Original Article

Serum vitamin D status in children of bronchial asthma

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Objective: To assess and compare serum vitamin D in pediatric asthmatic patients with non-asthmatic healthy children to observe its role in the progression of asthma

Methodology: This case control study was conducted in Physiology Department of Basic Medical Sciences Institute, Karachi, from 2013 to April 2015 with the association of National Institute of Child Health (NICH). It included 170 children of age between 6-14 years of both gender. All subjects were equally grouped into controls and cases. Controls were recruited from school and diagnosed cases of asthma were selected from NICH as per Global Initiative for Asthma Guideline. Serum vitamin D was estimated by ELISA kit. Asthma was assessed by spirometry. Data were analyzes by SPSS version 21.

Results: Vitamin D in controls was 17.91 ±0.48ng/ml and in cases was 15.18±0.21ng/ml ($p<0.001$). Serum levels of mild and moderate asthmatics with insufficient vitamin D were 16.5± 0.24ng/ml and 14.31±0.41ng/ml respectively and deficient vitamin D of both groups were 7.3± 0.15ng/ml and 6.8± 0.44ng/ml respectively. Significant indirect association was found between vitamin D and age ($r = -0.326$, $p=0.01$). vitamin D was directly related with FEV1($r=0.274$.$p= 0.04$).

Conclusion: In asthma, serum insufficient or deficient vitamin D levels result in increased inflammatory state of airways, which may impair the natural immune defense system of lungs. (Rawal Med J 202;45:607-610).

Keywords: Vitamin D, asthmatics, spirometry.

INTRODUCTION

Asthma is an inflammatory disease of airways resulting in breathlessness, cough and wheeze.[1] Globally, prevalence of childhood asthma is increased up to 8.6%.[2] In Pakistan, 20% of children are affected by asthma.[3]

Vitamin D has ability to do functions against inflammation and displays an important part in the mediation of defense mechanism of our body.[4] In skin, cholesterol is converted into previtamin D and then into vitamin D. It's first hepatic hydroxylation converts it into 25-hydroxy- D and then by renal 1-α hydroxylase to 1,25 dihydroxy D_3. There are some other areas besides kidneys where 1-α hydroxylase is present.[5] Airways epithelial cells have 1-α hydroxylase enzyme, which can synthesize physiologically active vitamin D, which is able to produce anti-microbial peptides, cathelicidins which decrease the infection and inflammation and provides strong innate immunity to airways.[6] Previous studies observed vitamin D deficient serum levels were associated with asthma and other allergic disorders.[7] In some areas where sunlight is sufficient or where food is fortified with vitamin D, it's deficiency had still happened.[8] Lack of Vitamin D is very common in asthmatic kids in Mediterranean countries and in North America.[9] It is directly linked with forced vital capacity.[10] This study was conducted to observe the effects of different levels of vitamin D on asthma severity that may be helpful in future to add vitamin D supplementation in addition to the routine treatment of asthma.

METHODOLOGY

This case control study was conducted in Physiology Department of, BMSI, JPMC, Karachi, from 2013 to April 2015 with the association of NICH. Ethical approval was obtained from IRB of NICH. Written permission was taken from children's parents. Total 170 participants were recruited and divided into 85 diagnosed asthmatic children as cases from NICH and 85 healthy school going boys and girls as controls. Cases were further subgroups as mild and moderate asthmatics. Sample

size was calculated by Open Epi formula with 20% prevalence.[3] All controls were apparently healthy having no history of asthma episode. All cases were diagnosed by the rules of Global Initiative for Asthma Guideline.[11] The subjects having history of vitamin D intake or medicines that modify serum vitamin D and patients who have chronic pulmonary diseases were excluded from study.

BMI as determined by formula, weight in kg/height in m². It is divided[12] into underweight = <18.5 kg/m², normal = 18.5-24.9 kg/m², over weight = 25-29.9 kg/m² and Obese = ≥30 kg/m.²

Vitamin D was estimated by Vitamin D ELISA kit. It is divided into Sufficient ≥30 ng/ml, Insufficient 20 to 29 ng/ml and deficient vitamin D <10 ng/ml.[13] Spirometry was performed by Vitalograph spirometer and at least three values of FVC and FEV1 were taken.

Statistical Analysis: Un paired t test was used to compare means. Chi square was performed to analyze the comparison of different categorical variables. Pearson correlation was used to determine correlation. Level of significance was $p<0.05$. Data were analyzed with SPSS version 21.

RESULTS

Table 1 represents the descriptive data of subjects. Besides age and gender distribution, comparison of all variables in both groups are significant ($p<0.05$). Table 2 shows comparison of mean values of vitamin D in asthmatic patients and healthy children. In control group, it was 17.91±0.51 and in cases was 15.18±0.22 ($p<0.001$).

Table 1. Biophysical characteristics and frequency of vitamin D status of two groups.

