ORIGINAL ARTICLE

Association Between Oxidative Stress, Serum Antioxidant Status and Vitamin D in Asthmatic Children

Adel Ahadi[1], Leyla Katebi[2],Shahab Bohlouli[3], Afshan Sharghi[4]

[1] Department of Pediatrics, Faculty of Medicine, Ardabil University of Medical Science, Ardabil, Iran.
[2] Faculty of Medicine, Ardabil University of Medical Science, Ardabil, Iran.
[3] Department of Pharmacology, Faculty of Pharmacology, Ardabil University of Medical Science, Ardabil, Iran.
[4] Department of Community Medicine, Faculty of Medicine, Ardabil University of Medical Science, Ardabil, Iran.

ABSTRACT

Introduction: The role of vitamin D in prevention of many diseases have been confirmed by many studies recently. The aim of this study was to determine the levels of oxidative and anti-oxidative markers after administration of vitamin D in asthmatic children. **Methods:** This randomized clinical trial study has been done on 60 asthmatic children who randomly divided into two groups. One group group received a single dose of vitamin D (5000 ng/ml) and another group received placebo with the same dose in the form of prescribed vitamin D. The levels of 25 (OH) D were measured at the baseline and also levels of vitamin D, glutathione peroxidase 1 (GPx1) and Total Oxidative Capacity (TOC) were measured 10 days after prescription single dose of vitamin D. **Results:** The amount of Vitamin D at baseline in two drug and placebo groups were similar but at the end of 10 days in the drug group with 54.8±20.92 significantly higher than placebo group with 30.73±12.98. The GPx1 levels at the end of 10 days in the drug group with 44.2±30.9 significantly more than placebo group with 29.5±12.9. Overall TOC amount at the end of 10 days in the drug group with 15.29±3.38 IU was similar to placebo group with 15.06±3.53 IU. The levels of vitamin D in rural children was significantly more than urban children. **Conclusion:** The results showed that, vitamin D could significantly increase the amount of GPx1, hence it can be used as an appropriate drug in the treatment of asthmatic children.

Keywords: Vitamin D, Asthma, Glutathione, Children

Corresponding Author:
Afshan Sharghi, MD
Email: afshan.sharghi@arums.ac.ir

INTRODUCTION

Today due to changing lifestyle from rural to urban, non-communicable and chronic diseases such as asthma and allergy are increasing (1). Since 1970, this increase has been quite obvious in developed countries, so that every year about 5-7% added to the prevalence of asthma (2). Iran in term of the prevalence of asthma is among countries with a moderate outbreak in the world and this rate is between 5% to 15% (About 6.5 million people in Iran). Asthma is a major health problem in children and adolescents at worldwide . In recent years, the prevalence of asthma in many countries have been increased during recent years. This disease is one of the major causes of student absenteeism and causes a learning disruption in patients (3-4).

"Asthma is a chronic inflammatory disease of the airways " in which, multiple cells especially mast cells , eosinophils and lymphocytic cells play a role (5 page.72). In susceptible people, this inflammation causes frequent wheezing, asthma, chest tightness and coughing (6). These symptoms are commonly associated with stenosis in the airways, which was partially reversible. This inflammation increases the response of the airways to various stimulus. Various environmental factors such as air pollution , cigarette and infectious agents can lead to lung injury through oxidative stress, which in the pathway of oxygen metabolism, leads to free radicals and cell damage (7 page.31).

Regarding the nature of asthma inflammation, the role of oxidative stress is systematically and topically determined " in the pathogenesis of this disease". During asthma and asthma attacks, the antioxidant capacity of the serum decreases dramatically (8 page.195). Oxidative stress could be due to inhalation oxidants from the outside and or to increase the Reactive oxygen Species (ROS) in the body (9 page.307). Due to the association of ROS with various pathophysiological changes in asthma, these substances play a crucial role in the incidence and severity of asthma symptoms . Among the effects of

ROS in the lungs of asthma patients, we could pointed to the increase of the lipid peroxidation, increase the sensitivity and secretion of airways and increase vascular permeability (10). An imbalance in ROS levels can cause air constraints and increase airway sensitivity . In addition to the role of inflammatory cells that increase the production of ROS, the lack of antioxidants in the airways of patients with asthma can also exacerbate this imbalance and as a result, increase inflammatory response in patients (11-13).

