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NEW THOUGHTS ON VITAMIN D IN PREGNANCY, LACTATION, AND INFANCY

Vitamin D is best known as a key modulator of calcium absorption and bone mineralization. Emerging evidence suggests that Vitamin D may also play critical roles in cardiovascular health, immunomodulation, and the regulation of growth and differentiation of cells in the prostate, breast, colon, lung, and keratinocytes. Lifestyle changes over the past generation have caused a decline in Vitamin D status of mothers and babies. Reduced sun exposure due to fears of skin cancer and changing dietary patterns (less milk, more sodas) have resulted in a substantial reduction of both Vitamin D intake and synthesis. As a result Vitamin D deficiency has increased in the general population and has been shown in numerous studies to be common in both mothers and babies. New guidelines for Vitamin D intake and supplementation have recently been published to counteract this growing problem. The following article will review the rationale and guidelines for nutrient supplementation of Vitamin D during pregnancy, lactation, and the first year of life.

PHYSIOLOGY OF VITAMIN D

Humans obtain Vitamin D by dietary sources and by skin exposure to sunlight. Most foods contain low levels of naturally occurring Vitamin D. The exceptions are fatty fish such as salmon and mackerel and Vitamin D fortified foods such as milk, dairy products, calcium fortified juices, and cereal grains. The traditional supplement of cod liver oil in infants was an early attempt to increase dietary sources of Vitamin D. Generally, the primary source of Vitamin D intake comes from sun exposure. Factors such as skin pigmentation, duration of exposure, environmental factors such as smog or clouds, use of sunscreens (particularly those greater than SPF 8), and degrees latitude north of the equator all have an impact on the effectiveness of the exposure on Vitamin D synthesis. It is thought that residents of Iowa, who live at latitude of ~40°, are exposed to insufficient UV energy for Vitamin D synthesis from the months of November through February. Once incorporated into the body, Vitamin D must undergo two hydroxylations to become active. The first hydroxylation occurs in the liver generating 25-hydroxyvitamin D

(25-OH-D). The second hydroxylation occurs in the kidney and generates 1, 25-hydroxyvitamin D (1, 25-OH-D). The rate of the first hydroxylation step is limited by Vitamin D availability and the rate of the second by serum calcium. Therefore, the best compound to measure to assess Vitamin D status is 25-OH-D. Studies vary widely in their definition of the values indicative of deficiency and insufficiency. Currently accepted standards are >30 ng/ml (>75 nmol/L) 25-OH-D for Vitamin D sufficiency, 21-29 ng/ml (52-72 nmol/L) 25-OH-D for Vitamin D insufficiency, and <20 ng/ml 25-OH-D for Vitamin D deficiency (<50 nmol/L).

VITAMIN D IN PREGNANCY

A significant percentage of women enter pregnancy in a Vitamin D insufficient state. Bodnar et al measured the Vitamin D status of a large number of healthy pregnant women (200 white / 200 black) at 4-21 weeks gestation and at pre-delivery in Pittsburgh, PA during 1997-2001. Pittsburgh has latitude similar to Keokuk, IA. Mothers were classified as Vitamin D deficient (<37.5 nmol/L 25-OH-D), Vitamin D insufficient (37.5-80 nmol/L 25-OH-D), and Vitamin D sufficient (>80 nmol/L 25-OH-D). The researchers found that 5% and 42.1% of white women and 29.2% and 54.1% of black women were Vitamin D deficient and insufficient respectively. Other studies completed in Boston, MA and Winnipeg, Canada demonstrated similar results.

Recent studies provide intriguing evidence that Vitamin D deficiency in mothers may be associated with increased complications for the health of the pregnancy and the health of the newborn. Bodnar et al found a dose-response relationship between serum Vitamin D levels and risk for pre-eclampsia. As serum 25-OH-D concentrations declined by 50 nmol/L there was a two-fold increase in risk for pre-eclampsia. Mere wood et al postulated a relationship between maternal Vitamin D status and need for primary C-section. They theorized that Vitamin D deficiency would alter calcium metabolism thereby affecting muscle strength and function. They enrolled 253 healthy women between 2005 and 2007 at Boston Medical Center to determine the relationship between Vitamin D status and the need for primary C-section. Overall incidence of primary C-section in the entire group was 17%. Primary C-sections were required in 14% and 28% of Vitamin D sufficient and insufficient women respectively.

Vitamin D deficiency in mothers may also influence outcomes in the infant. Weiler et al measured the Vitamin D status of healthy mothers and babies admitted to the Winnipeg Health Sciences Center, Winnipeg, Canada from August 2001 to April 2003. She found that 70% of Vitamin D deficient mothers (25-OH-D <37.5 nmol/L) delivered a Vitamin D deficient infant. Vitamin D status has also been associated with fetal growth. Mannion et al evaluated the impact of milk consumption and Vitamin D intake of 2091 mothers in Calgary, Alberta on the birthweight of their infants. Using serial dietary recalls, the researchers divided mothers into groups that consumed >250 ml of milk daily and <250 ml milk daily. After controlling for other variables they found that

each additional cup of milk consumed per day was associated with a 41 g increase in birthweight. As it was conjectured that the increased weight gain might be due to increased protein intake, the researchers also compared daily Vitamin D intake to weight gain. Once again, after controlling for other variables, they also found a positive association between Vitamin D intake as weight gain with each additional microgram (40 IU) of Vitamin D consumed per day associated with an 11 g increase in birthweight.

