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A STUDY OF VITAMIN D AS A THERAPEUTIC TOOL IN BRONCHIAL ASTHMA

By

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ABSTRACT

Background: Asthma is heterogeneous disease usually characterized by a chronic airway inflammation; it is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and intensity together with variable expiratory air way limitation.

Objective: To assess the level of serum vitamin D and its effect on IL-10 production in patients with bronchial asthma and the effect of vitamin D supplementation for controlling of bronchial asthma and improving symptoms.

Subjects and Methods: This study was conducted on 50 subjects; 28 males and 22 females with mean ages 46.7 ± 14.4 years. All subjects of the study were selected from the outpatient clinic and chest Department, Mostafa Kamel Military Hospital over the period through March 2021 to June 2021. The subjects were divided into two groups: Group 1A (n = 20): Were subjected to pulmonary function test & had bronchial asthma symptoms (Studied during attacks); and had vitamin D supplementation; Group 1B (n = 20): Were subjected to pulmonary function test & & had bronchial asthma symptoms (Studied in-between the attacks attacks); and had vitamin D supplementation and Group 2 (n = 10): Were subjected to pulmonary function test & were apparently healthy (Control group); and had vitamin D supplementation; serum vitamin D (25 hydroxycholecalciferol), were measured by radioimmunoassay's before and after 12 weeks of vitamin D supplementation.

Results: Serum levels of vitamin D, IL-10 and FEV1 were significantly lower in asthmatic patients than in controls and in asthmatic patients during attack than those in between attack; there was highly statistically significant difference between vitamin D (Before and after vitamin D supplementation) in both studied patients; there was a statistically significant difference between FEV1 (Before and after vitamin D supplementation) in both studied patients; there was a statistically significant difference between IL-10 (Before and after vitamin D supplementation) in both studied patients and there was highly statistical positive correlation between (Vitamin D, IL-10 & FEV1) in studied patients before and after vitamin D supplementation.

Conclusion: There was a strong inverse relationship between serum vitamin D and pulmonary functions. Vitamin D deficiency occurred in the majority of bronchial asthma patients and therefore a decreased serum vitamin D level was considered an additional risk factor for respirator functions and bronchial asthma exacerbation, vitamin D supplementations increased levels of IL-10, which is essential for controls of inflammatory states associated with lung inflammatory disorders, such as asthma and interstitial lung disease.

Keywords: Vitamin D, Hydroxycholecalciferol, Bronchial asthma and IL-10.

INTRODUCTION

The factors particularly responsible for asthma are not very clear because of its different presentation in both adults and children. Interleukins IL-4, IL-5, and IL-13 (T-helper cell type-2 cytokines) are regulated in the asthmatic airway and are related with increased eosinophilia, mast cell degranulation and increased levels of immunoglobulin E (IgE) *(Bradding et al., 2010* and *Holt & Strickl, 2010)*.

Vitamin D is a fat-soluble nutrient and a secosteroid hormone which is widely recognized as a modulator of calcium absorption and bone health and further regulates neuromuscular function, cellular differentiation, insulin secretion and blood pressure *(Looman et al., 2018)*. Several dietary hypotheses have been proposed in context with asthma and among them vitamin D status is of particular interest. Studies suggest that there is a probable relationship between vitamin D status and asthma-related symptoms presumably via the immune-modulatory effects of vitamin D *(Herr et al., 2011* and *Nurmatov et al., 2011)*.

Vitamin D metabolites are important immune-modulatory hormones and are able to suppress Th2-mediated allergic airway disease. Some genetic factors that may contribute to asthma are regulated by vitamin D, such as vitamin D receptor (VDR), human leukocyte antigen genes (HLA), human Toll-like receptors (TLR), matrix metalloproteinases (MMPs), a disintegrin and metalloprotein-33 (ADAM-33) and poly (ADP-ribosyl) polymerase- 1 (PARP-1) *(Moore et al., 2010* and *Niloufer & Kashmira, 2017)*.