Vitamin D is a fat-soluble vitamin with hormonal function that is well known for its role in calcium , phosphorous homeostasis and bone metabolism (14). Over the past decades , studies showed that many non-skeletal diseases are associated with vitamin D deficiencies and on the other hand , vitamin D receptors have been found in many tissues of the body (15 page.85). Vitamin D play a role in regulating the immune system , proliferation and cellular differentiation . Deficiency of this vitamin is a risk factor for many chronic diseases such as various cancers , autoimmune diseases, infectious , cardiovascular , hypertension and type 1 and 2 diabetes (16). In many body tissues , in addition to the presence of vitamin D receptors , there is also an alpha 1– hydroxylase enzyme that converts 25-hydroxyvitamin D into its active form 1 and 25-hydroxyvitamin D. So, vitamin D can have paracrine and antioxidant effects (17 page.298). On the other hand, vitamin D improves airway availability and produces antimicrobial peptides. Many studies showed the role of vitamin D in modulating immune responses (18-19).

The importance of equilibrium between oxidants and antioxidants in the creation and control of asthma has been studied in many studies and most studies have shown that this balance has significant role in the various pulmonary diseases, including asthma (20-23).

A study showed that the levels of vitamin D in asthmatic patients was significantly lower than healthy people (8). The low level of vitamin D in asthmatic patients could be a reason for increasing their respiratory infections and asthma attacks. In asthmatic patients, the insufficient levels of vitamin D were associated with higher rate of referral patients to emergency of hospitals and then their hospitalization (24). A study by Korn et al concluded that the low level of vitamin D in asthmatic patients could be associated with their more asthma attacks during their life (25).

Due to lack of more studies about the association between antioxidants and vitamin D in asthmatic children by conducting this study we want to measure firstly the level of Vitamin D and secondly evaluate the impact of vitamin D prescribing in the levels of oxidative and anti-oxidative markers in asthmatic children.

MATERIALS AND METHODS

Study design and samples

This randomized clinical trial study was done on 60 asthmatic children who admitted in the pediatric ward of Bu-Ali hospital in Ardabil city. Patients were randomly divided into two groups (drug and placebo groups) based on randomized block design method. Before administering the drug, 2-3 cc blood samples were taken at the baseline to measure the level of 25 hydroxyvitamin D for all patients. Intervention group received a single dose of oral 50,000IU cholecalciferol tablets (VitaD50000) in the form of capsule and the placebo group was given placebo with the same dose in the form of prescribed vitamin D (empty capsule form). After ten days, 25 hydroxyvitamin D, GPx1 and TOC were measured in both groups again. Two groups in term of age, gender and history of hospitalization were matched.

Study measurements

Blood samples were collected into both empty and anticoagulated tubes containing ethylenediaminetetraacetic acid (EDTA). The serum was then separated from the cells by centrifugation at 3000 rpm for 10 min. Serum samples for measurement of serum 25(OH) D3 and TOC levels were stored at -80°C until they were used.

A single measurement of 25(OH) D concentrations was conducting using the highperformance liquid chromatography method with Agilent 1100 bio analyzer (Waldbronn, Germany, Roche).

The TOC levels were evaluated spectrophotometrically using the ADVIA 2400 bio analyzer (Tarrytown, NY, Siemens). All blood sample measurements were performed at the Department of Biochemistry, Ardabil Research Hospital, Ardabil, Iran.

Serum levels of GPx1 and CRP were measured using ELISA kits (Abcam, Cambridge, UK and R&D SYSTEMS, Minneapolis, MN, USA, respectively) following manufacturers' instructions.

Inclusion and exclusion criteria

Children with asthma who hospitalized in the Bu-Ali hospital of Ardabil city were entered in the study and children who uses high dose of vitamin D during recent three months and without tend to participated in the study were excluded.

Statistical analysis

Data collected by a checklist and collected data were analyzed in SPSS version 16 descriptive statistical methods as form of tables and figures. Firstly data were checked for normality by K-S test and used analytical statistics including Chi-square and T-test for analysis data. Also Pearson's correlation analysis was done to

determine the correlation between vitamin D amount and select variables.