Variable	Control n=85		Case n =85	P value
	Mean± SD		Mean ± SD	
Age (years)	10.84±1.73		10.06±2.23	0.074
BMI(kg/m²)	18.33		15.01	<0.001
Girls	40 (42%)		38(40%)	0.094
Boys	45(58%)		47(60%)	
ED/Hospitalization in last 6 months	No	85(100%)	36(42.3%)	<0.001
	Yes	0 (0%)	49(57.6%)	
Family history of asthma	No	58(68.2%)	22(25.8%)	<0.001
	Yes	27(31.7%)	63(74.1%)	
Vitamin D Insufficient level(10-29ng/ml)	75(88%)		60(70.5%)	<0.004
Vitamin D deficient level(<10 ng/ml)	10(11%)		25(29.4%)	

Table 2. Comparison of mean serum vitamin D level in two groups.

Variable	Control Mean± SD	Case Mean ±SD	p- value
Vitamin D Level (ng/ml)	17.91±0.51	15.18±0.22	<0.001

Table 3. Comparison of serum vitamin D levels within subgroups.

Variable	Mild Asthma n=21 Mean± SD	Moderate Asthma n= 64 Mean± SD	P value
Vitamin D insufficient level (ng/ml)	16.5± 0.24	14.31±0.41	<0.001
Vitamin D deficient level (ng/ml)	7.3± 0.15	6.8± 0.44	<0.001

Table 4. Correlation of serum vitamin D levels with biophysical and pulmonary function test in case group.

Variable	Case	
	Correlation (r)	P value
Age (years)	-0.336	0.03*
BMI (kg/m²)	-0.162	0.78
FVC(L)	0.174	6.25
FEV1(L)	0.274	0.04*
FEV1/FVC %	0.144	0.77

Vitamin D insufficient levels between mild and moderate asthmatics revealed significant result ($p<0.001$) as well as comparison of deficient level shows significant differences in these subgroups ($p<0.001$) (Table 3). Table 4 shows the association of vitamin D with Age, BMI, FEV1, FVC and FEV1/FVC%. Negative relationship of age with vitamin D ($r=-0.336$, $p=0.03$) while positive correlation of FEV1 with vitamin D were noticed ($r=0.274$, $p=0.04$).

DISCUSSION

We noticed that no one among our subjects had normal serum levels of vitamin D. In our country, vitamin D insufficiency is very common in both genders and in all ages.[14] Nearly 20% of general pediatric population of Pakistan is affected by asthma.[3] We found significantly lower mean vitamin D levels in asthmatic children than control subjects. Hatami et al[15] and Jat and Khairwa[16] found similar results. But Maalmi et al[17] did not discover major

difference in the mean values of serum vitamin D levels in healthy subjects and asthmatics.

In the present study, out of 85 participants, 75 controls had insufficient while only ten had deficient vitamin D but in cases, 60 had insufficient whereas 25 had deficient levels of vitamin D. The cases had very low levels of this vitamin when severity of asthma increased from mild to moderate state. Similar results were noticed by Korn et al[18] and according to them serum vitamin D decreased as the severity of asthma increased. They also found that all their study subjects including controls had low levels of vitamin D.

We correlated vitamin D levels with biophysical parameters and pulmonary function test in asthmatic pediatric patients which revealed significant positive correlation of FEV1 with vitamin D. Somashekar et al[19] also observed direct relationship of vitamin D with FEV1%. In contrast, Maalmi et al[17] noticed mild association with FVC but not with other pulmonary function test. Another study from Turkey showed decrease FEV1 in asthmatic patients with decrease vitamin D.[20] They found that lack of vitamin D were related with uncontrolled asthma control and poor lung function test.

Correlation of age with vitamin D revealed statistically significant inverse correlation but not with BMI. Alyasin et al[21] also found that young age and less vitamin D was associated with worsening of asthmatic condition. Same results were found by Somashekar et al[19] but Brehm et al[22] reported contradictory results.

Vitamin D differentiates T cells into regulatory T cells and increase their secretion mainly interleukin 10 which is an anti inflammatory cytokine. Meanwhile it decreases the production of inflammatory cytokines. That's why, lack of vitamin D results in imbalance between inflammatory and anti-inflammatory state of airways resulting in poor asthma control. After binding to its receptor, VDR, vitamin D prevents the secretion of antibodies by B cells and Th-1 and Th-17 differentiation by T lymphocytes and both of these are inflammatory cytokines.[23] Chronic asthma results in physical variations in the structure of airways. This is produced due to the sustained inflammatory condition which later causes healing. Vitamin D prevents the alteration of structural modifications of bronchial smooth muscle and recovers lung functions.[24]

CONCLUSION

Vitamin D deficiency is very common in our population both in healthy and asthmatic children. In asthma, its serum level becomes insufficient or even deficient with high frequency as compared to control group which may lead to worsening of disease. Therefore, vitamin D supplementation should be included in the regular treatment as an anti-inflammatory therapy which is the basic cause in the development of asthma.

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