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The Convergence of Two Epidemics: Vitamin D Deficiency in Obese School-aged Children[1]

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ABSTRACT

Problem: Vitamin D deficiency (VDD) and obesity are two interrelated global epidemics that affect school-aged children. This article will review the relationship between VDD and obesity in school-aged children and implications it has for the pediatric nurse (PN).
Eligibility criteria: Original articles of studies, review articles and meta-analyses were selected from the past 5 years and pooled for review. These included obese school-aged children who had vitamin D insufficiency. The latest guidelines concerning the issue were also included.
Sample: Children 6–12 years of age with obesity and vitamin D insufficiency.
Results: This review strongly implies obesity in children being a strong risk factor for VDD. Prevention of VDD starts with lifestyle changes and adequate dietary intake of fortified foods and current screening recommendations for VDD are inconsistent. Vitamin D supplementation is recommended with inadequate intake or deficient serum 25-hydroxyvitamin D levels or signs of hypocalcemia. Supplementation doses differ based on whether VDD is being prevented or being treated and in obese children, the Endocrine Society recommends a dose that is two to three times higher than for normal weight children. Subclinical signs and symptoms of VDD include musculoskeletal pain, fractures, reduced bone density and reduced immunity.
Conclusions: Whereas obesity is a strong risk factor for VDD, more research is needed to clarify the role of VDD as a risk factor for obesity.
Implications: The PN plays an essential role in preventing, screening for, assessing for, treating and counseling on VDD in obese school-aged children.

In the face of our current global obesity epidemic (World Health Organization, 2012), we are faced with yet another global epidemic of vitamin D deficiency (VDD). VDD is a worldwide major public health concern across the lifespan (Palacios & Gonzalez, 2014), with children being at greater risk (van Schoor & Lips, 2011). According to the 2001–2006 National Health and Nutrition Examination Survey (NHANES), about one in five children aged 1–11 years have VDD (Mansbach, Ginde, & Camargo, 2009). Suboptimal levels of vitamin D (VitD) affects school-aged children 6–11 years old (73%) more than younger children (63%) (Mansbach et al., 2009). Having sufficient VitD levels in childhood and adolescence is important because osteoporosis risk may be traced back to these periods and bone mass accrual in these periods may be the most important adjustable factor of lifetime bone health (Golden, Abrams, & Committee on Nutrition, 2014). These periods are considered the most important adjustable determinant of future bone health (Golden et al., 2014). Obesity adds another layer of risk for VDD in school-aged children (Turer, Lin, & Flores, 2013). This article will review the relationship between VDD and obesity in school-aged children and implications it has for the pediatric nurse (PN).

Background

In this review, obesity is defined according to body mass index (BMI) parameters established by the Centers for Disease Control and Prevention, where overweight is having a BMI ≥ 85th to <95th percentile and obesity is having a BMI ≥ 95th percentile (Centers for Disease Control and Prevention, 2015). In contrast, the parameters for VDD are less clear, due to differing definitions set forth by the Institute of Medicine (IOM) and Endocrine Society (ES). Table 1 reviews these differences.

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Table 1
Vitamin D status definitions based on serum 25(OH)D levels.

Status	IOM (IOM, 2011b)		Endocrine Society (Holick et al., 2011)	
	nmol/l	ng/ml	nmol/l	ng/ml
Deficiency	<30	<12	≤50	≤20
Insufficiency	30–49	12–19	52.5–72.5	21–29
Sufficiency	≥50	≥20	≥75	≥30
Reason for concern	>125	>50	–	–

Note. IOM = Institute of Medicine.

