU/L after 6 months, and 873.5 IU/L after 7 months. Milk level changes paralleled maternal vitamin D status changes. Maternal serum 25-OH-vitamin D levels in the 6,400 IU group increased from 34 to 58.8 mcg/L over the 7-month study period. The authors suggested that the increase in both milk and serum levels towards the end of the 7-month study period in both groups was due to increased outdoor activity and sun exposure coinciding with warmer months.[23] Based on the average milk concentration of 374.4 IU/L

after 4 months of treatment in the 6,400 IU daily group, an exclusively breastfed infant would ingest about 60 IU/kg (1.5 mcg/kg) daily. This dosage could potentially meet the 10 mcg daily requirement for the average sized 5-month-old infant.

Forty exclusively breastfeeding mothers in the Northern US were given oral vitamin D_3 150,000 IU one time or 5000 IU daily for 28 days. Their infants were between 4 and 28 weeks old at study enrollment. Average milk vitamin D_3 levels in the single dose group increased from below the limit of quantification (<280 IU/L) at baseline to approximately 1600 IU/L after 1 day, decreasing to 440 IU/L by 7 days after the dose, to undetectable again by day 14. Average milk D_3 levels in the once daily group increased from undetectable at baseline to 320 IU/L by day 3 and remained at about 320 IU/L for the remaining 28-day study period; 25-OH-vitamin D was not detected in milk in either group.[11] Based on the reported average level, an exclusively breastfed infant would receive approximately 50 IU/kg (1.2 mcg/kg) daily from a maternal daily dosage of 5,000 IU D_3.

In a mother taking long-term vitamin D_2 100,000 IU daily during pregnancy and lactation to maintain normal calcium and phosphorus status after a prepregnancy thyroid-parathyroidectomy, plus a daily prenatal vitamin containing 400 IU vitamin D, breastmilk antirachitic activity at 14 days postpartum was 6,700 IU/L. Milk vitamin D_2 concentration was 126 mcg/L and 25-OH-vitamin D_2 was 8.3 mcg/L.[29] These values are approximately 800 times and 80 times higher, respectively, than those normally seen in lactating women taking a 400 IU daily of vitamin D_2 supplement.[8] Vitamin D_3 forms were undetectable in milk. The mother's serum vitamin D_2 and 25-OH-vitamin D_2 levels were 500 times normal levels.

Eighty-five breastfeeding mothers in Finland were given an oral vitamin D_2 or D_3 supplement of 1000 IU daily, 2000 IU daily or no supplementation. Milk was collected at 8, 15, and 20 weeks postpartum. Milk levels were highest in September, and higher in September and May than December and February. Supplementation significantly increased milk antirachitic activity in winter months compared to no supplementation, but not in summer. Median hindmilk antirachitic activity in February was 51 IU/L in the 1,000 IU daily group and 92 IU/L in the 2,000 IU daily group. The range was 20 to 190 IU/L in both groups. For the nonsupplemented mothers in February, the median milk level was 35 IU/L ranging from 15 to 100 IU/L. Median hindmilk antirachitic activity in September was 136 IU/L in the 1,000 IU group, and 114 IU/L in the unsupplemented group, with a range of approximately 50 to 320 IU/L in both groups.[9] Diet, daily sunlight exposure, and maternal vitamin D status were not controlled for, and likely explain the highly variable milk levels reported. The positive effect of supplementation on vitamin D levels in winter but not in summer seen in this study has been also reported in pregnant mothers and their serum 25-OH-vitamin D levels.[30]

Thirty-six women in the Netherlands were randomized to receive a daily vitamin D supplement of either 400 IU, 1400 IU, 2400 IU, or 3400 IU beginning at 20 weeks gestation and continued for 4 weeks postpartum. A single breastmilk sample was collected at 4 weeks postpartum. Median milk levels were 33 IU/L, 83 IU/L, 150 IU/L, and 156 IU/L, respectively. Analyses confirmed a linear relationship between maternal dosage and milk level. The authors calculated that it would take a daily maternal dose of 8500 IU (21 mcg) to achieve milk levels sufficient to deliver the target 400 IU (10 mcg) daily to the breastfed infant.[31]

One hundred ninety mothers in Qatar were randomized to receive either 600 IU or 6000 IU vitamin D beginning within 4 weeks postpartum. Baseline milk levels were similar in both groups at around 20 IU/L. At 4 months postpartum, median milk levels were 12 IU/L and 186 IU/L, respectively. At 7 months postpartum they were 14.3 IU/L and 144 IU/L, respectively. Based on the milk levels in the 6000 IU (150 mcg) high-dose group, an exclusively breastfed infant would receive approximately 30 IU/kg (0.75 mcg/kg) daily of vitamin D.[32]