Vitamin D plays a role in asthma and exerts its action through either genomic and/or non-genomic ways. Many Studies have shown that 1,25 (OH)2 D causes increases in IL-10 and decreases in IL-12 production with down regulation of costimulatory molecules, such as CD40 and CD80/86 all resulting in decreased T-cell activation. IL-10 can be released by Tregs, and acts to suppress both TH1 and TH2 responses *(Luong and Nguyễn, 2012)*.

This is accomplished through inhibition of antigen-presenting cell function and cytokine production. There are two main types of Tregs. The first are naturally occurring CD4+, CD25+, and the second are inducible IL-10 and TGF-β producing Tregs. While studying the effects of 1,25 (OH)2 D in Tregs, it was discovered that 1,25 (OH)2 D was involved in up-regulation of IL-10 and TLR9. When a TLR9 agonist, was added to cells incubated with 1,25 (OH)2 D, there was a decrease in IL-10 production. This is thought to be the mechanism by which 1,25 (OH)2 D allows for both response to infection and regulation of inflammation *(Urry et al., 2013)*.

When 1,25 (OH)2 D is present, it both allows for an initial innate immune response to infection via TLR9 with initial down regulation of IL-10, and increases IL-10 via Tregs to control the inflammatory response to protect the host from collateral damage. 1,25 (OH)2 D has also been shown to interact with TLR1 and TLR2 to enhance innate immunity *(Gauzzi et al., 2011)*.

The aim of this study was to assess the level of serum vitamin D and its effect on IL-10 production in patients with bronchial asthma and the effect of vitamin D supplementation for controlling of

bronchial asthma and improving symptoms.

SUBJECTS AND METHODS

This study was prospective randomized controlled clinical trial (RCT); conducted on 50 subjects; 28 males and 22 females with mean ages 46.7 ± 14.4 years. All subjects of the study were selected from the outpatient clinic and chest Department, Mostafa Kamel Military Hospital over the period through March 2021 to June 2021.

The subjects were divided into two groups: Group 1 (Study group): Composed of 40 individuals having bronchial asthma, and subdivided into: group 1A, 20 patients with bronchial asthma during the attack, 12 males and 8 females, with mean ages 49.35 ± 14.91 years and group 1B, patients in between attacks, 10 males and 10 females, with mean ages 46.20 ± 15.12 years while Group 2 (Control group): Was composed of 10 apparently healthy individuals with nearly matched age and sex, 6 males and 4 females, with mean ages 42.40 ± 11.84 years.

Inclusion criteria:

1. Bronchial asthma patient.
2. Age between 18 – 70 years of age.
3. Sex, no predilection between males and females.

Exclusion criteria:

1. Diabetic patients.
2. Patients with COPD.
3. Patients with chronic liver diseases and renal diseases.
4. Patients under vitamin D or calcium treatments.

All patients and controls were subjected to the following:

A. Clinical Assessment:

a) Patient's demographics: Age, sex, smoking, body mass index.

b) Occupation: Job necessitates exposure to allergens.

c) Family history: Similar condition.

d) Complete history and physical examination to evaluate exclusion criteria.

e) Clinical assessment to diagnosis bronchial asthma.

B. Plain chest X-Ray (Postero-anterior view), showed hyper inflated chest and electrocardiogram.

C. Pulmonary function tests:

a) Showed obstructive pattern with reduced Forced expiratory volume in 1 second (FEV1) FEV1/Forced vital capacity (FVC) less than 80 % of predicted:

b) Reversibility test: ‘Reversibility’ generally refers to rapid improvements in FEV1 (Or PEF), of more than 12 % and more than 200 ml from baseline measured after 15 – 20 minutes after inhalation of a rapid-acting bronchodilator 200 – 400 mcg albuterol, greater confidence if more than 15 % and 400 ml - Excessive variability in twice daily peef over two weeks.

D. Laboratory assessment:

a) CBC (Blood eosinophils), liver enzymes (AST and ALT) and renal function tests (urea and creatinine).

b) Fasting and PP blood glucose.

c) Lipid profile (LDL-HDL-triglycerides).

d) Serum vitamin D (25 hydroxycholecalciferol), measured by radioimmunoassay before and after 12 weeks of vitamin D supplementation.

e) Serum level of IL – 10 measured by radioimmunoassay before and after 12 weeks of vitamin D supplementation.

f) Serum Calcium & Phosphorus assay.