Vitamin D Deficiency and Obesity

Obesity and Other Risk Factors for Vitamin D Deficiency

There is strong evidence that obesity is a risk factor for VDD. Being overweight or obese was found to be independently associated with VDD and reduced VitD levels (Gutierrez Medina et al., 2015; Kelly, Brooks, Dougherty, Carlow, & Zemel, 2011; Turer et al., 2013). Turer et al. (2013) evaluated 6–18 year old children enrolled in the 2003–2006 NHANES and found increasingly higher prevalence of VDD with increasing BMI. This study reported that children who were overweight, obese or severely obese (BMI ≥ 99th percentile) were about twice as likely as children of healthy weight to have VDD. Similarly, Vimaleswaran et al. (2013) found that each BMI unit increase correlated with a 1.15% decrease in serum 25-hydroxyvitamin D (25(OH)D) levels. Serum 25(OH)D levels are lower and VitD insufficiency (<30 ng/ml) is more prevalent in obese children when compared to non-obese children (Liu et al., 2016; Motlaghzadeh et al., 2016). Furthermore, Vimaleswaran et al. (2013) found a causal relationship between obesity and reduced serum 25(OH)D (see Table 2). In their sample of 90 obese and non-obese children aged 2–14 years, Motlaghzadeh et al. (2016) administered 50,000 IU of $VitD_3$ once weekly for six weeks. They found a lower therapeutic response in their obese children, which may be due to sequestration of VitD by adipose tissue and decreased serum 25(OH)D bioavailability (IOM, 2011a). In addition to obesity, other risk factors include winter months, darker skin (e.g., African-Americans, Hispanics), use of sunscreen, covered skin, latitude, poverty, and increasing age (Golden et al., 2014; Gutierrez Medina et al., 2015; IOM, 2011a; Kelly et al., 2011; Olson, Maalouf, Oden, White, & Hutchison, 2012; Turer et al., 2013; Vehapoglu et al., 2015).

Effects of Vitamin D Deficiency in Obesity

It has been suggested that VitD may regulate metabolism of adipose tissue (Pyrzak, Witkowska-Sedek, Krajewska, Demkow, & Kucharska, 2015). In a retrospective chart review of 32 obese children with VitD insufficiency who received supplementation, the children had decreased BMI after serum levels reached sufficiency (>30 ng/ml; Grunwald et al., 2017). Suboptimal serum 25(OH)D levels were associated with high adiposity and a two to three times higher risk of being obese (Cediel, Corvalan, Aguirre, de Romana, & Uauy, 2016). Findings were similar in a nationally representative sample of 2492 children from the 2005–2006 NHANES (Moore & Liu, 2016). In contrast, a randomized controlled trial that administered 4000 IU of $VitD_3$ or a placebo daily for six months to 35 obese children with VitD insufficiency found no difference in BMI between the two groups (Belenchia, Tosh, Hillman, & Peterson, 2013). A meta-analysis by Vimaleswaran et al. (2013) also failed to establish a reverse causal relationship between VDD and obesity but found obesity to be a causal risk factor for reduced VitD. While there is evidence for the role of VDD in increasing obesity risk, more studies are needed to clarify this relationship. Details of the reviews and studies discussed here are found in Tables 2 and 3.

VitD more clearly predicts other risk factors of metabolic syndrome (Challa, Makariou, & Siomou, 2015; Ekbom & Marcus, 2016; Erol, Bostan Gayret, Hamilçıkan, Can, & Yiğit, 2017; Kelishadi, Farajzadegan, & Bahreynian, 2014; Liu et al., 2016; Pyrzak et al., 2015). A systematic review by Kelishadi, Farajzadegan et al. (2014) found higher VitD to be associated with healthier lipid profiles in children. VDD was a secondary factor in the development of dyslipidemia (Erol et al., 2017) and those with VDD had higher cholesterol and triglyceride levels (Ekbom & Marcus, 2016; Liu et al., 2016). Reduced VitD levels were also associated with higher blood pressure (Challa et al., 2015; Pyrzak

Table 2
Findings from review articles and clinical guidelines: effects of VDD in obese school-aged children.