The current advisable intake for Vitamin D during pregnancy is 200 IU/d. It is generally believed, however, that this level is insufficient to maintain Vitamin D status during the course of pregnancy. Lee et al measured the plasma 25-OH-D levels of 40 healthy mother/baby dyads admitted to Boston Medical Center, Boston, MA from October 2002 to February 2003. Mothers had no history of parathyroid or renal disease. Sixty-two percent of the mothers were African American, 92% of the mothers reported consuming milk in their diet, and 70% of mothers reported the use of a maternal vitamin containing 400 IU Vitamin D. In this population, 50% of mothers were found to be Vitamin D deficient as measured by a 25-OH-D level <30 nmol/L. *It is now thought that a supplement of 400 IU will have little impact on mothers' Vitamin D levels.* In fact, mothers who enter pregnancy in a Vitamin D deficient state will still be deficient at delivery despite daily intakes of 800-1600 IU/d Vitamin D. The American Academy of Pediatrics currently recommends that health care providers should assess Vitamin D status of the pregnant woman during her pregnancy by measuring Vitamin D levels. They suggest that Vitamin D supplements should be prescribed as needed on an individualized basis in order to ensure maternal Vitamin D levels remain >80 nmol/L.

VITAMIN D IN LACTATION

Similar to pregnancy the current advisable intake for Vitamin D during lactation is 200 IU/d. Unlike some nutrients such as protein and calcium, Vitamin D levels in mothers' milk are directly related to maternal Vitamin D status. Wagner et al found that administration of 400 IU/d Vitamin D had minimal impact on the mother's Vitamin D status or the Vitamin D content of her milk. Supplements of 1000-2000 IU/d demonstrated some improvement in maternal and infant Vitamin D stores, but Vitamin D content of the breastmilk was still insufficient to meet the full needs of the infant. Maternal and infant adequacy was achieved only when the dose of supplement was increased to 6400 IU/d. Hollis et al postulate that changing the source of Vitamin D from Vitamin D2 (plant-based) to Vitamin D3 (fish-based) may enhance the effectiveness of oral supplements as Vitamin D3 is the compound secreted in breastmilk. At this time, however, studies are still needed to identify the appropriate, safe dose of supplement to maintain maternal levels and meet the infant's need for Vitamin D. *For this reason, it is currently recommended to supplement the infant with Vitamin D rather than attempt high-dose maternal supplementation.*

VITAMIN D IN INFANCY

Infants can not only be born with Vitamin D deficiency, they can also develop Vitamin D deficiency postnatally due to reduced intake and limited sun exposure. Infants at highest risk for postnatal deficiency are in solely breast fed infants who also have darker skin pigmentation. Ziegler et al assessed the Vitamin D status at 280 days of life in 84 breast fed infants living in Iowa. Using the strictest criteria for deficiency (<11nmol/L 25-OH-D) he found 23% of unsupplemented infants had laboratory signs of D deficiency. In contrast, none of the infants receiving Vitamin D supplements (through formula or a multivitamin containing 400 IU Vitamin D) were deficient. Vitamin D levels demonstrated seasonal variation with 70% of unsupplemented infants showing evidence of Vitamin D deficiency during the winter months.

In November 2008, the American Academy of Pediatrics revised their guidelines for Vitamin D supplementation in order to assure intake adequacy. Where previous guidelines were to begin supplements of 200 IU/d within the first few months of life, *new recommendations are to begin dosing immediately after birth at a dose of 400 IU/d.* Vitamin supplementation should continue until the infant transitions over to D fortified formula or whole milk and is consuming at least a quart/day of the D enriched feeding. *Formula fed or combination breast/formula fed infants should also receive a Vitamin D supplement of 400 IU/d until daily Vitamin D fortified formula intake exceeds 1 quart.*

SUMMARY

Changes in lifestyle have resulted in a significant decline in sun exposure which is our primary source of Vitamin D. As a result women are entering pregnancy with lower Vitamin D status and deliver infants with lower stores at birth. Assessing Vitamin D status during pregnancy and adjusting maternal supplementation as needed may enhance both maternal and fetal stores. Breastfeeding without the addition of a Vitamin D supplement puts infants at extremely high risk for deficiency, particularly during winter months and in darker skin populations. *All breast fed infants (solely and partially breast fed) should receive a Vitamin D supplement of 400 IU/day beginning in the first few days of life (before discharge to home).* Further studies must be completed to better identify the appropriate level of Vitamin D supplementation during both pregnancy and lactation.

~References available upon request

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