Ethical approval

The study was approved at the Ethics Committee of Ardabil University of Medical Sciences with code ARUMS.REC.92.20 and registered in the Iranian clinical trial system with code IRCT2014053117843N3.

RESULTS

Among the drug group, 70% and of control group 50% were boys. The average age of children in the drug group was 4.93±3.33 years and in the placebo group was 4.45±3.22 years and two groups were matched in term of age. In the drug group 63.3% and in the placebo group 56.7% were live in the village houses (Vila homes). There wasn't significant difference in anthropometric variables such as weight, Height and BMI between two groups.

Of all patients in drug group, 13% (43.3%) and of patients in placebo group, 20% (66.7%) had a history of allergy in their family. In both groups, 18 patients (60%) had a history of asthma in their family. In the drug group, 15 patients (50%) and in the placebo group,14 (46.7%) had history of hospitalization.

In the drug group, 15 patients (50%) and in the placebo group, 14 (46.7%) were Passive Smoker in their family . The average of hemoglobin at baseline in the drug group with 12.93±1.86 mg/dL was similar to the placebo group with 12.42±2.9 mg / dL (Table I).

Table I: The Mean count of blood markers in two group at baseline

Type of blood cell	Group	Mean±SD	p-value
WBC	Drug	11980±3469	0.01
	Placebo	9299±4352	
PMN	Drug	62±16.56	0.1
	Placebo	53±21.75	
Lymph	Drug	33±16.97	0.2
	Placebo	39±18.81	
Mono	Drug	2±1.61	0.45
	Placebo	2±1.43	
EOS	Drug	2±0.81	0.1
	Placebo	1±0.93	
Hb	Drug	12.93±1.86	0.4
	Placebo	12.42±2.91	
HCT	Drug	38.81±3.04	0.09
	Placebo	37.29±3.9	
ESR	Drug	23.1±12.97	0.2
	Placebo	19.03±13.66	
GPx1	Drug	44.2±30.9	0.02
	Placebo	29.5±12.9	
CRP	Drug	1.03±1.2	0.7
	Placebo	0.5±0.8	

The mean of vitamin D at the baseline in the placebo group with 29.61±13.9 ng/dl was higher than drug group with 18.68±10.6 ng/dl but the difference wasn't significant. The mean of vitamin D at the end of 10 days in the drug group with 54.8±20.92 ng/dl was significantly higher than the placebo group with 30.73±12.98 ng/dl. Of all patients, 3 patients (10%) in drug group and 4 patients (13.3%) in placebo group had normal level of vitamin D (Figure 1). The mean of glutathione antioxidants in 10-day after receiving the single dose of drug (vitamin D) with 44.16 µmol / g in the drug group higher than the placebo group with 29.88 µmol / g. The level of vitamin D was higher in rural patients than urban patients (P = 0.004) and in children with short sleeves significantly more than children with long sleeved lining (P = 0.014). However there was no relationship between type of home (P = 0.324), gender (P = 0.055) and CRP (more than one negative plus) (P = 0.427) with vitamin D levels (Table II) . The rate of coughing and wizing among patients during study were decreased significantly (Table III).

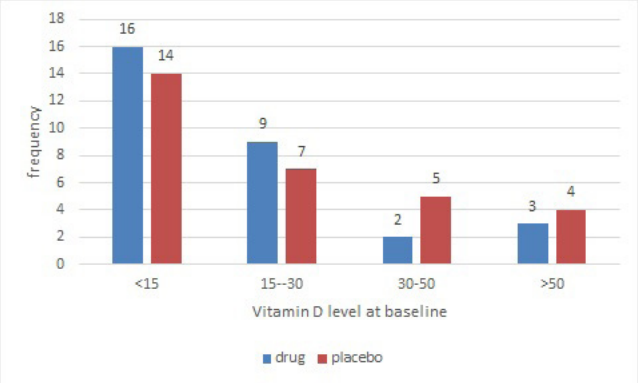

Figure 1: The levels of Vitamin D in children in two groups at baseline

Table II: Relation between Vitamin D level at baseline with patients characteristics