First author (year)	Study type	Purpose	Relevant findings
Kelishadi, Farajzadegan (2014)	Systematic review & meta-analysis	Review cross-sectional studies on relation of VitD and lipid profile in children/adolescents	Increased VitD a/w more favorable lipid profile
Vimaleswaran (2013)	Meta-analysis	Explore causality and direction of relation between obesity and VitD using bi-directional Mendelian randomization analysis	Causal relationship between obesity and reduced VitD Any effects of reduced VitD leading to obesity are likely small
Challa (2015)	Review	Review VDD effects on metabolic syndrome	Low VitD increases risk for metabolic syndrome, especially high BP and insulin resistance
Cianferotti (2012)	Review	Review subclinical VDD boundaries, skeletal and extraskeletal effects and supplementation	Extreme VDD presents as rickets and osteomalacia, both rare
Dobnig (2011)	Review	Review skeletal and extraskeletal effects of VDD	Low VitD a/w upper respiratory infections, cardiovascular disease, cancer
Moon (2014)	Review	Review VitD insufficiency effects on bone growth in infancy/childhood	Both fractures and low VitD levels individually common and may coexist Severe VDD → overt rickets, osteomalacia, symptomatic hypocalcemia, all relatively uncommon
Pyrzak (2015)	Review	Review clinical implications of VDD in obese children and adults	Low VitD: risk factor for cardiovascular disorders, metabolic syndrome, hypertension, diabetes, cancer, autoimmune and infectious diseases VitD may promote obesity via adipose tissue regulation
Golden (2014)	AAP clinical report	Update: bone health optimization update	VDD results in rickets in young children (peak 3–18 months) and increases fracture risk in older children
Wagner (2008)	AAP clinical report	Update: VDD and rickets prevention	Low VitD increases PTH, reducing bone mass and increasing fracture risk Clinical signs: abnormal immune function, increasing risk for acute infection and chronic diseases (cancer, psoriasis, diabetes, autoimmune) Extreme VDD → rickets (peak 3–18 months)

Note. AAP = American Academy of Pediatrics. ALP = alkaline phosphatase. a/w = associated with. PTH = parathyroid hormone. VDD = vitamin D deficiency. VitD = vitamin D.

Table 3
Review of original research studies: effects of VDD in obese school-aged children.