E. Vitamin - D supplementation; in the form of (Cholecalciferol vitamin D3) Devarol amp 200,000 international units, IM once per month, for 3 months.

Statistical analysis:

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

Description of all studied parameters in all studied groups at the onset of the study is shown in (Table 1).

Table (1): Demography of all studied parameters in all studied groups at the onset of the study

Variables		Group IA (n = 20)	Group IB (n = 20)	Control (n = 10)
Age (years)	**Mean± SD**	49.35±14.91	46.20±15.12	42.40±11.84
Sex (n, %)	**Male**	12 (60 %)	10 (50 %)	6 (60 %)
	Female	8 (40 %)	10 (50 %)	4 (40 %)
Vitamin D Before (ng/ml)	**Mean± SD**	18.65±7.39	21.50±7.79	38.40±15.44
IL-10 Before (pg/ml)	**Mean± SD**	4.09±1.17	4.33±1.12	7.70±1.52
FEV_1 Before (%)	**Mean± SD**	66.90±10.96	71.85±8.20	90.20±10.02
Hb (g/dl)	**Mean± SD**	11.10±1.84	12.25±0.92	12.65±1.25
WBCs (x 10^3/ul)	**Mean± SD**	9.10±2.38	7.45±1.93	7.70±2.41
PLT (x 10^3/ul)	**Mean± SD**	262.25±92.4	247.5±61.5	260±64.6
Urea (mg/dl)	**Mean± SD**	31.20±9.96	34.00±7.79	35.30±8.79
Creatinine (mg/dl)	**Mean± SD**	1.07±0.16	1.08±0.14	0.94±0.18
FBS (mg/dl)	**Mean± SD**	102.00±11.39	103.45±12.98	104.50±10.10
PPBS (mg/dl)	**Mean± SD**	137.10±19.39	149.20±19.18	134.00±21.57
ALT (U/L)	**Mean± SD**	33.20±6.69	32.70±4.90	37.30±5.83
AST (U/L)	**Mean± SD**	21.20±5.63	22.05±4.25	24.90±7.52

There was a Highly Statistical Significant Difference (p value < 0.001) between group IA and control group as regarding IL-10 and FEV1. Also, Statistically Significant Difference (p value < 0.05) between group IA and control group was noted, as regarding vitamin D and hemoglobin; No Statistical Significant Difference (p value > 0.05) between group IA and control group as regarding other studied parameters **(Table 2)**.

Table (2): Comparison between group IA and Control group as regard studied parameters

Variables		Group IA (n = 20)	Control (n = 10)	p value
Age (years)	**Mean±SD**	49.35±14.91	42.40±11.84	0.21
Sex (n, %)	**Male**	12 (60 %)	6 (60 %)	1.0
	Female	8 (40 %)	4 (40 %)	
Vitamin D Before (ng/ml)	**Mean±SD**	18.65±7.39	38.40±15.44	**0.008***
IL-10 Before (pg/ml)	**Mean±±SD**	4.09±1.17	7.70±1.52	**< 0.001****
FEV_1 Before (%)	**Mean±SD**	66.90±10.96	90.20±10.02	**< 0.001****
Hemoglobin (g/dl)	**Mean±SD**	11.10±1.84	12.65±1.25	**0.024***
WBCs (x 10^3/ul)	**Mean±SD**	9.10±2.38	7.70±2.41	0.14
PLT (x 10^3/ul)	**Mean±SD**	262.25±92.4	260±64.6	0.94
Urea (mg/dl)	**Mean±SD**	31.20±9.96	35.30±8.79	0.28
Creatinine (mg/dl)	**Mean±±SD**	1.07±0.16	0.94±0.18	0.06
FBS (mg/dl)	**Mean±±SD**	102.00±11.39	104.50±10.10	0.56
PPBS (mg/dl)	**Mean±±SD**	137.10±19.39	134.00±21.57	0.69
ALT (U/L)	**Mean±SD**	33.20±6.69	37.30±5.83	0.11
AST (U/L)	**Mean±SD**	21.20±5.63	24.90±7.52	0.14

*p-value < 0.05 is considered significant. **p-value < 0.001 is considered highly significant.