Characteristics	Group	Mean	SD	p-value
Residence place	Urban	18.94	12.2	0.004
	Rural	63.64	35.1	
Type of home	Vila	17.9	7.8	0.3
	Apartment	28.3	12.3	
Type of sleeve dress	Long sleeves	14.8	9.3	0.014
	Short sleeves	86.1	30.5	
Hospitalization history	+	24.3	12.8	0.98
	-	23.9	17	
Gender	Boy	16.1	10.7	0.055
	Girl	36.3	17.8	
CRP	+	19.7	8.2	0.43
	-	27.3	14.1	

There was a significant and positive correlation between vitamin D levels at the baseline and 10 days late in drug group patients (Figure 2) . Also, the relation between levels of vitamin D at baseline and 10 days later with GPx1 levels after 10 days based on Pearson

Table III: Frequency of clinical symptoms in two group by time

Time of study	Symptoms	asthma			Wiz			Cough		
		n	%	p	n	%	p	n	%	p
Baseline	Drug	21	70	0.6	27	90	0.6	30	100	1
	Placebo	23	76.7		28	93.3		30	100	
End of study	Drug	4	13.3	0.7	1	3.3	0.04	3	10	0.028
	Placebo	5	16.7		6	20		10	33.3	

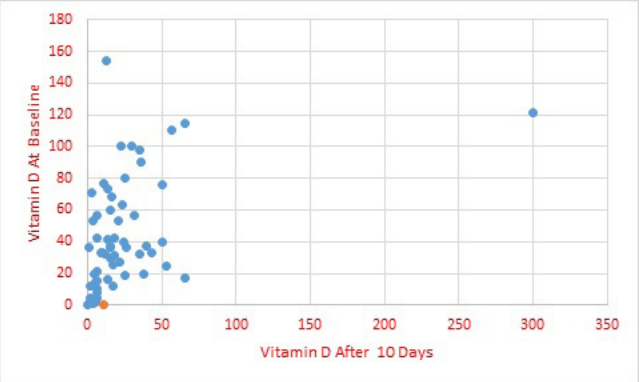

Figure 2: Correlation between Vitamin D level at baseline and After 10 days

correlation wasn't significant (Table IV). In Drug group, the correlation between vitamin D at baseline and vitamin D after 10 days with GPx1 levels after 10 days wasn't significant (Figure 3).

Table IV: Correlation between vitamin D at baseline and 10 days later with other variables

Variable 1	Variable 2	r	Sig
Vitamin D at baseline	Age at baseline	0.43	-0.104
Vitamin D at baseline	WBC at baseline	0.54	0.082
Vitamin D at baseline	ESR at baseline	0.77	0.039
Vitamin D at baseline	Vitamin D after 10 days	0.001	0.43
Vitamin D at baseline	GPx1 after 10 days	0.43	-0.103
Vitamin D after 10 days	GPx1 after 10 days	0.72	-0.048