First author (year), country	Study type	Purpose	Sample	VDD definition (ng/ml)	Relevant results
Belenchia (2013), USA	Randomized controlled trial	Determine if supplementation would improve insulin resistance	35 obese 9–19 year-olds (M = 50%) with insufficiency to receive 4000 IU/day D_3 or placebo for 6 months	VDD < 20 Insufficiency ≤30	Children with supplementation had decrease in insulin resistance ($p = 0.03$) VitD vs. placebo: no difference in BMI or glucose
Cediel (2016), Chile	Cross-sectional	Evaluate relation between 25(OH)D, adiposity and insulin resistance	435 Chilean prepubertal children (M = 47%) taken from Growth and Obesity Chilean Cohort Study	Suboptimal <30	Suboptimal VitD a/w high adiposity ($p < 0.05$) and insulin resistance ($p < 0.05$) Suboptimal VitD: 3–4× greater risk of insulin resistance, independent of BMI
Ekbom (2016), Sweden	Prospective cross-sectional	Investigate relation between VitD and markers of glucose metabolism	202 Swedish obese 4–17 year-olds (M = 51%) with VDD or non-deficiency	VDD < 12	VDD children had higher TC ($p = 0.05$), higher TG ($p = 0.003$), more frequent insulin resistance ($p = 0.05$) VDD is a factor of impaired fasting glucose, independent of age and season ($p < 0.05$)
Erol (2017), Turkey	Cross-sectional	Determine if VDD is risk factor for dyslipidemia	108 obese 8–14 year-olds (M = 41%) with dyslipidemia or non-dyslipidemia	VDD < 20	VDD is secondary factor in formation of dyslipidemia ($p = 0.04$)
Grunwald (2017), USA	Retrospective & prospective	Determine if treatment/correction of VDD leads to changes in metabolic profile	Retrospective arm: 32 obese 3–20 year-olds (M = 44%) with insufficiency Prospective arm: 7 obese children with insufficiency Both arms treated with various VitD regimens and experienced correction (>30 ng/ml)	VDD < 20 Insufficiency ≤30	Retrospective arm: BMI *Z*-score lower after correction ($p = 0.01$). No change in metabolic profile. Prospective arm: no change in metabolic profile after correction
Gutierrez Medina (2015), Spain	Cross-sectional	Analyze relation between: VDD and puberty, VDD and insulin resistance	120 Spanish obese 6–17 year-olds (M = 57%) and 50 lean controls (M = 48%) Each group subdivided: prepubertal and pubertal	VDD < 20	Obese prepubertal children with VDD had significantly higher HOMA vs. those without VDD ($p < 0.05$)
Kehler (2013), USA	Retrospective cohort	Audit notes for VDD children presenting to ED. Analyze age, ethnicity, CC, biochemical findings	89 infants-16 year-olds Majority Pakistani (37%) and Black African (11%)	Low <20 Very low <10 (83%)	Most common CCs: abdominal pain (19%), seizure (17%), limb pain (15%)
Kelishadi, Salek (2014), Iran	Randomized controlled trial	Assess supplementation on insulin resistance and cardiometabolic risk factors	50 obese 10–16 year olds to receive 300,000 IU D_3 weekly or placebo for 12 weeks	Insufficiency ≤30	VitD vs. placebo: VitD group had improved TG ($p = 0.02$), insulin resistance ($p = 0.02$), cardiometabolic risk factors ($p = 0.04$)
Kelly (2011), USA	Cross-sectional	Determine relation between VitD and fasting glucose, insulin sensitivity	85 obese and non-obese 4–18 year-olds (M = 55%) Majority White (48%), African American (45%)	VDD < 10	Reduced VitD a/w higher fasting glucose ($p = 0.005$), insulin ($p = 0.007$), & HOMA ($p = 0.02$), independent of age & obesity
Liu (2016), China	Cross-sectional	Examine relation between 25(OH)D and obesity	443 obese and non-obese <18 year-olds (M = 64%)	VDD ≤ 20	VDD a/w higher TC ($p = 0.002$), insulin ($p < 0.001$) and HOMA ($p < 0.001$), independent of BMI
Moore (2016), USA	Cross-sectional	Evaluate relation between 25(OH)D and measures of adiposity	2492 obese and non-obese 6–18 year-olds from NHANES 2005–2006 (M = 51%)	Used both ES and IOM criteria	Suboptimal 25(OH)D: 2–3× greater risk of obesity
Nwosu (2013), USA	Prospective cross-sectional	Determine relation between VitD and CVD markers	45 overweight and non-overweight 3–12 year-olds (M = 58%)	VDD < 20	VitD negatively a/w LDL ($p = 0.016$) and TC/HDL ratio ($p = 0.028$)
Olson (2012), USA	Cross-sectional	Examine relation between VitD and glucose metabolism and BP	411 obese 6–16 year-olds (M = 43%) Majority Hispanic (49%), African American (27%), White (21%) 89 matched non-overweight controls (M = 32%)	VDD < 20	Obese children: VitD inversely a/w HOMA ($p = 0.001$) and 2-h glucose ($p = 0.04$), independent of age and obesity VitD not a/w HbA1c ($p = 0.18$), SBP ($p = 0.14$), DBP ($p = 0.86$)
Torun (2013), Turkey	Retrospective	Evaluate clinical and biochemical findings in VDD and insufficiency	193 Turkish obese and non-obese 7–11 year-olds (M = 52%) with VDD or insufficiency (≤ 20 ng/ml)	VDD < 10	Main complaint: skeletal pain (leg 57%, chest 28%) Few biochemical signs of osteomalacia detected
Vehapoglu (2015), Turkey	Prospective cohort	Examine relation between VitD and growing pains Evaluate VitD supplementation on pain resolution	120 Turkish non-overweight Turkish 4–12 year-olds (M = 43%) with growing pains (i.e., limb pain)	VDD < 10	87% had VitD insufficiency (<20 ng/ml) 27% accompanying abdominal pain, 30% concurrent headaches 3-month supplementation significantly reduced growing pain intensity ($p < 0.001$)
Wang (2016), China	Cross-sectional	Examine relation between HOMA & 25(OH)D	278 Chinese non-overweight and overweight/obese 8–18 year-olds (M = 50%)	VDD < 12	Lower 25(OH)D a/w with worse HOMA for non-overweight ($p < 0.001$) and overweight/obese ($p < 0.001$)