There was a highly statistically significant difference (p value < 0.001) between group IB and control group as regard IL-10 and FEV1 (Before). Also, a Statistically significant difference (p value < 0.05) between group IB and control group as regard vitamin D (before), creatinine and ALT; and No statistically significant difference (p value > 0.05) between group IB and control group as regard other studied parameters **(Table 3)**.

Table (3): Comparison between group IB and Control group as regard studied parameters

Variables		Group IB (n = 20)	Control (n = 10)	p value
Age (years)	**Mean±SD**	46.20±15.12	42.40±11.84	0.49
Sex (n, %)	**Male**	10 (50 %)	6 (60 %)	0.6
	Female	10 (50 %)	4 (40 %)	
Vitamin D Before (ng/ml)	**Mean±SD**	21.50±7.79	38.40±15.44	**0.007***
IL-10 Before (pg/ml)	**Mean±SD**	4.33±1.12	7.70±1.52	**< 0.001****
FEV1 Before (%)	**Mean±SD**	71.85±8.20	90.20±10.02	**< 0.001****
Hemoglobin (g/dl)	**Mean±SD**	12.25±0.92	12.65±1.25	0.32
WBCs (x 10^3/ul)	**Mean±SD**	7.45±1.93	7.70±2.41	0.76
PLT (x 10^3/ul)	**Mean±SD**	247.5±61.5	260±64.6	0.61
Urea (mg/dl)	**Mean±SD**	34.00±7.79	35.30±8.79	0.68
Creat (mg/dl)	**Mean±SD**	1.08±0.14	0.94±0.18	**0.027***
FBS (mg/dl)	**Mean±SD**	103.45±12.98	104.50±10.10	0.82
PPBS (mg/dl)	**Mean±SD**	149.20±19.18	134.00±21.57	0.059
ALT (U/L)	**Mean±SD**	32.70±4.90	37.30±5.83	**0.031***
AST (U/L)	**Mean±SD**	22.05±4.25	24.90±7.52	0.19

*p-value < 0.05 is considered significant. **p-value < 0.001 is considered highly significant.

There was a statistically significant difference (p value < 0.05) between group I A and group IB as regard hemoglobin and WBCs and No statistically significant difference (p value > 0.05) between group I and group I as regard other studied parameters **(Table 4)**.

Table (4): Comparison between group IA and group IB as regard studied parameters

Variables		Group IA (N = 20)	Group IB (N = 20)	p value
Age (years)	**Mean±SD**	49.35±14.91	46.20±15.12	0.51
Sex (n, %)	**Male**	12 (60 %)	10 (50 %)	0.52
	Female	8 (40 %)	10 (50 %)	
Vitamin D Before (ng/ml)	**Mean±SD**	18.65±7.39	21.50±7.79	0.24
IL-10 Before (pg/ml)	**Mean±SD**	4.09±1.17	4.33±1.12	0.5
FEV1 Before (%)	**Mean±SD**	66.90±10.96	71.85±8.20	0.11
Hb (g/dl)	**Mean±SD**	11.10±1.84	12.25±0.92	**0.019****
WBCs (x 10^3/ul)	**Mean±SD**	9.10±2.38	7.45±1.93	**0.021****
PLT (x 10^3/ul)	**Mean±SD**	262.25±92.4	247.5±61.5	0.55
Urea (mg/dl)	**Mean±SD**	31.20±9.96	34.00±7.79	0.32
Creatinine (mg/dl)	**Mean±SD**	1.07±0.16	1.08±0.14	0.81
FBS (mg/dl)	**Mean±SD**	102.00±11.39	103.45±12.98	0.7
PPBS (mg/dl)	**Mean±SD**	137.10±19.39	149.20±19.18	0.055
ALT (U/L)	**Mean±SD**	33.20±6.69	32.70±4.90	0.78
AST (U/L)	**Mean±SD**	21.20±5.63	22.05±4.25	0.59

* p value < 0.001 is considered highly significant, ** p value < 0.05 is considered significant.