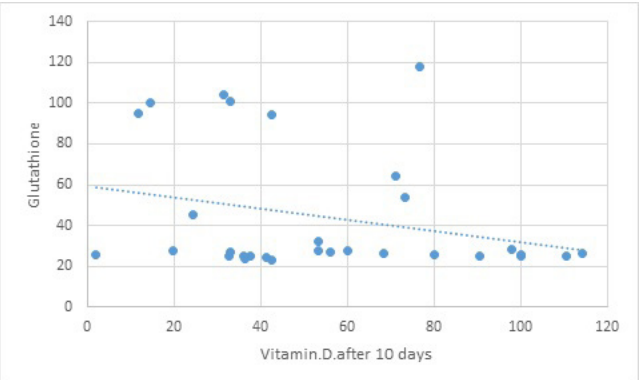

Figure 3: Correlation between Vitamin D after 10 days and GPx1 in drug group

DISCUSSION

The mean of vitamin D in the drug group significantly increased from 18.7 at baseline to 54.8 after 10 days (P=0.001) but in the placebo group the changes from 29.61 at baseline to 30.73 after 10 days wasn't significant. Also, it was found that vitamin D could significantly reduce the rate of coughing and Wiz in patients. In Freishtat et al study, the mean of vitamin D in the case and control groups was 18.5 ng/ml and 40.4 ng/ml , respectively (p=0.002, OR=1.21, CI:1.07-49.5) [23]. Of all patients, 86% in case group and 19% in control group had vitamin D amount less than 30 ng/ml and the difference between two groups was significant (p=0.001). In our study, 83.3% of drug group and 70% of placebo group had vitamin D amount less than 30 ng/ml which was similar to Freishtat et al study (23). In Searing et al study, mean of vitamin D was 31 ng / mL. Of all patients 47% had a vitamin level less than 30 ng / ml and 17 % of patients had a vitamin D level less than 20 ng / mL which was similar to our study results (24). In Brehm et al study, the mean of vitamin D was 35.7 ng / ml and 3.4% of patients had vitamin level less than 20 and 24.6% of patients had vitamin D less than 30 (22 page.55). In the study of Korn et al, serum vitamin D levels in the asthmatic individuals was 25.6 ng / ml and in healthy subjects was 26.2 ng / ml (P = 0.778) (25) . Among the asthmatic populations, 35.4% had normal vitamin levels, 31.8% between 20-30 and 32.9% less than 20. The level of vitamin D in patients with intermittent asthma was 31.1 ng / ml, mild asthma was 27.3 ng / ml, moderate asthma was 26.5 ng / ml and severe asthma was 26.4 ng / ml and there was a significant relationship between asthma severity and vitamin D levels (P = 0.046). Menon et al in a study, found that mean of vitamin D was 28.64 ng / ml in asthmatic patients and 28.42 ng / ml in healthy people and no significant difference was observed between two groups (P = 0.930) (26). In a study by Gupta et al, in asthmatic patients, 90% had vitamin D levels less than 75 ng / ml and 78% less than 50 ng / ml (27). Patients in the asthmatic group, had an average vitamin D of 36 ng / ml , which was 48 ng / ml in the control group (P = 0.03) . Unlike most studies, this study did not show any significant relationship between asthma and vitamin D levels . In this study, glutathione levels significantly were higher in asthmatic patients than placebo recipients. The total oxidation capacity (TOC) in the drug group was 15.29 and in the placebo group was 15.06 .

In our study, the amount of GPx1 in asthmatic children was significantly higher than other children. Similar to

our study, Ahmed Ansari et al in a study showed that there was a significant positive association between post-intervention levels of 25(OH) D and GPx1 in the intervention group. They concluded that vitamin D supplementation favourably enhanced GPx1 levels in adult with prediabetes, particularly in males (28). Also, the amount of TOC between two groups was similar. Due to lack of more studies about the association between antioxidants and vitamin D in asthmatic children, we have not any more evidence for confirm this relation. In this study we only discussed on the amount of oxidants and anti-oxidants in asthmatic patients. In Ahmad et al study, the glutathione peroxidase (GPx) in asthmatic patients significantly lower than the healthy controls (29). Varshavski et al in a study showed that the level of glutathion in asthmatic patients was significantly lower than healthy control people (p=0.002) and prescription of oral glutathione to these patients leads to a decrease in the extracellular oxidative status in these patients (30). Mak et al in a study showed that the level of glutathione in asthmatic patients which was significantly lower than healthy control people (11). In the study of Shokry et al, glutathione levels in patients with asthma reached from 47.86 at baseline to 48.2 two days after treatment but the difference between asthmatic patients and healthy people wasn't significant (31). In the study of EMECEN et al, TOS levels in patients with asthma were 3.31 µmol H2O2 Equiv/ L and its level in asthmatic patients wasn't significantly different from that of healthy subjects (32).

The results of this study showed that the level of vitamin D in rural children and children with short sleeves were significantly higher than children in urban area and children with long sleeves (p=0.004 v.s. p=0.014) but the relation between levels of vitamin D and variables such as gender, type of living and the level of CRP wasn't significant. Also, there was a significant relationship between vitamin D levels at baseline and 10 days later . In a study by Ahmadabadi et al, it was found that vitamin D level wasn't significantly related to gender of patients (P = 0.08) (33). The average vitamin D level in girls was 14.44 ng / dl and in boys 22 ± 8.26 ng / dl . Also, there was a correlation between the level of this vitamin and age of children (P = 0.04). In brehm et al study, the relation between age and gender with levels of vitamin D was statistically significant (p=0.008 v.s p= 0.04) (22).

