Serum 25-Hydroxyvitamin D3 Concentrations and Carotid Artery Intima-Media Thickness Among High-Risk Children

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Background

- Single-center, retrospective, observational studies showed that vitamin D deficient states in adults have been found to be associated with hypertension, diabetes, atherosclerosis, myocardial infarction, congestive heart failure, stroke and decreased kidney function[1].
- Even among adolescents, deficient vitamin D states are associated with hypertension, hyperglycemia, and metabolic syndrome[2].
- However, a recently released report from the Institute of Medicine showed that although vitamin D is key for bone health, there is no unequivocal evidence that it provides other benefits[3].
- Certain deleterious vascular effects have been described in adults with deficient vitamin D states, however there is no data pertaining to this in children[4].

Objective

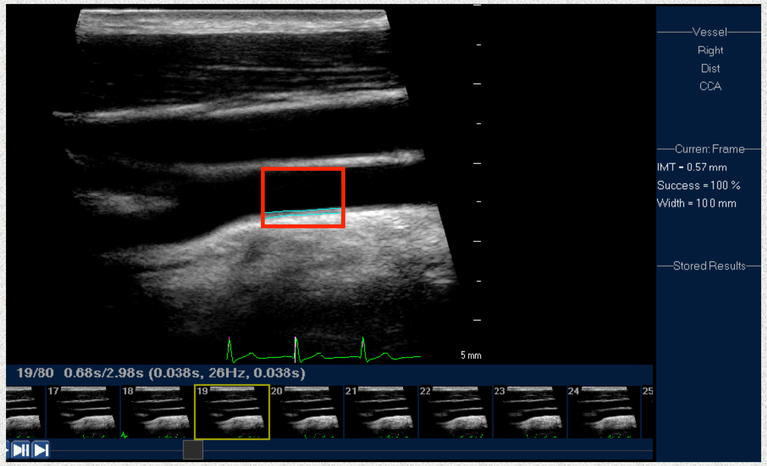
- To determine whether there is a correlation between serum vitamin D levels and carotid artery intima-media thickness - CIMT (a noninvasive tool for assessment of subclinical atherosclerosis) in high-risk children.

Methods

- A PubMed literature search was conducted back to 1966 using the following search terms: "vitamin D," "cardiovascular," "pediatric," and "carotid artery intima-media thickness." There were no studies describing CIMT and vitamin D status in children.
- Children's Mercy Institutional Review Board's permission was obtained prior to commencement of this study.
- This study involved a chart review of 74 children aged 6-22 years old who visited the Children's Mercy Hospital Preventive Cardiology and Lipid Clinic between January 1, 2009 and December 31, 2010.
- Demographic and anthropometric data including age, sex, race, weight, height, and BMI were gathered. Family history of premature heart disease and history of tobacco smoke exposure were ascertained via an interview. Systolic blood pressure (SBP), fasting lipid profile, insulin and serum 25-hydroxyvitamin D3 data was collected. The season in which the vitamin D levels were measured was recorded as Spring/Summer (March-August) or Fall/Winter (September-February).
- Ultrasound images of the common carotid artery to measure CIMT were obtained.
- Vitamin D was used as a continuous predictor variable and in addition categorized into three levels (Insufficient - < 20 ngm/ml, Borderline - ≥20 to ≤ 30 ngm/ml, Sufficient - > 30 ngm/ml) to examine its relationship with maximum and mean CIMT.
- A univariative (ANOVA) and multivariative analysis (general linear model) were performed comparing vitamin D and maximum and mean CIMT using SAS program.

CIMT

- CIMT measurements were taken from the far wall of both the left and right common carotid arteries using a semi-automated, edge detection software (Philips, QLAB)[5]. This software was used to measure the CIMT within a 10-mm-wide box that was placed along the far wall of the common carotid artery within 2 cm of the carotid bifurcation.