There was a statistically significant difference (p-value < 0.05) between IL-10 (Before and after vitamin D supplementation) in studied patients. The mean IL-10 (Before) was 4.9 ± 1.9 while it was 6.1 ± 1.8 after vitamin D supplementation. In addition, this table shows Statistically Significant Difference (p-value < 0.05) between FEV1 (Before and after vitamin D supplementation) in studied patients. The mean FEV1 (Before) was 73.5 ± 12.9 while it was 79.8 ±10.8 after vitamin D supplementation **(Table 5)**.

Table (5): Comparison of IL-10 and FEV1 (before and after vitamin D supplementation) in the studied groups

Variables		Before (n = 50)	After (n = 50)	p value
IL-10	**Mean ± SD**	4.9 ± 1.9	6.1 ± 1.8	**0.001***
FEV_1 (%)	**Mean ± SD**	73.5 ± 12.9	79.8 ± 10.8	**0.009***

* p value < 0.05 is considered significant.

There was a highly statistically significant (p value < 0.001) correlation between (Vitamin D, IL-10 & FEV1) in studied patients before vitamin D supplementation.

There was a highly statistical significant (p value < 0.001) correlation between (Vitamin D vs. IL-10) and (IL-10 vs. FEV1) in studied patients after vitamin D supplementation; and also shows a statistical significant (p value < 0.05) correlation between (Vitamin D vs. FEV1) in studied patients after vitamin D supplementation **(Table 6)**.

Table (6): Correlation study between (Vitamin D, IL-10 & FEV1) in studied patients before and after vitamin D supplementation.

		(r)	p value
Before	**Vitamin D vs IL-10**	0.8	**< 0.001****
	Vitamin D vs FEV_1	0.58	**< 0.001****
	IL-10 vs FEV_1	0.78	**< 0.001****
After	**Vitamin D vs IL-10**	0.77	**< 0.001****
	Vitamin D vs FEV_1	0.46	**0.001***
	IL-10 vs FEV_1	0.74	**< 0.001****

(r): Pearson correlation coefficient, *p value < 0.05 is considered significant, **p value < 0.001 is considered highly significant.

There was a statistically significant difference (p value < 0.05) between FEV1 (Before and after vitamin D supplementation) in patients during attack and a highly statistically significant difference (p value < 0.001) between Vitamin D and IL-10 (Before and after vitamin D supplementation) in patients during attack.

There was a statistically significant difference (p value < 0.05) between IL-10 and FEV1 (before and after vitamin D supplementation) in-between the attack and a highly statistically significant difference (p value < 0.001) between vitamin D (Before and after vitamin D supplementation) in-between the attack.

There was a no statistically significant difference (p value > 0.05) between studied laboratory data (Before and after vitamin D supplementation) in the control group **(Table 7)**.

Table (7): Comparison of studied laboratory data (before and after Vitamin D supplementation) in patients during attack, between the attack and control group

			Before (n = 20)	After (n = 20)	p value
During the attack (1A)	**Vitamin D**	**Mean± SD**	18.65±7.39	30.35±7.10	**< 0.001****
	IL-10	**Mean± SD**	4.09±1.17	5.24±1.30	**< 0.001****
	FEV_1	**Mean± SD**	66.90±10.96	74.00±10.23	**0.002***
Between the attack (1B)	**Vitamin D**	**Mean± SD**	21.50±7.79	31.90±6.68	**< 0.001****
	IL-10	**Mean± SD**	4.33±1.12	5.69±1.08	**0.005***
	FEV_1	**Mean± SD**	71.85±8.20	79.30±6.51	**0.041**
Control group	**Vitamin D**	**Mean± SD**	38.40±15.44	44.80±11.98	0.314
	IL-10	**Mean± SD**	7.70±1.52	8.86±1.49	0.102
	FEV_1	**Mean± SD**	90.20±10.02	92.70±8.73	0.559

*p value < 0.05 is considered significant, **p value < 0.001 is considered highly significant.