Note. a/w = associated with. BMI = body mass index. BP = blood pressure. CC = chief complaint. CVD = cardiovascular disease. DBP = diastolic blood pressure. ED = emergency department. ES = Endocrine Society. HbA1c = hemoglobin A1c. HOMA = homeostasis model assessment index of insulin resistance. IOM = Institute of Medicine. LDL = low-density lipoprotein. M = male. NHANES = National Health and Nutrition Examination Survey. SBP = systolic blood pressure. TC = total cholesterol. TC/HDL = total cholesterol/high-density lipoprotein. TG = triglycerides. VDD = vitamin D deficiency. VitD = vitamin D. 25(OH)D = serum 25-hydroxyvitamin D.

et al., 2015) and VitD sufficiency was found to protect against cardiovascular disease (Nwosu, Maranda, Cullen, Ciccarelli, & Lee, 2013).

Two randomized controlled studies have found that VitD supplementation lowered cardiometabolic risk factors and insulin resistance in obese children and adolescents (Belenchia et al., 2013; Kelishadi, Salek, Salek, Hashemipour, & Movahedian, 2014). While both Belenchia et al. (2013) and Kelishadi, Salek et al. (2014) used different VitD dosages, serum 25(OH)D levels reached sufficiency levels at which insulin resistance improved. The retrospective chart review of 32 obese children by Grunwald et al. (2017) described earlier found

no improvements in metabolic profile (i.e., homeostatic model assessment of insulin resistance, HbA1c, lipid levels) following correction of VitD insufficiency. These findings were repeated when they prospectively followed seven obese children who were given VitD supplementation and achieved sufficiency. The difference in findings may be a result of the small sample size in both retrospective and prospective arms, retrospective design, and lack of a control sample in Grunwald et al. (2017). Nonetheless, more randomized controlled studies are needed to determine if VitD supplementation, particularly in school-aged children, will improve cardiometabolic risk factors.

A number of cross-sectional studies have shown that reduced serum 25(OH)D levels are associated with increased or more prevalent insulin resistance in obese school-aged children (Ekbom & Marcus, 2016; Gutierrez Medina et al., 2015; Kelly et al., 2011; Liu et al., 2016; Olson et al., 2012; Wang, Wang, Wen, Tao, & Zhao, 2016). In particular, Gutierrez Medina et al. (2015) found that obese children with VDD had significantly higher insulin resistance than obese children with VitD sufficiency, suggesting a more direct relationship between VDD and insulin resistance. This direct relationship was also suggested in Wang et al. (2016), as reduced serum 25(OH)D levels were associated with worse insulin resistance in both their overweight and non-overweight children. Suboptimal VitD levels put children at a three to four time greater risk for insulin resistance (Cediel et al., 2016). Reduced serum 25(OH)D levels also affected glucose levels where children had higher two-hour glucose levels after an oral glucose tolerance test (Olson et al., 2012) and higher fasting glucose (Ekbom & Marcus, 2016; Kelly et al., 2011).

While VitD primarily promotes bone health, there is increasing evidence that VDD has extraskeletal effects, having associations with autoimmunity, metabolic syndrome, cancer, cardiovascular and infectious diseases (Dobnig, 2011; Pyrzak et al., 2015; Wagner, Greer, Section on Breastfeeding, & Committee on Nutrition, 2008).

Prevention

The American Academy of Pediatrics (AAP), ES, and IOM recommend that children 1–18 years of age have an intake of 600 IU of VitD daily (Golden et al., 2014; Holick et al., 2011; Ross et al., 2011). The daily upper limit in 4–8 year olds is 3000 IU and in 9–18 year olds is 4000 IU (Golden et al., 2014; Holick et al., 2011). The ES suggests that children with obesity and those on certain medications (i.e., antiepileptics, antifungals, glucocorticoids, antiretrovirals) be given at least two to three times more the usual recommended daily intake of VitD, in order to meet their body's needs (Holick et al., 2011). The AAP proposes this as well, however, no conclusive recommendations exist (Golden et al., 2014).