In a Danish study of 48 breastfeeding women with normal vitamin D status, 70 to 80% of whom were taking a 400 IU daily supplement, vitamin D and 25-OH-vitamin D milk levels were highest in July, approximately 3 nmol/L and 1.5 nmol/L, respectively, and lowest in February (<1 nmol/L for both). More milk samples collected in winter months were below the vitamin D detection limit of 0.14 nmol/L than in summer (49% vs 24%). The

median total vitamin D antirachitic activity in milk was 130 IU/L in the summer months and 80 IU/L in winter. Breastmilk concentrations correlated with maternal median serum 25-OH-vitamin D concentrations, which were at their highest in July (90 nmol/L) and lowest in February (50 nmol/L).[10]

Five white-skinned, lactating mothers were exposed to artificial UVB light at approximately the same exposure as 30 minutes of clear, midday, midlatitude, summer sun. Their average breastmilk vitamin D_3 levels increased from 0.15 mcg/L prior to exposure to a peak of 0.85 to 3.7 mcg/L 2 to 3 days after exposure. Vitamin D_3 milk levels were still slightly above baseline, 0.24 to 0.4 mcg/L, at 14 days after exposure. Milk 25-OH-vitamin D_3 and vitamin D_2 did not significantly increase.[13]

Four hundred and sixty-seven women in Toronto, Canada had their vitamin D status evaluated during pregnancy at 28 to 31 weeks gestation, and again at 3 and 12 months postpartum. Two-thirds of the women studied had serum 25-OH-vitamin D <75 nmol/L throughout the study, and less than half were taking a standard vitamin D supplement. Their outdoor activity levels were considered low to moderate. Seasonal variation accounted for only a 5.4 nmol/L increase in serum 25-OH-vitamin D for those pregnant during winter and postpartum during spring and summer.[33] Although breastmilk vitamin D levels were not measured, this study suggests that seasonal changes in maternal blood and milk vitamin D levels are minimal in women living at high latitudes with low serum vitamin D levels, average outdoor exposure, and casual vitamin D supplementation.

A study comparing ten black and fifteen white exclusively breastfeeding mothers in a northern US city reported average milk levels of 34 IU/L and 64 IU/L, respectively. Vitamin D_3, D_2, and 25-OH-vitamin D_3 levels were all significantly lower in the milk of the black mothers, but 25-OH-vitamin D_2 was similar between the two groups. The vitamin D_3 milk level was significantly lower in the black mothers even when controlling for their less self-reported outdoor exposure. Maternal average daily vitamin D intake was similar between the two groups, but daily intake of vitamin D_2 contained in prenatal vitamins was higher in the white mothers, which resulted in a higher proportion of their total vitamin D intake coming from D_2. The average maternal serum 25-OH-vitamin D level was 27 mcg/L in black mothers and 45 mcg/L in white mothers, which was not significantly different.[14] This study suggests that skin pigmentation-related D_3 synthesis efficiency differences can result in lower milk vitamin D_3 and 25-OH-vitamin D_3 levels in darker skinned mothers despite similar vitamin D intake and similar baseline vitamin D status.

Infant Levels. When a mother has underlying vitamin D deficiency, her breastfed infant will likely have deficient 25-OH-vitamin D serum levels (<20 mcg/L) if the mother is taking only 400 to 1000 IU (10 to 25 mcg) daily,[19,34,35] and insufficient serum levels (20 to 30 mcg/L) when the mother is taking 2000 IU (50 mcg) daily.[27,36] But, the infant can potentially achieve sufficient serum levels (>30 mcg/L) when the mother takes 4,000 IU (100 mcg) or more daily.[32,37] When a breastfed infant is given a daily 400 IU supplement directly, average infant serum levels are sufficient (>30 mcg/L) without being excessive (>100 mcg/L) if the mother is also taking a daily 400 to 2,000 IU (10 to 25 mcg) supplement.[38] Pregnant women living in higher latitudes with underlying normal vitamin D status who take a 2,000 IU daily vitamin D supplement beginning in the second trimester of pregnancy will usually have infants born with sufficient vitamin D status, which can be maintained for at least 8 weeks postpartum through exclusive breastfeeding without infant supplementation.[39]

Forty exclusively breastfeeding mothers in the Northern US were given vitamin D_3 150,000 IU one time or 5000 IU daily for 28 days. Their infants were between 4 and 28 weeks old and 68% were vitamin D deficient at study enrollment. In the single dose group, average infant serum 25-OH-vitamin D levels increased from 16.3 mcg/L at baseline to 38.7 mcg/L at day 28.[11] A nearly identical increase was observed in the once daily group; from 16.9 mcg/L to 39.2 mcg/L.