DISCUSSION

In the present study out of 50 patients 5 patients (10%) were suffering from vitamin D deficiency while 30 (50%) were suffered from vitamin D insufficiency while 24 (35%) show normal levels of vitamin D. In the present study: serum levels of vitamin D, IL-10 and FEV1 were significantly lower in asthmatic patients than in controls and in asthmatic patients during attack than those in between attack. These items improved after vitamin D supplementation. The results of this study were matched with a cross-sectional survey on 75 Italian asthmatic children found that the prevalence of vitamin D-deficiency was 53.3% *(Chinellato et al., 2011)*.

In another survey from North America, 17% of asthmatics had vitamin D deficiency and a positive correlation was observed between vitamin D levels and lung function. Moreover, a cohort study revealed that low serum 25 (OH)2 D levels at the age of 6 years predicted asthma-associated symptoms (uncontrolled asthma and decreased lung function) at 14 years of age *(Ali and Nanji, 2017)*.

A study in Canada involving people aged 13 to 69 years found that those with vitamin D levels below 50 nmol/L (20 ng/mL) were 50 % more likely to have current asthma than those with levels between 20 and 30 ng/ml. Those with low levels were also twice as likely to have ever had asthma (20). A study in Turkey found that children with asthma had much lower vitamin D levels than other children and spent less time in the sun *(Uysalol et al., 2017)*.

In our study highly statistically significant difference between Vitamin D (Before and after Vitamin D supplementation) in both studied patients, also there is a statistically significant difference between FEV1 (Before and after Vitamin D supplementation) in both studied patients. In agreement with our result, a study in India with children with moderate to severe bronchial asthma found that taking 60,000 IU of vitamin D3 per month significantly increased peak expiratory flow rate and reduced the requirement of steroids, emergency visits and the number of exacerbations. A vitamin D supplement randomized controlled trial with adults with baseline vitamin D level of 19 ng/mL treated with 100,000 IU once, followed by 4000 IU/d for 28 weeks, had about a 40 % lower number of asthma exacerbations *(Yadav and Mittal, 2015)*.

On the other hand, a study done in New Zealand revealed that low blood 25 (OH) D levels were not associated with asthma incidence *(Mirzakhani et al., 2015)*. Although, it is challenging to formulate a relationship between them due to certain limitations of these studies such as the presence of bias (Selection bias), confounders (Physical activity, sex, age, etc.) and small sample size. The above-mentioned limitations might have caused a spurious relation between vitamin D and asthma. The effect of vitamin D on bronchial asthma could be related to Vitamin D has been shown to reduce airway smooth muscle (ASM) mass, subepithelial deposition, and goblet cell hyperplasia. Similarly, an inverse correlation exists between ASM mass and serum 25 (OH) D in pediatric patients with asthma *(Hibler et al., 2015)*, whereas

addition of vitamin D derivatives to cultures of human ASMs impairs proliferation of cells Furthermore, vitamin D has been shown to reduce production of extracellular matrix proteins from fibroblasts and reduce expression of enzymes implicated in airway remodeling, namely ADAM33 and MMP9 *(Yang et al., 2015)*.

Vitamin D receptors are located in multiple lung cell types and have beneficial effects on asthma control. Several mechanisms are used to promote these effects including reducing hyperplasia and airway smooth muscle proliferation, decreasing inflammation, promoting lung immunity, slowing cell cycling and enhancing the effects of exogenous steroids *(Iqbal and Freishtat, 2011)*. An inverse relationship between vitamin D status and serum IgE levels as demonstrated by *Umar et al. (2018)*. Studies have concluded that decreased level of serum 25 (OH) D is correlated with an increased prevalence, hospitalization, and increased emergency visits along with declined lung function and increased airway hyper-responsiveness in asthmatic children *(Amor-Carro et al., 2020)*. Clinical trials conducted in recent times have shown the protective influence of vitamin D supplementation among asthmatic patients *(Urashima et al., 2013)*.