Adequate VitD intake from food and lifestyle changes should be encouraged in overweight and obese children to prevent VDD (see Table 4). While fatty fish is an excellent natural source of VitD (National Institutes of Health [NIH], 2016b), fortified foods are the primary source of dietary VitD in the U.S. (e.g., milk which is fortified with 100 IU/8 oz.; Golden et al., 2014; IOM, 2011a; NIH, 2016b). Physical activity should be encouraged, while screen time and soda/juice intake (may otherwise replace milk intake) should be limited (Olson et al., 2012; Turer et al., 2013). While physical activity promotes outdoor sun exposure, an American Academy of Dermatology (AAD) position statement (2010) stated that no safe level of sun exposure exists that allows for both optimal VitD synthesis and does not increase skin cancer risk. Therefore, it is wise to limit skin exposure to sunlight and to apply sunscreen prior to sun exposure (AAD, 2010; NIH, 2016a).

Screening

Guidelines are inconsistent on whether children with obesity should undergo VDD screening. The AAP recommends screening with persistent low impact fractures or conditions that decrease bone density (BD; Golden et al., 2014; Misra, Pacaud, Petryk, Collett-Solberg, & Kappy, 2008); however, more research is needed to make screening recommendations for children with obesity or of African-American and Hispanic backgrounds (Golden et al., 2014). In contrast, the ES recommends that children with risk factors (e.g., obesity, African-American, Hispanic) be screened for VDD (Holick et al., 2011). Conditions that should prompt screening for VDD include rickets, osteomalacia, osteoporosis, chronic kidney disease, liver failure, malabsorption syndromes, hyperparathyroidism, tuberculosis and other granulomatous diseases, and some lymphomas. The ES also recommends screening patients who are taking certain medications, including antiepileptics, antifungals, glucocorticoids, cholestyramine and antiretrovirals. When screening for VDD, the recommended screening measure is serum 25(OH)D (Fraser & Milan, 2013; Golden et al., 2014).

Liquid chromatography tandem mass spectrometry (LC-MS/MS) is the gold standard for serum 25(OH)D measurement, however, the immunoassay is the method of choice due to convenience, lower cost, and greater efficiency (Fraser & Milan, 2013; Yetley et al., 2010). Immunoassays developed by different manufacturers have varying sensitivities and specificities: Abbott (sensitivity 90.9%, specificity 97.8%), Beckman (sensitivity 90.9%, specificity 87.6%) and Roche (sensitivity 72.7%, specificity 94.4%) (Saleh, Mueller, & von Eckardstein, 2016). Of note, the Roche assay's low sensitivity suggests risk for false negatives. Variability (10–20%) exists between different assay methods and between laboratories using the same assay (U.S. Preventive Services Task Force [USPSTF], 2014). Complicating factors include natural fluctuations of serum 25(OH)D, that it is a negative acute phase reactant (VitD lower with inflammation), and interferences from heterophilic serum antibodies (USPSTF, 2014). With international standardization underway through the VitD Standardization Program, future improvements in VitD measurement look promising (Binkley & Sempos, 2014; USPSTF, 2014).

Table 4
Role of the pediatric nurse.

Prevention	RDA for 1–18 year olds with normal weight: 600 IU/day
	RDA for 1–18 year olds with obesity: 2–3× higher (ES)
	Dietary counseling:
	≥2–3 cups of milk daily (Turer et al., 2013)
	Some yogurts, cheeses, breakfast cereals, soy beverages
	Fatty fish (e.g., salmon, sardines)
	Limit soda/juice intake
	≤2 h daily of screen time
	≥2 h weekly of physical activity
Screening	Recommended by ES
Assessment	Look for subclinical signs/symptoms:
	Bone pain (e.g., limb pain), fractures
	Slipped capital femoral epiphysis
	Abnormal immune function
	Other: abdominal pain, headache, seizure
	Assess total VitD intake (diet and supplementation)
	Assess risk factors for VDD
	Assess signs of hypocalcemia
Treatment	Goal: to achieve serum 25(OH)D > 20 ng/ml (AAP) or >30 ng/ml (ES)
	Normal weight: 2000 IU/day or 50,000 IU/week of D_2 or D_3 for ≥6 weeks.
	Maintenance: 600–1000 IU/day
	Obese: 6000–10,000 IU/day. Maintenance 3000–6000 IU/day (ES)
	Monitor levels annually and adjust dose accordingly

Note. AAP = American Academy of Pediatrics. ES = Endocrine Society. RDA = recommended dietary allowance. VDD = vitamin D deficiency. VitD = vitamin D.