Eighteen fully breastfeeding women in the southeast US with nondeficient vitamin D status were given either 2,000 or 4,000 IU daily vitamin D beginning at 1 month postpartum. Mothers were instructed to minimize sun

exposure. After 3 months, average infant serum 25-OH-vitamin D levels increased from 7.9 to 27.8 mcg/L in the 2,000 IU daily group and from 13.4 to 30.8 mcg/L in the 4000 IU daily group.[26] This study demonstrates that, on average, a 4,000 IU daily vitamin D supplement in lactating women who have nondeficient underlying vitamin D status can achieve marginally normal status in their breastfeeding infant without giving additional vitamin D directly to the infant. Such a strategy would not necessarily be effective in every mother-infant pair, and therefore infant serum 25-OH-vitamin D monitoring is recommended to confirm efficacy when using this strategy.

One hundred forty-eight exclusively breastfeeding women in the Northeast and Southeast U.S. were given either 400 or 6,400 IU daily of vitamin D_3 beginning within 4 to 6 weeks of delivery. Average baseline maternal serum 25-OH-vitamin D levels were >50 nmol/L, and average infant levels were <50 nmol/L (range undetectable to 113.8 nmol/L). Infants of mothers in the 400 IU daily group were given a 400 IU daily vitamin D supplement, while those in the 6,400 IU daily group were given placebo. After 4 and 7 months, most infants in both groups had serum 25-OH-vitamin D levels >75 nmol/L, achieving normal vitamin D status. The average levels at 4 months were 109 and 106.9 nmol/L in the 400 IU daily and 6,400 IU daily groups, respectively. At 7 months, average levels were 109.1 and 108.5 nmol/L, respectively, and the percentages of infants with levels <50 nmol/L were 4.3% and 4.2%, respectively.[40] Maternal and infant serum 25-OH-vitamin D levels were 20 to 25 nmol/L lower on average when mothers were obese (BMI 30 kg/sq. m or greater) compared to mothers who were not overweight (BMI less than 25 kg/sq. m). An association between maternal weight and lower levels was significant even after adjusting for maternal race, education and insurance status. This study suggests that obese mothers may require higher vitamin D supplementation dosages.[41]

One thousand three hundred healthy, non-obese, pregnant women in Dhaka, Bangladesh were randomized to receive an oral tablet of 4,200 IU, 16,800 IU, 28,000 IU of vitamin D3, or placebo once weekly beginning prenatally between 17- and 24-weeks gestational age. The placebo group and some in the 28,000 IU group continued to receive their assigned treatment for 26 weeks postpartum while the others stopped treatment after delivery. Baseline maternal vitamin D status was similar across all participants with 65% biochemically vitamin D deficient. Breastfeeding duration was similar between each of the groups. The median duration of exclusive breastfeeding was 12 to 14 weeks. Infant vitamin D supplementation was uncommon (<10%). One thousand one hundred sixty-four infants were available for analysis. At 3 and 6 months postpartum, average infant total 25-OH-vitamin D3 blood levels were approximately 90 nmol/L (36 mcg/L) and fewer than 5% of had blood levels indicating deficiency (< 50 nmol/L or < 20 mcg/L) in the group given postpartum maternal supplementation, compared to 40 to 50 nmol/L (16-20 mcg/L) and 50 to 60%, respectively, in the other groups.[42] Partial or no breastfeeding was associated with higher levels in the non-postpartum supplemented groups, likely due to vitamin D fortification of the available infant formula. Levels were similar regardless of breastfeeding status among infants in the postpartum supplementation group.[43] This study suggests that maternal postpartum vitamin D supplementation of 28,000 IU (700 mcg) once weekly is effective at improving infant vitamin D status when feeding breastmilk..

