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Original article

Is there any link between vitamin D and left atrial diameter in children?

Zeynep Cerit[1], Şule Gökçe[2], Levent Cerit[3]

[1]Department of Pediatric Cardiology, Near East University Faculty of Medicine, Nicosia, Cyprus - E-mail: drcerit@hotmail.com; [2]Department of Pediatrics, Ege University Faculty of Medicine, Izmir, Turkey; [3]Department of Cardiology, Near East University Faculty of Medicine, Nicosia, Cyprus

Summary. Vitamin D (vitD) deficiency has been found associated with rickets/osteomalacia, autoimmune diseases, cardiovascular system diseases, and infectious diseases. Growing evidence demonstrated that vitD has a key role in the renin-angiotensin-aldosterone system. Although there is a strong association between left atrial diameter and serum vitD level in adults, there is scarce data in children. Therefore, we aimed to assess the association between serum vitD level and left atrial diameter in children. We performed a prospective study with 97 children in routine control without any complaint. All patients were evaluated for the echocardiographic evaluation in the outpatients clinic, and the children were divided into two groups as vitamin D deficiency group (vitamin D<20ng/ml) and control group (vitamin D≥20ng/ml). Demographic data, echocardiographic parameters, and serum vitD level were analysed. A p-value of <0.05 was considered significant. The study population included 97 children, and the prevalence of vitD deficiency was found 46.3%. Although left atrial diameter was increased in children with vitD deficiency, there was no significant difference between the two groups with regard to left atrial diameters. Left atrial diameter was significantly associated with BMI z-score (r=0.301), age (r=0.307)(P<0.001), interventricular septum (r=0.209), weight (r=0.184), vitD (r=0.127). On multivariate analysis, BMI z-score was significantly associated with left atrial diameter. BMI z-score is independently associated with left atrial diameter. Although left atrial diameter was increased in patients with vitD deficiency, serum vitamin D level was not found an independently associated with the left atrial diameter.

Key words: vitamin D, left atrial diameter, Body Mass Index

Background

Left atrial (LA) diameter has important prognostic information in the adult population as well as in a variety of cardiovascular disease such as atrial fibrillation, stroke, congestive heart failure, myocardial infarction (1). Vitamin D (vitD) has established roles in calcium and bone metabolism. Vitamin D deficiency was found associated with increased risk of cardiovascular disease, hypertension, obesity, and increased LA diameter (2-12). Additionally, there is a strong association between obesity and LA diameter. In the same manner, the strong association between obesity and LA diameter in children (13,14).

Taking this into account, we aimed to evaluate the association between serum vitD level and LA diameter in children.

Methods

Patients

The study population included 45 children with vitamin D deficiency (<20ng/ml) and 42 children (control group ≥20ng/ml). All children were consecutively recruited from healthy child policlinics.

The medical records of 97 children were evaluated with regard to the association between serum vitD

levels and LA diameter. The epidemiological and demographic data including age, gender, weight, height, body mass index (BMI) were analysed. The exclusion criteria of this study were a history of diabetes, hypertension, inflammatory disease, malignancy, connective tissue disorders or skeletal dysplasia, more than mild valvular stenosis or regurgitation, cardiomyopathy and/or ventricular dysfunction.

Anthropometry

Height was measured with a standard wall-mounted stadiometer to the nearest centimetre, and weight was measured with calibrated electronic scales. BMI was calculated as weight (kg)/height (m)2. BMI z-score, and it's the corresponding percentile were determined by comparison with U.S growth charts from the Centers for Disease Control and Prevention (15).

Echocardiographic evaluation

Echocardiographic evaluations were performed with two-dimensional guided M-mode echocardiography obtained in the parasternal short and long-axis views, in accordance with the recommendations by the American Society of Echocardiography (16).

Left ventricular posterior wall (LVPW) thickness in diastole, interventricular septum (IVS) thickness were obtained by M-mode. Two-dimensional and colour Doppler imaging were routinely performed to diagnose valvular stenosis or regurgitation and other structural defects.

Laboratory studies

Levels of 25-hydroxy (OH) vitD was measured following a fasting period of eight hours. Serum 25-(OH) vitD levels were measured by chemiluminescence immunoassay using a Lıaıson analyser (DiaSorin Inc). VitD deficiency was defined as serum levels of 25-(OH) VitD < 20 ng/ml. The study protocol was approved by the local ethics committee.

Statistical analysis

Statistical analysis was performed with the SPSS version 20.0 for personal computers (Chicago, IL, USA). All continuous variables were tested for normality. Results were expressed as mean±standarddeviation (SD) or as the median. Student T-test or Mann–Whitney U test was used to compare continuous variables and chi-square test for categorical variables. Univariate logistic regression analyses were conducted to identify the independent predictors of left atrial diameter. Multiple linear regression was undertaken with LA diameter entered as dependent variables into separate models; independent variables were determined from the univariate analysis and entered in a step-wise fashion. A p value<0.05 was considered statistically significant in all the calculations.

Results

The study population included 97 children, and the prevalence of vitamin D deficiency was found 46.3%. The two groups were comparable for age, gender, height, left ventricular ejection fraction, systolic and diastolic blood pressure (Table1).