Clinical Presentation

Stages of Vitamin D Deficiency

Three stages of VDD progression exist (Wagner et al., 2008). In stage one, hypocalcemia with euphosphatemia result from decreased serum 25(OH)D. Calcitriol remains the same or increases. In stage two,

parathyroid hormone (PTH) is released to sustain serum calcium levels through bone demineralization. Eucalcemia, hypophosphatemia, and mildly elevated alkaline phosphatase (ALP) levels result. In stage three, severely decreased serum 25(OH)D leads to hypocalcemia, hypophosphatemia, elevated ALP levels, and evidence of bone demineralization.

Subclinical Signs and Symptoms

Subclinical manifestations of VDD are more common, although subtle, than overt rickets or osteomalacia (Haroon & FitzGerald, 2012). These include musculoskeletal pain, fractures and decreased immunity. Furthermore, bone deformities are less evident in school-aged children with VDD than in infants and toddlers due to greater epiphyseal plate fusion (Torun, Genc, Gonullu, Akovali, & Ozgen, 2013). Whereas the VitD boundaries related to rickets and osteomalacia are clear and have been defined by the ES and IOM, those in association with these subclinical signs and symptoms are less clear (Cianferotti & Marcocci, 2012).

Musculoskeletal pain, particularly extremity pain, appears to be a common subclinical presentation among children with low VitD. In Vehapoglu et al. (2015), 86.6% of children presenting with growing pains (i.e., recurrent limb pain lasting greater than six months) had VitD insufficiency. VitD supplementation resulted in a significant pain decrease, suggesting insufficiency as the underlying cause. Limb pain was also a common presentation in children with VDD presenting to the emergency department (Kehler, Verma, Krone, & Roper, 2013). Chief complaints of skeletal pain of the leg (57%) and chest (28%) were found in Torun et al. (2013) in their sample of 193 Turkish obese and healthy weight 7–11 year olds with VDD or insufficiency. Other symptoms include abdominal pain, headaches and seizures (Kehler et al., 2013; Vehapoglu et al., 2015). Table 3 reviews these studies in greater detail.

Fractures and reduced BD may be another subclinical sign. The increased PTH levels in VDD in school-aged children and adolescents suggest increased risk for fractures and reduced BD, especially during rapid bone growth (Wagner et al., 2008). According to the AAP, increased fracture risk from VDD should be a concern in the school-aged and adolescents (Golden et al., 2014). Clarke and Page (2012) found VDD to be associated with fractures and slipped capital femoral epiphysis. In reviewing the effects of VitD insufficiency on fracture risk and BD, Moon, Harvey, Davies, and Cooper (2014) suggested that providers be careful about attributing fractures to low VitD levels (in the absence of increased PTH or ALP), as both fractures and low VitD levels individually are common in the general population and may be present at the same time. The PN should recognize that while VDD increases fracture risk and decreases BD, a challenge remains when there is VitD insufficiency.

VDD may also potentially be present with abnormal immune function, resulting in increased risk for acute infections and chronic diseases, including cancers and cardiovascular, metabolic, and autoimmune diseases (Dobnig, 2011; Pyrzak et al., 2015; Wagner et al., 2008).

Rickets and Osteomalacia

Rickets and osteomalacia are rare VDD extreme conditions (Cianferotti & Marcocci, 2012; Moon et al., 2014; Wagner et al., 2008). Clinical signs of rickets include bone enlargement (e.g., skull, ends of long bones, rib cage), curved spine and femur, and generalized muscle weakness (Wagner et al., 2008).