In our study the correlation between GPx1 and other parameters such as BMI , Hb and HCT,wasn't significant which was not similar to Ahmed et al study because they found an inverse correlation between GPx1 and BMI in all patients not in intervention group (28).

CONCLUSION

Our study results showed that administration a single dose of vitamin D significantly could increase the anti-oxidant levels in asthmatic patients. Hence, by increasing the level of these antioxidants, it may be possibly to reduce oxidative degradation in asthmatic patients . Also, it can be used as an appropriate drug in these patients . Future studies could be recommended for done in future in other places as a multicenter studies by considering other markers and their relation with vitamin D.

AKNOWLEDGEMENTS

Author would like to thanks all children and their parents who participated in the study.

REFERENCES

1. Hallstrand TS, Bates PW, Schoene RB. Aerobic Conditioning in Mild Asthma Decrease the Hyperpnoea of Exercise & Improves Exercise & Ventilatoty Capacity. Chest. 2000; 118 (5): 1460-1469.
2. Bradly J, Moran F. Pulmonary Rehabilitation Improves Exercise Tolerance in Patients with Bronchiectasis. Aust J of Physiother. 2006;52(1):65.
3. Weiner P, Magadle R, Berar-Yanay N, Davidovich A, Weiner M. The Cumulative Effect of Long-Acting Bronchodilators, Exercise, and Aspiratory Muscle Training on the Perception of Dyspnoea in Patients with Advanced COPD. Chest. 2000;118(3):672-678.
4. Troosters T, Gosselink R, Decramer M. Short-and Long-Term Effects of Outpatient Rehabilitation in Patients with Chronic Obstructive Pulmonary Disease: A Randomized Trial. Am J Med. 2000;109(3):207-212.
5. Nadeem A, Chhabra SK, Masood A, Raj HG. Increased oxidative stress and altered levels of antioxidants in asthma. J Allergy Clin Immunol. 2003; 111(1): 72-8.
6. MacPherson JC, Comhair SA, Erzurum SC, Klein DF, Lipscomb MF, Kavuru MS, et al. Eosinophils are a major source of nitric oxidederived oxidants in severe asthma: characterization of pathways available to eosinophils for generating reactive nitrogen species. J Immunol. 2001; 166(9): 5763-72.
7. Mirzarahimi M, Ahadi A, Bohlooli SH, Namakikhalajan E, Barak M. Antioxidant levels in cord blood of term neonates and its association with birth weight. Iranian Journal of Child Neurology.2016;10(1):31-34.
8. Cluzel M, Damon M, Chanez P, Bousquet J, Crastes de PA, Michel FB, et al. Enhanced alveolar cell luminol-dependent chemiluminescence in asthma. J Allergy Clin Immunol. 1987; 80(2): 195-201.
9. Calhoun WJ, Salisbury SM, Bush RK, Busse WW. Increased superoxide release from alveolar macrophages in symptomatic asthma. Am Rev