In addition, increased intake of vitamin D during pregnancy has an influence on asthma in children and adults. Evidence from the researches concludes that asthma exacerbations and resistance to common therapies are some of the major challenges to reduce asthma-related morbidity and mortality *(Al-Ghobain et al., 2018)*. Our results reported that there is a statistically significant difference between IL-10 (Before and after Vitamin D supplementation) in both studied patients and highly statistical positive correlation between (Vitamin D, IL-10 & FEV1) in studied patients before and after vitamin D supplementation. In agreement with our results, studies have shown that 1,25 (OH)2 D causes increases in IL-10 and decreases in IL-12 production with down regulation of co-stimulatory molecules, such as CD40 and CD80/86 all resulting in decreased T-cell activation *(Ma et al., 2015)*.

IL-10 can be released by Tregs, and acts to suppress both TH1 and TH2 responses *(Yang et al., 2012)*. In the *Fahy and Dickey (2013)* study have shown that IL-10 producing alveolar macrophages (IMs) prevent lung inflammation by regulating neutrophil infiltration and goblet cell mucus production by down-regulating IL-13 and Th17-related genes. It is noteworthy that patients with lung inflammatory disorders, such as cystic fibrosis, asthma, and interstitial lung disease, show decreased IL-10 levels. Thus, additional studies are needed to determine whether IL-10-producing IMs are decreased in these disorders. Neutrophilic asthma is steroid resistant and has more severe inflammation compared with that of eosinophilic asthma. Therefore, alternative therapeutic interventions that resolve activation of lung neutrophils are desired to improve clinical outcomes. In the future, a clinical study will be needed to characterize IM function in asthma patients as well as healthy individuals, as IMs may offer a novel therapeutic target for neutrophilic asthma *(Kawano et al., 2016)*.

IL-10 inhibits the inflammatory response, and defective production or action of IL-10 is linked to the development of chronic inflammatory disorders, including inflammatory bowel disease *(Iyer and Cheng, 2012)*. Genome-wide association studies identified IL-10 as an important risk gene for asthma. Accordingly, lower levels of IL-10 are observed in asthma patients *(Jahromi et al., 2014)*.

In the lung, IL-10 inactivates neutrophils, eosinophils, and mast cells. In addition, alveolar macrophages (AMs) exhibit IL-10 dependent suppression of CD80 and CD86 expression and thereby suppress the activation of adaptive immunity. Moreover, transfer of dendritic cells (DCs) or CD4+ T cells engineered to secrete IL-10 prevents experimental lung inflammation. Thus, IL-10 is critically involved in lung inflammation and asthma (Mittal and Roche, 2015). No statistically significant difference between other studied laboratory data (Before and after vitamin D supplementation) in studied subjects.

CONCLUSION

In the present study, there was a strong direct relationship between serum vitamin D and pulmonary functions. Vitamin D deficiency occurred in the majority of bronchial asthma patients and therefore a decreased serum vitamin D level is considered an additional risk factor for respiratory functions and bronchial asthma exacerbation. Vitamin D supplementations increased levels of IL-10, which is essential for controlling of inflammatory states associated with lung inflammatory disorders, such as asthma. We recommend further studies on large geographical scale and larger sample size to emphasize our conclusion. It is recommended that to consider vitamin D supplementation and its efficacy as a new important line of treatment in patients with bronchial asthma, thereby prophylactic administration of vitamin D could be useful and researches have to be done to approve this theory. In addition, assessment of vitamin D effect and IL-10 on type of recurred cells on tracheobronchial tree.

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دراسة على فيتامين (د) كوسيلة علاجية فى مرضى الربو الشُعَبى

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خلفيـــة البحـــث: الرَبـــو الشُـــعبي هـــو مـــرض مـــزمن يتميـــز عـــادةً بالتهـــاب فـــي مجـــرى التـــنفس، ويـــؤدي إلـــي أعـــراض بالجهـــاز التنفســـي مثـــل الأزيـــز، ضـــيق التـــنفس، شَـــدَة الصَـــدر والسُـــعال والتـــي غالبـــا مـــا تحـــدث فـــي فتـــرة الليـــل أو الصـــباح البـــاكر؛ والعوامـــل المســـؤولة عـــن الرَبـــو الشُـــعبي غيـــر واضـــحة؛ ويرجـــع ذلـــك لإخـــتلاف صـــورة المـــرض بين البالغين والأطفال.