Treatment

The 2014 AAP clinical guidelines on bone health promotion recommend supplementation with inadequate VitD intake (see section on "Prevention") or VDD (Golden et al., 2014). Therefore, if an obese child has inadequate dietary intake of VitD, supplementation is recommended. According to the AAP, screening for serum 25(OH)D is not necessary as supplementation is more cost-effective than screening and following up on serum 25(OH)D (American Academy of Pediatrics, 2017). Furthermore, clinical manifestations of hypocalcemia warrant supplementation (Misra et al., 2008).

Both the AAP and ES recommend that children 1–18 years old with VDD should be supplemented with 2000 IU/day or 50,000 IU/week of $VitD_2$ or $VitD_3$, with each regimen lasting at least six weeks, and followed by maintenance therapy of 600–1000 IU/day (Golden et al., 2014; Holick et al., 2011). The goal of this therapy depends on which VitD sufficiency definition is used and is aimed to achieve serum 25(OH)D levels >20 ng/ml (Golden et al., 2014) or >30 ng/ml (Holick et al., 2011). After treatment completion, serum levels should be obtained with these goals in mind (Golden et al., 2014). In obese children, the ES recommends a dose two to three times higher with at least 6000–10,000 IU/day until VitD levels are >30 ng/ml, followed by maintenance therapy of 3000–6000 IU/day (Holick et al., 2011). Serum levels need to be monitored at least annually (Misra et al., 2008) and dose adjusted accordingly to maintain sufficiency (Holick et al., 2011).

Role of the Pediatric Nurse

Clinical

Prevention is key in avoiding VDD in obese school-aged children and can start with obesity prevention, knowing that obesity is a risk factor for VDD, as was discussed previously in "Obesity and Other Risk Factors for Vitamin D Deficiency." Obesity prevention in children starts early in the prenatal period, as maternal obesity is a strong and consistent risk factor of childhood obesity (Daniels, Hassink, & Committee On Nutrition, 2015). General principles from a clinical report by the AAP on primary prevention of obesity include monitoring growth starting from birth, encouraging breastfeeding during infancy, and supporting adults to increase physical activity and healthy eating in their children, while also decreasing a sedentary lifestyle (Daniels et al., 2015). Counseling on lifestyle and adequate VitD intake from food addresses both issues of obesity and risk for VDD and offering supplementation may be protective in obesity especially when dietary VitD intake from food is inadequate (Turer et al., 2013). The ES supports VDD screening in obese children, whereas the AAP does not, and suggests that their daily VitD needs and supplemental doses for VDD be two to three times higher than healthy weight children (Holick et al., 2011). The PN should assess subclinical signs and symptoms, total VitD intake including from food and supplementation, risk factors for VDD, and signs of hypocalcemia. History and physical exam will enable the PN to know if VDD screening is needed. Table 4 summarizes the role of the PN.

Patient Education

The PN should counsel children and families on the importance of VitD in promoting calcium absorption in the body and bone mineralization; with sufficient VitD levels, calcium resorption from bones is prevented. The PN should identify obesity as a strong risk factor and counsel on protective factors, namely that of a healthy lifestyle and adequate dietary VitD intake according to the Recommended Dietary Allowance (RDA; i.e., daily intake that meets the needs of ≥97.5% of the population). Patients should learn how to read nutrition labels to determine whether foods are fortified with VitD to ensure adequate intake. Physical activity needs to be emphasized and even 10 min of high-impact activities (e.g., walking, jumping) three times/week increases BD (Golden et al., 2014). Lastly, counsel on subclinical manifestations of VDD, especially limb pain and fractures.

Future Research

Universally agreed upon VDD parameters are needed, as well as definitive recommendations specific to children with obesity (i.e., RDA,

screening, treatment). The contribution of VDD to obesity and extraskeletal benefits of VitD need more research, along with parameters within which these extraskeletal benefits are optimized. Lastly, more research will determine whether there are safe levels of unprotected sun exposure that will increase serum 25(OH)D.

Conclusion

Obesity is a strong risk factor for VDD and VDD in obese children predicts metabolic syndrome. The PN can prevent VDD in obese children through lifestyle and dietary changes, screen for VDD based on history and physical exam, assess for subclinical manifestations, treat when indicated and provide counseling.

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