There was a significant difference between two groups with regard to weight, LVPW, IVS, LA diameter, and body mass index z-score (39.7±8.7 vs 30.8±9.1 p<0.001, 6,1±1.3 vs 5.1±0.9 p=0.004, 6.5±1.1 vs 5.1±1.1 p<0.001, 32.9±3.7 vs 27.7±2.9 p=0.002, 2.8±0.39 vs 1.4±0.21 p<0.001; respectively)(Table1).

The univariate regression analyses are shown

Table 1. Characteristics of patients

Patient Characteristics	Serum Vitamin D Level		P
	<20 ng/ml (45)	≥20ng/ml (42)	
Age (years)	8.9±3.1	9.1±2.8	0.531
Female gender, %	46	44	0.729
Weight (kg)	39.7±8.7	30.8±9.1	**<0.001**
Height (cm)	136.4±8.3	134.9±9.1	0.623
BMI z-score	2.8±0.39	1.4±0.21	**<0.001**
Left atrial diameter (mm)	32.9**±3.7**	27.7±2,9	**0.002**
LVPW (mm)	6.1±1.3	5.1±0.9	**0.004**
IVS (mm)	6.5**±1.1**	5.1**±1.1**	**<0.001**
Ejection fraction (%)	69.8**±5.7**	68.7**±4.9**	0.385
SBP (mmHg)	109**±9.4**	107**±8.9**	0.728
DBP (mmHg)	56.7**±5.8**	54.9**±5.1**	0.683

BMI; body mass index, LVPW; left ventricular posterior wall, IVS; interventricular septum, SBP; systolic blood pressure, DBP; diastolic blood pressure

in Table 2. LA diameter was significantly associated with BMI z-score (r=0.301, P<0.001), age (r=0.307, P<0.001), IVS (r=0.209, P<0.001), weight (r=0.184, P<0.001), vitD (r=0.127, P<0.001). On multivariate analysis, BMI z-score was significantly associated with left atrial diameter (Table 3).

Discussion

In our study, we found that BMI z-score is independently associated with the left atrial diameter in children. Although LA diameters were increased in patients with vitD deficiency, serum vitD level was not found an independently associated with the LA diameter.

LA enlargement is associated with an increased risk of cardiovascular diseases including atrial fibrillation, stroke, heart failure, and sudden cardiac death (1-12). Increased BMI is also associated with several cardiovascular diseases (17). In the Framingham Heart Study, BMI was found strongly correlate with LA diameter (18). Additionally, Pritchett et al. (19) demonstrated that BMI was significantly associated with LA diameter, after adjustment for age and gender.

Table 2. Univariate associations with left atrial diameter

Characteristics	Left atrial diameter	p
Age (years),	0.307	**<0.001**
BMI z-score	0.201	**<0.001**
Weight (kg)	0.184	**<0.001**
LVPW (mm)	0.138	0.428
IVS (mm)	0.313	**<0.001**
Vitamin D (ng/ml)	0.127	**<0.001**

BMI; body mass index, LVPW; left ventricular posterior wall, IVS; interventricular septum

Table 3. The relationship between left atrial diameter and age, vitamin D, IVS, and BMI z-score by multivariate analysis.

Predictor Variables	B(standardized coefficient)	p
Age (years)	0.562	**<0.001**
Vitamin D (ng/ml)	0.037	0.237
IVS (mm)	0.051	0.362
BMI z-score	0.462	**<0.001**

BMI; body mass index, IVS; interventricular septum

In the same manner, Daniels et al. (20) found that BMI was a significant predictor of LA diameter in multiple regression models that incorporated height, systolic blood pressure and left ventricular geometry. Hirschler et al. (21) demonstrated significant univariate correlations between the LA area and BMI, waist circumference, blood pressure and a measure of insulin resistance. In the stepwise multivariate analysis, BMI was not tested but in a model incorporating waist circumference, blood pressure, LV mass and HOMA–IR, waist circumference was the only significant independent predictor of LA size. Di Salvo et al. (22) have revealed that obese children had larger LA dimensions and lower atrial strain rate, suggesting an impaired atrial function in this group, in comparison with controls. In our study, we found that BMI z-score was found independently associated with LA diameter.

VitD regulates inflammatory responses and upregulates the expression of anti-inflammatory cytokines, such as interleukin-10, according to in vitro experiments. Also, vitD regulates the activity of the renin-angiotensin aldosterone system (RAAS). Activated RAAS can lead to oxidative stress and inflammation, both of which could culminate in AF. It is assumed that tissue angiotensin II may induce apoptosis of the cardiomyocytes and contribute to changes in atrial structure (23-25).

There is a strong association between vitD and LA diameters in adults. But there is scarce data about the association between vitD and LA diameters in children. In our study, although LA diameters were increased in patients with vitD deficiency, serum vitD level was not found an independently associated with the LA diameter.

Some limitations might be seen in the current study. Firstly, the small sample size. Secondly, we did not determine the parathyroid hormone and calcium levels of the study population.

In conclusion, consistent with previous studies, we found that BMI z-score is independently associated with the LA diameter in children. Although LA diameters were increased in patients with vitD deficiency, serum vitD level was not found an independently associated with the LA diameter. Further studies with a larger number of children are required to clarify the association between serum vitD level and LA diameter.

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Correspondence:
Levent Cerit, MD
Associate Professor of Cardiology
Near East Hospital University Hospital, Near East Boulevard, Nicosia, Cyprus
Tel.: 00903926751000
E-mail: drcerit@hotmail.com