Caspian J Intern Med 2013; 4(1): 624-626
Jabbari A, et al.

Comment

Vitamin D serum level and chronic obstructive lung disease

This refers to Dr. Monadi M. and his colleague's manuscript published in your valuable Journal about serum vitamin D level in patients suffered from chronic obstructive pulmonary disease (COPD) entitled "Relationship between serum vitamin D and forced expiratory volume in patients with chronic obstructive pulmonary disease" (1).

The mean age of patients entered into study was 67.4±11.5 years (1). The patients participated in this study belong to elderly age (geriatric) and not from general population. Epidemiological studies suggest that vitamin D insufficiency is related to a number of disorders frequently observed among the elderly, such as breast, prostate and colon cancers, type 2 diabetes, and cardiovascular disorders including hypertension (2) this underling disease could affect on pulmonary function test potentially.

Researcher did not exclude these patients from their investigation. Epidemiological studies support the importance of adequate vitamin D status for the maintenance of pulmonary health and function; low levels of serum 25-hydroxyvitamin D3 (25-OHD) are associated with an increased incidence or poor control of asthma, respiratory infection and chronic obstructive pulmonary disease (COPD) (3).

Serum level of 25-hydroxyvitamin D considered as Serum vitamin D level although, the researchers did not offer any references for their decision but it was wise because Individual vitamin D status is usually estimated by measuring plasma 25-OHD levels (2). Researchers considered serum 25-OHD levels less than 20 ng/ml as vitamin D deficiency; levels between 21 and 29 ng/ml as insufficient and serum level more than 30 as sufficient without references mention (1).

Reference values from normal populations are not applicable for the definition of vitamin D insufficiency or deficiency. Instead vitamin D insufficiency is defined as the lowest threshold value for plasma 25-OHD (around 50 nmol/L) that prevents secondary hyperparathyroidism, increased bone turnover, bone mineral loss, or seasonal variations in plasma PTH. Vitamin D deficiency is defined as values below 25 nmol/L (2) an investigation categorized the serum plasma level of 25OHD as follow: levels less or equal to 30 nmol/L as deficiency, between 30-50 nmol/L as insufficiency, and serum level more than 50 nmol/L as sufficiency (4).

Forced expiratory volume in first second (FEV1) in COPD's patients is dependent on many factors so; there are many confounding factors about it. Vitamin D binding protein (VDBP) is a glycosylated α-globulin protein synthesized by many tissues including the liver, kidneys, gonads and fat, and also by neutrophils. It binds circulating vitamin D with high affinity (3). VDBP genetic polymorphisms have been associated with chronic obstructive pulmonary disease (COPD).

The genetic association of VDBP with COPD may be mediated by effects on macrophage activation, since VDBP relates to FEV1, and affects macrophage activation (5). The role of VDBP is less well understood. There was not mentioned who the confounding factors like smoking, steroid usage, VDBP or serum calcium level was controlled. Although, the research methodology and design of study (like, sample size) was not appropriate; the authors concluded "a relationship between serum 25-OHD concentration and FEV1 volume in patients with COPD" (1) and suggested "optimization of serum vitamin D levels in COPD" (1).

Based on our experiences, suggestion like this must be derived from a clinical trial on COPD's patients with low serum25-OHD level after prescription of Vitamin (Vit.) D and observation of FEV1 improvement.

Researcher after observation a possible correlation between serum 25-OHD level and volumes of FEV1 in patients suffered from COPD although; that was not significant from statistical point of view; deduced "a dose response pattern of relationship between serum 25-OHD concentrations and FEV1 volumes" (1).

We fully support the valuable conclusion of the author about a positive relationship between serum 25-OHD levels and FEV1 in patients with COPD, but it should also be noted that prescription of supplementary of Vit. D needs more evidence. Further studies with an appropriate sample size is

necessary for Determine the optimum serum level of 25-OHD in COPD's patients.