One hundred ninety mothers in Qatar were randomized to receive either 600 IU or 6000 IU vitamin D beginning within 4 weeks postpartum. Infants of the mothers in the low-dose group were given 400 IU daily while those in the high-dose group received daily placebo. At 4 and 7 months postpartum, average infant serum 25-OH-vitamin D levels rose from around 30 nmol/L in both groups to 105 to 109 nmol/L in the low maternal dose (with direct infant supplementation) and to 81 to 92 nmol/L in the high-dose group (without direct supplementation). The number of infants with serum levels of 50 nmol/L or greater were about 90% in both groups.[32]

In a Turkish study of 90 exclusively breastfed infants, the effects of maternal vitamin D_3 400 IU daily supplementation beginning during pregnancy and continuing postpartum was compared to no postpartum maternal vitamin D supplementation. Sun exposure of 3 or more days per week of at least 15 minutes daily was

associated with a 5 mcg/L increase in serum 25-OH-vitamin D. Routinely wearing concealing clothing was associated with a 5 mcg/L decrease. Milk levels were not measured.[44]

In 38 exclusively breastfeeding women in the Northern U.S. participating in a 6-month long prospective study to determine risks of vitamin D deficiency and rickets in breastfed infants, investigators reported a significant positive correlation between weekly maternal and infant UVB exposure and infant 25-OH-vitamin D_3 levels among all participants. In a subset of 13 infants born in winter and not given any vitamin D, average levels increased 13 mcg/L to 25.1 mcg/L between 6 weeks and 6 months of age, coinciding with increased UVB exposure over that time.[35]

In a study of 115 exclusively breastfed infants in northern India born with severe vitamin D deficiency (cord serum 25-OH-vitamin D <11 mcg/L), whose mothers were given 60,000 IU of oral vitamin D_3 or placebo once daily for 10 days beginning on the day of delivery, average infant serum 25-OH-vitamin D levels at 6 months of age were twice as high (30 vs 15 mcg/L) in the supplemented group compared to the placebo group. The frequency of severe deficiency at 6 months of age was lower in the supplemented group compared to the placebo group (8% vs 44%).[45]

One hundred fifty-two vitamin D-deficient mothers in northern India were randomized to receive 120,000 IU (3000 mcg) of vitamin D one time within 7 days postpartum followed by the same dose at 6, 10, and 14 weeks postpartum to coincide with scheduled infant immunization, or placebo. Infants of mothers in the placebo group received vitamin D 400 IU (10 mcg) daily, while those in the treatment group received placebo. At 14 weeks, 70% were still exclusively breastfeeding in both groups. The median 25-OH-vitamin D serum levels were approximately 61 nmol/L in both groups, and 60% of infants had serum levels over 50 nmol/L in both groups.[37]

In a similar study in the same region of India, 114 mothers were randomized to receive vitamin D3 60,000 IU (1,500 mcg) or placebo as a single dose starting between 24 and 48 hours after delivery, and then repeated at 6, 10, and 14 weeks postpartum. At baseline, around 90% of all mothers and infants had vitamin D deficiency. Over 90% of participants were exclusively breastfeeding. None of the infants were directly supplemented during the 6-month study period and sun exposure was similar between the two groups. At 6 months of age, average infant serum 25-OH-vitamin D level was 19 mcg/L in the treatment group and 6 mcg/L in the placebo group, while vitamin D deficiency was present in 5% and 91% of infants, respectively. None of the infants were directly supplemented during the 6-month study period and sun exposure was similar between the two groups.[46]

Two hundred twenty healthy, non-obese, postpartum mothers in Rajasthan, India were randomized to receive 120,000 IU or 12,000 IU of vitamin D3 once a month for 12 months beginning in the first postpartum month. Mothers and infants were followed for 1 year. Exclusive breastfeeding in all participants at enrollment was implied but feeding status throughout the study was not reported. All infants had vitamin D deficiency at baseline. The median total 25-OH-vitamin D serum level in the infants of mothers in the high dose group increased from 7.1 mcg/L at baseline to 36.5 mcg/L at 12 months. Infants in the low dose group increased from 4.8 mcg/L to 17 mcg/L.[47]

Effects in Breastfed Infants

Maternal daily doses of 400 to 6,400 IU (10 to 160 mcg) have not been associated with any short-term biochemical abnormalities in breastfed infants.[11,19,34-36,38,40,48]

An 11-day-old, exclusively breastfed, term, female neonate experienced asymptomatic, mild hypercalcemia (total serum calcium 11.4 mg/dL). The mother was taking maintenance vitamin D_2 100,000 IU daily to maintain normal calcium and phosphorus status after a pre-pregnancy thyroid-parathyroidectomy, plus a prenatal vitamin containing 400 IU daily vitamin D (form not specified) during pregnancy and lactation. Vitamin D_2 and 25-OH-vitamin D_2 levels in cord blood and in milk at 14 days of age were both markedly elevated. Serum vitamin

D levels were not measured in the infant.[29] The combination of high daily breastmilk vitamin D_2 intake plus a high infant serum level present at birth likely contributed to the abnormal calcium value.