Results (n=74)

Table 1 - Demographic Data

Age, years	13.7 ± 3.1
Sex, male	45%
Race, white	62%
Family history	45%
Tobacco smoke exposure	30%
Fall/Winter Season	50%

Table 2 - Anthropometric Data

BMI, kg/m^2	26.9 ± 6.3
BMI, *Z* score	1.4 ± 1.1
SBP mm Hg	117 ± 10

Table 3 - Laboratory Data

Total cholesterol, mg/dL	215 ± 45
High Density Lipoprotein Cholesterol, mg/dL	46 ± 60
Triglycerides, mg/dL	195 ± 302
Insulin, uIU/mL	17 ± 22
25-Hydroxyvitamin D3, ngm/mL	**26 ± 9**

Table 4 - CIMT Data

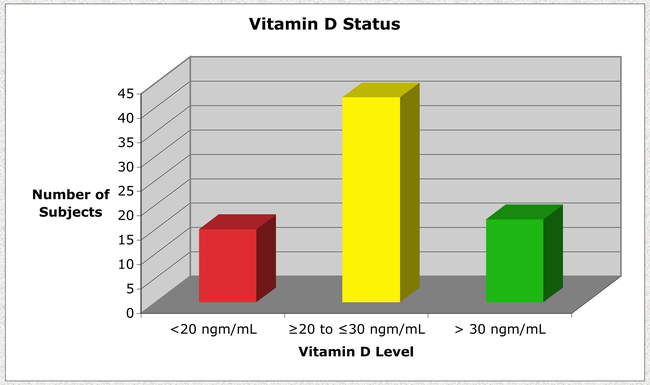
CIMT maximum (mm)	0.54 ± 0.06
CIMT mean (mm)	0.48 ± 0.04

- Data are presented as mean±SD or percentages.

- Seven modifiable atherosclerosis promoting risk factors were analyzed as predictor variables with respect to their relationship with maximum and mean CIMT:
  --1- BMI ≥ 95th percentile for age and sex
  --2- SBP ≥ 95th percentile for age, sex, and height
  --3- Total cholesterol ≥ 170 mg/dL
  --4- Triglycerides ≥ 100 mg/dL
  --5- High Density Lipoprotein Cholesterol ≤ 45 mg/dL
  --6- Insulin ≥ 18 uIU/mL
  --7- Exposure to tobacco smoke

Mean Risk Factor Score = 3.3 ± 1.6

Results



- ***There was a significant association between SBP and mean CIMT (p = 0.04).***
- ***With univariative analysis, there was no association between vitamin D levels and maximum (p = 0.90) or mean (p = 0.89) CIMT .***
- ***With multivariative analysis adjusting for risk factor score, there was no association between vitamin D levels and maximum (p = 0.40) or mean (p = 0.23) CIMT.***

Conclusions

- In this cohort, there was no correlation between vitamin D status and CIMT.
- We found SBP to correlate with mean CIMT suggesting that hypertension is a strong atherosclerosis-promoting risk factor beginning in childhood.

Limitations

- The sample size was limited as children were required to have a serum vitamin D level and carotid artery ultrasound performed during the same visit. It is possible that we were not able to prove the hypothesis due to small sample size and low power.
- There were no healthy controls as all the subjects presenting to the clinic had cardiac risk factors.
- This study is a retrospective and observational, therefore, it cannot establish causation.

Bibliography

1. Kenrick J, et al. 25-Hydroxyvitamin D deficiency is independently associated with cardiovascular disease in the Third National Health and Nutrition Examination Survey. *Atherosclerosis* 2009; 205:255-260.
2. Reis J, et al. Vitamin D status and cardiometabolic risk factors in the United States adolescent population. *Pediatrics* 2009; 124:e371-9.
3. Institue of Medicine. (2010). Dietary Reference Intakes for Calcium and Vitamin D. http://www.iom.edu/Reports/2010/Dietary-Reference-Intakes-for-Calcium-and-Vitamin-D.aspx
4. Targher G, et al. Serum 25-hydroxyvitamin D3 concentrations and carotid artery intima-media thickness among type 2 diabetic patients. *Clin Endocrinol* (Oxf) 2006; 65:593-7.
5. Le J, et al. Vascular age is advanced in children with atherosclerosis-promoting risk factors. *Circ Cardiovasc Imaging* 2010; 3:8-14.