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Reply to comment:

Dear editor;

We appreciate the comments by Jabbari,et al about our article entitled " Relationship between serum vitamin D and forced expiratory volume in patients with chronic obstructive pulmonary disease (1) published in a recent issue of Caspian Journal of Internal Mediciene (CJIM).

Vitamin D deficiency is linked to several skeletal as well as extraskeletal conditions which can result in vitamin D deficiency or being affected by vitamin D deficiency (2-4). The aim of our study was to determine the relationship between serum 25-hydroxyvitamin D (25-OHD) and forced expiratory volume in 1 second (FEV1) in patients with chronic obstructive pulmonary disease (COPD) but not the causes of vitamin D deficiency in COPD or the role of vitamin D in the development of COPD.

A number of conditions such as cardiovascular diseases, colon cancer, diabetes and hypertension have been observed to be the consequences of vitamin D deficiency (2). These conditions in contrast to Dr Jabbari statement do not affect FEV1 volume or the relation between FEV1 and vitamin D level. However, a number of diseases such as multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and COPD, vitamin D deficiency were associated with higher activity or disease severity (5-8). Nevertheless disability and lack of physical activities due to several systemic diseases including COOD may lead to vitamin D deficiency as well. For these reasons patients with heart failure or other conditions which had a possible contributive role on FEV1 volume were excluded from the study.

We confirm the definition of vitamin D deficiency as 20ng/ml (50nmol /l) as described by Jabbari et al, in their comment. However, all investigators have accepted serum 25-OHD levels less than 20 ng/ml being considered as deficiency, serum levels at 20-29 as insufficiency and serum concentrations at 30 ng/ml and higher as sufficient levels (9,10). Levels of serum 25-OHD less than 25nmol/l as vitamin D deficiency has not been accepted only by a few investigators whereas, this cut of point has been regarded as severe deficiency (10).

Irrespective to COPD, FEV1 may be affected by asthma, restrictive airway disease, infections and some other paranchymal diseases of the lungs. Although we did not included these conditions, but inclusion of a number of

patients with subclinical disease could not be ignored. However; the confounding effect of conditions mentioned by Dr Jabbari should be minimal or non-significant because, the distribution of these conditions are expected to be similar across different levels of vitamin D Furthermore, the population of our study were derived from the same source and are expected to have similar disease characteristics with unique distribution. Therefore, the possible confounding effects are believed to affect all patients with different levels of vitamin D similarly and so the results should not be affected.

Jabbari et al suspected of confounding effects of smoking, vitamin D binding globulin protein (VDBP), and polymorphism. It does not seem that VDBP, or polymorphism has additional effects beyond vitamin D deficiency. Smoking in itself is an important etiologic factor of COPD which affect airways and more than 70% of our study populations were smokers. Similarly, genetic polymorphism in vitamin D binding proteins affects pulmonary airways by mechanisms of deficiency.

A direct or indirect effect of calcium on airway patency has not been shown yet. Jabbari et al, are concern about restoration of serum vitamin D levels in COPD without performing clinical trial. Whereas, normalization of serum vitamin D in any subjects particularly in patients with COPD does not require clinical trial. We should treat all suspected patients blindly; even healthy individuals with vitam D deficiency should be treated without any delay. Serum 25-OHD should be raised to 30 ng/ml or higher irrespective to FEV1status.

Correction of vitamin D in COPD is not limited to lung butc involve several extra pulmonary system including bone and muscle. Vitamin D in patients with COPD increases muscle strength, improves bone mass and decreases the risk of bone fractures (1). The results of our study are in consistent with earlier publication. Despite, many studies which have addressed the relationship between serum vitamin D and pulmonary function this issue requires further studies.

Additionally, we conducted a clinical trial to determine the efficacy of vitamin D supplementation on FEV1 in patients with COPD (unpublished data). In this study, mean decline from baseline in FEV1 among vitamin D treated patients was significantly lower compared with the control group who did not receive vitamin D. Our study should a beneficial effect of vitamin D treatment in COPD and suggest earlier diagnosis as well as treatment of vitamin D deficient COPD. Nevertheless, these findings should be confirmed by further prospective clinical trials.

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