Respir Dis. 1987; 135: A224.
10. Marcal LE, Rehder J, Newburger PE, Condino- Neto A. Superoxide release and cellular gluthatione peroxidase activity in leukocytes from children with persistent asthma. Braz J Med Biol Res. 2004; 37(11): 1607-13.
11. Mak JC, Leung HC, Ho SP, Law BK, Lam WK, Tsang KW, et al. Systemic oxidative and antioxidative status in Chinese patients with asthma. J Allergy Clin Immunol. 2004; 114(2): 260-4.
12. Misra M, Pacaud D, Petryk A. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics. 2008; 122:398.
13. Weisberg P, Scanlon KS, Li R, Cogswell ME. Nutritional rickets among children in the United States: review of cases reported between 1986 and 2003, Am J Clin Nutr, 2004; 80:1697S.
14. McAllister JC, Lane AT, Buckingham BA. Vitamin D deficiency in the San Francisco Bay Area. J Pediatr Endocrinol Metab. 2006; 19:205.
15. Mylott BM, Kump T, Bolton ML, Greenbaum LA. Rickets in the Dairy State. WMJ. 2004; 103:84.
16. Agrawal T, Gupta GK, Agrawal DK. Vitamin D supplementation reduces airway hyperresponsiveness and allergic airway inflammation in a murine model. Clin Exp Allergy. 2013;43(6):672-83.
17. Nanzer AM, Chambers ES, Ryanna K, Richards DF, Black C, Timms PM et al. Enhanced production of IL-17A in patients with severe asthma is inhibited by 1α,25-dihydroxyvitamin D3 in a glucocorticoid-independent fashion. J Allergy Clin Immunol. 2013 May 15; (13): 526-5.
18. Liao MF, Chen CC, Hsu MH. Evaluation of theserum antioxidant status in asthmatic children. Acta Paediatr Taiwan. 2004; 45(4): 213-7.
19. Hanta I, Kuleci S, Canacankatan N, Kocabas A. The oxidant-antioxidant balance in mild asthmatic patients. Lung . 2003; 181(6): 347-52.
20. Kirkham P, Rahman I. Oxidative stress in asthma and COPD: antioxidants as a therapeutic strategy. Pharmacol Ther. 2006; 111(2): 476-94.
21. Comhair SA, Erzurum SC. Antioxidant responses to oxidant-mediated lung diseases. Am J Physiol Lung Cell Mol Physiol. 2002; 283:L246.
22. Brehm JM, Schuemann B, Fuhlbrigge AL, Hollis BW. Serum vitamin D levels and severe asthma exacerbations in the Childhood Asthma Management Program study. J Allergy Clin Immunol. 2010;126(1):52-8.
23. Freishtat RJ, Iqbal SF, Pillai DK, Klein CJ, Ryan LM, Benton AS, et al. High prevalence of vitamin D deficiency among inner-city African American youth with asthma in Washington, DC. J Pediatr. 2010;156(6):948-52.
24. Searing DA, Zhang Y, Murphy JR, Hauk PJ, Goleva E, Leung DY.Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use. J Allergy Clin Immunol. 2010;125(5):995-1000.
25. Korn S, Hьbner M, Jung M, Blettner M, Buhl R.Severe and uncontrolled adult asthma is associated with vitamin D insufficiency and deficiency. Respir Res. 2013 Feb 22;14(1):25.
26. Menon J, Maranda L, Nwosu BU. Serum 25-hydroxyvitamin D levels do not correlate with asthma severity in a case-controlled study of children and adolescents. J Pediatr Endocrinol Metab. 2012;25(7-8):673-9.
27. Gupta A, Bush A, Richards D, Hawrylowicz C, Saglani S. Serum vitamin D levels and severe therapy resistant asthma in children. Arch Dis Child. 2011;96:A13.
28. Mohammed Ghouse Ahmed Ansari, Shaun Sabico, Mario Clerici, Malak Nawaz Khan Khattak, Kaiser Wani, Sara Al-Musharaf, et al. Vitamin D Supplementation is Associated with Increased Glutathione Peroxidase-1 Levels in Arab Adults with Prediabetes. Antioxidants (Basel). 2020 Feb; 9(2): 118.
29. Ahmad A, Shameem M, Husain Q. Relation of oxidant-antioxidant imbalance with disease progression in patients with asthma. Ann Thorac Med. 2012;7:226-32.
30. Varshavskiĭ BIa, Trubnikov GV, Galaktipmpva LP, Koreniak NA, Koledeznaia IL, Oberemok AN. Oxidant-antioxidant status of patients with bronchial asthma during inhalation and systemic glucocorticoid therapy. Ter Arkh. 2003;75(3):21-4.
31. Shokry DM. Oxidant-antioxidant balance in childhood asthma. Egypt J Pediatr Allergy Immunol. 2013;11(1):35-40.
32. Emecen O. Evaluation of oxidant/antioxidant status and ECP levels in asthma. Turk J Med Sci. 2010; 40 (6): 889-895.
33. Ahmadabadi F, Sharghi A, Alipour R. Study on Correlation between serum vitamin D levels and markers of severity of asthma in asthmatic children (aged 5-15) in Ardabil 2010- 2011, Desertation, Ardabil University of Medical Science, 2010.