الهـــدف مـــن البحـــث: تقيـــيم مســـتوى فيتـــامين (د) فـــي الـــدم وتـــأثيره علـــى إنتـــاج انترلـــوكين-10 فـــي المرضـــى الـــذين يعـــانون مـــن الرَبـــو الشُـــعبي وتـــأثير مكمـــلات فيتامين (د)؛ للسيطرة على الرَبو الشُعبي وتحسين أعراضه.

المرضـــي وطـــرق البحـــث: تـــم إختيـــار جميـــع الأشـــخاص الـــذين شـــملتهم الدراســـة مـــن العيـــادات الخارجيـــة وقســـم الصـــدر، بمستشـــفى مصـــطفى كامـــل العســـكري فـــي الفتـــرة مـــن مـــارس 2021 إلـــى يونيـــو 2021؛ وتـــم تقســـيم المرضـــي إلـــى مجمـــوعتين: المجموعـــة الأولـــي (مجموعـــة الدراســـة): تتـــألف مـــن 40 شخصًـــا يعـــانون مـــن الرَبـــو الشُـــعبي، تـــم تقســـيمهم إلـــى مرضـــى المجموعـــة (1-أ) المصـــابين بـــالرَبو الشُـــعبي أثنـــاء وجـــود الأعـــراض، ومرضـــى المجموعـــة (1-ب) المصـــابين بـــالرَبو الشُـــعبي مـــا بـــين وجـــود الأعـــراض. المجموعـــة الثانيـــة (مجموعـــة القيـــاس): تضـــم 10 أفـــراد يتمتعـــون بصحة جيدة مع اختلاف العمر والجنس.

نتـــائج البحـــث: وقـــد كشـــفت النتـــائج الرئيســـية للدراســـة أن مســـتويات فيتـــامين (د) و إنترليـــوكين-10 و حجـــم الزفيـــر القســـري بعـــد الدقيقـــه الأولـــي أقـــل فـــي المرضـــى المصـــابين بـــالربو بشـــكل ملحـــوظ مقارنـــةً بمرضـــى الربـــو أثنـــاء وجـــود الأعـــراض مقارنـــة بالمســـتويات التـــي تســـبق الإصـــابة بـــه؛ كمـــا كـــان هنـــاك فـــرق إحصـــائي كبيـــر بـــين فيتـــامين (د) (قبـــل وبعـــد إعطـــاء فيتـــامين (د) فـــي كـــل مـــن المرضـــى الـــذين شـــملتهم

الدراسة؛ وظهر فرق ذو دلالة إحصائية بين حجم الزفير القسري بعد الدقيقه الاولي](قبل وبعد إعطاء مكملات فيتامين (د) [في المرضى الذين شملتهم الدراسة؛ وكذا ظهر فرق ذو دلالة إحصائية بين إنترلوكين-10] (قبل وبعد إعطاء مكملات فيتامين (د) (في كل من المرضى الذين شملتهم الدراسة؛ وكان هناك ارتباط إيجابي إحصائي للغاية ما بين فيتامين (د) و إنترليوكين-10 و حجم الزفير القسري بعد الدقيقه الأولي في المرضى الذين خضعوا للدراسة قبل وبعد إعطاء مكملات فيتامين (د).

الاستنتاج: هناك علاقة عكسية قوية بين فيتامين (د) والوظائف التنفسية؛ حيث يحدث نقص فيتامين (د) في غالبية مرضى الرَبو الشُعبي وبالتالي يعتبر انخفاض مستوى فيتامين (د) في الدم عامل خطر إضافي لوظائف الجهاز التنفسي وتفاقم الرَبو الشُعبي، كما زادت مكملات فيتامين (د) من مستويات إنترليوكين-10، وهو أمر ضروري لتثبيط الالتهابات فى الحالات المرتبطة بالإضطرابات الإلتهابية في الرئة، مثل الربو وأمراض الرئة الخلالية.

الكلمات الدالة: فيتامين د، هيدروكسي كولي كالسيفيرول، الربو القصبي و إنترلوكين-10.