In a study in northern India, short-term maternal use of oral 60,000 IU vitamin D_3 once daily for 10 days beginning after birth was not associated with any differences in serum calcium or phosphorus levels, or of urinary calcium/creatinine ratios, in their exclusively breastfed infants at 14 weeks and 6 months of age compared to infants of mothers given placebo. Infants of mothers given vitamin D had a lower frequency of biochemical rickets compared to placebo (0 vs 17%), but no difference in the frequency of radiological rickets (3.6% vs 3.4%).[45]

One hundred fifty-two mothers in northern India, most of whom were vitamin D deficient, were randomized to receive 120,000 IU (3000 mcg) of vitamin D one time within 7 days postpartum followed by the same dose at 6, 10, and 14 weeks postpartum to coincide with scheduled infant immunization, or placebo. Infants of mothers in the placebo group received 400 IU (10 mcg) of daily vitamin D while those in the treatment group received placebo. At 14 weeks, infant growth parameters and serum biochemical indicators of bone mineral and liver homeostasis were similar between the two groups. At 9 months, dental growth and diarrheal or respiratory illness frequency were also not different.[38]

One hundred fourteen vitamin D deficient mothers in northern India were randomized to receive vitamin D3 60,000 IU (1,500 mcg) or placebo as a single dose starting between 24 and 48 hours after delivery, and then repeated at 6, 10, and 14 weeks postpartum. Over 90% of participants were exclusively breastfeeding. At 6 months of age, 6 infants in the control group and no infants in the treatment group developed biochemical rickets, while 2 infants and 1 infant, respectively, developed radiological rickets. Infants of mothers in the treatment group reportedly had normal serum calcium and phosphorus concentrations at 6 months of age, although specific results were not given, and this outcome was not reported for the control group.[46]

One hundred ninety mothers in Qatar were randomized to receive either 600 IU or 6000 IU vitamin D beginning within 4 weeks postpartum. Infants of the mothers in the low-dose group were given 400 IU daily while those in the high-dose group received daily placebo. At the scheduled 4- and 7-month postpartum study visits, infant growth parameters, serum calcium and parathyroid hormone levels, and parent reported infant health status, were not different between the two groups.[32]

Two hundred twenty healthy, non-obese, breastfeeding mothers in Rajasthan, India were randomized to receive 120,000 IU or 12,000 IU of vitamin D3 once a month for 12 months beginning in the first postpartum month. Infants in both groups had normal serum calcium, phosphate, and alkaline phosphate levels at baseline and at 12 months. There was no significant differences in growth parameters, bone mineral content or density between the two groups at 12 months. [47]

One thousand three hundred pregnant women in Dhaka, Bangladesh were randomized to receive an oral tablet of 4,200 IU, 16,800 IU, 28,000 IU of vitamin D3, or placebo once weekly beginning prenatally between 17- and 24-weeks gestational age. The placebo group and some in the 28,000 IU group continued to receive their assigned treatment for 26 weeks postpartum while the others stopped treatment after delivery. Baseline maternal vitamin D status was similar across all participants with 65% biochemically vitamin D deficient. Breastfeeding duration was similar between each of the groups. The median duration of exclusive breastfeeding was 12 to 14 weeks. Infant vitamin D supplementation was uncommon (<10%). One thousand one hundred sixty-four infants were available for analysis. There were no differences between the groups in infant growth at 1 year postpartum. There were also no differences in infant mortality, hospitalizations, respiratory tract infections, rickets, serum calcium status, or early childhood bone mineral density and grip strength. Infant hypercalcemia and hypercalciuria occurred rarely (0-1%) and did not differ between groups.[42]

One hundred forty-eight exclusively breastfeeding postpartum patients were given either 400 or 6,400 IU daily of vitamin D3 beginning within 4 to 6 weeks of delivery. Average baseline infant serum 25-OH-vitamin D was <50

nmol/L (range undetectable to 113.8 nmol/L). Infants of mothers in the 400 IU daily group were given a 400 IU daily vitamin D supplement, while those in the 6,400 IU daily group were given placebo. There were no differences between the two groups in biochemical markers of calcium status, bone mineral content or density at 1, 4, or 7 months of age.[49,50]

Emerging evidence suggests adequate infant delivery of vitamin D through breastmilk from maternal supplementation during pregnancy and lactation is important for regulation of the developing infant immune system.[51,52]

Effects on Lactation and Breastmilk

Relevant published information was not found as of the revision date.

Alternate Drugs to Consider

Calcitriol

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Substance Identification

Substance Name

Vitamin D

CAS Registry Number

67-97-0; 50-14-6

Drug Class

Breast Feeding

Lactation

Milk, Human

Vitamins