

Vitamin D Status And Parathyroid Hormone In Albanians

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Abstract: Vitamin D is a fat soluble organic compound, acting like a hormone and playing a crucial role in calcium homeostasis in the human body. Both vitamin D and parathyroid hormone are essential in calcium metabolism. This paper aims the assessment of the current situation of vitamin D status and parathyroid hormone in Albanians, during the period of time from 2009 to 2014. All the individuals involved in this study were taken under examination through blood sampling (10 ml/person) to check for the present value of vitamin D and PTH as well as other parameters, such as calcium, phosphate, etc. PTH and vitamin D levels were measured by electrochemiluminescence immunoassay, while total calcium and phosphate values were measured by Turbidimetry method on Coobas 6000 system. The values of 25(OH) D and PTH were correlated with age, gender and electrolytes. From the results, we notice a high prevalence of vitamin D insufficiency in the group with primary hyperparathyroidism (18.15±8.75 ng/ml), low levels of vitamin D in the group with secondary hyperparathyroidism (15.71±4.45 ng/ml) and in the group with hypoparathyroidism (15.83±9.31 ng/ml). We noticed also a negative correlation between 25(OH) D and PTH levels. In conclusion, we can say that, from this study, it is noticed a high prevalence of vitamin D deficiency in Albanians, and we can recommend regular blood tests at a certain age, in order to prevent other diseases linked to low levels or insufficiency of vitamin D.

Keywords: 25-(OH)₂-D Vitamin, Parathyroids, PTH, Hypoparathyroidism, Hyperparathyroidism

Introduction

Vitamin D is a fat soluble organic compound, acting like a hormone and playing a crucial role in calcium homeostasis in the human body. Vitamin D and PTH level affect directly the calcium concentration in serum and in the extracellular level. Calcium homeostasis is largely regulated through an integrated hormonal system that controls calcium transport in the gut, kidney, and bone. It involves two major calcium-regulating hormones and their receptors—PTH and the PTH receptor (PTHR) (Potts JT, Gardella TJ, 2007) and 1,25(OH)₂D and the vitamin D receptor (VDR) (Jurutka PW., et al 2001)—as well as serum ionized calcium and the calcium-sensing receptor (CaR) (Brown EM., 2007). The increased PTH also stimulates the kidney to increase secretion of 1,25(OH)₂D, which activates the VDR in gut to increase calcium absorption, in the parathyroid glands to decrease PTH secretion, and in bone to increase resorption (Peacock M., 2010).

Regarding the vitamin D, the major source of it, is the skin synthesis, contributing to more than 90% of vitamin D serum concentration (Bellavia D., 2016). The precursors of vitamin D in the body are also very important, so diet plays a key role to vitamin D level too. Fortified foods or vitamin D supplementation is considered also. There are many studies about what is considered normal and abnormal vitamin D concentration, vitamin D deficiency, insufficiency, normality or increased.

Although there is a variation of the ideal values to establish adequate levels of vitamin D, many experts agree that levels of 25(OH)D below 20 ng/mL are classified as deficient, levels between 20 and 29 ng/mL as

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insufficiency, and those between 30 and 100 ng/mL as sufficiency (Maeda S. S., 2014; Yanoff L. B., et al 2006). Chronic vitamin D inadequacy in adults can result in compensatory hyperparathyroidism, leading to increased bone turnover, enhanced bone loss, and increased risk of fragility fracture (Guilsun K. et al, 2012). It has also been reported that serum 25(OH)D levels decline with age earlier in women than in men and less efficiently prevent compensatory hyperparathyroidism in older adults (Dawson-Hughes B., et al 2005). In this study, we assessed and analyzed the current situation of vitamin D status and parathyroid hormone in Albanians, as well as calcium and phosphates, in the role of the two main electrolytes affecting directly the PTH and vitamin D concentration as a result of the bifunctional mechanism of calcium and PTH homeostasis. Our focus was the albanian population, including patients with parathyroid problems and the healthy population, represented by the control group.

Method

A group of 969 individuals was enrolled in this study during the period of time from 2009 to 2014. 500 individuals were representing the control group, which was chosen randomly. 290 individuals were diagnosed with primary hyperparathyroidism, 115 individuals were dialysis patients suffering from secondary hyperparathyroidism and 64 individuals were diagnosed with hypoparathyroidism. All details of the clinical and biochemical parameters of these patients were recorded. A 10 ml fasting blood sample was collected for the determination of 25-hydroxyvitamin D, PTH, total serum calcium and inorganic phosphates in serum. Serum concentration of 25(OH) D and PTH were measured by the Electrochemiluminescence immunoassay and serum calcium and inorganic phosphate were measured by colorimetric methods on Coobas 6000 system. The reference values of vitamin D, used in this study are as follows: <20 ng/ml (deficiency), 20-29 ng/ml (insufficiency), 30-100 ng/ml (sufficiency) and >100 ng/ml (increased). The reference value of PTH was from 15-65 mg/dl (normal), the reference value for serum calcium, was 8.6-10.2 mg/dl and for serum phosphate it was 2.6-4.5 mg/dl.

Datas were expressed as mean±standard deviation and median. Statistical analysis is done using the nonparametric test of Spearman correlation. Significance level was set for the values of $p < 0.000$.

Results and Discussion

The focus of our study was the Albanian population. We have included the healthy population (represented by the control group) and a group of individuals diagnosed with different parathyroid problems, such as: primary hyperparathyroidism, secondary hyperparathyroidism and hypoparathyroidism. The first group, control group is represented by 500 "healthy" individuals; the second group is represented by 405 individuals with hyperparathyroidism, of whom 290 with primary hyperparathyroidism and 115 dialysis patients diagnosed with secondary hyperparathyroidism. The fourth group is represented by 64 patients with hypoparathyroidism.

Control Group

78 individuals from the control group (15.6%), have resulted with primary hyperparathyroidism problems and 9 individuals (1.8%), with hypoparathyroidism. PTH values within this group range from 3.16 mg/dl to 206 mg/dl. The average value of PTH in the subgroup with increased PTH levels is 82.12 (± 23.98) mg/dl, while for the subgroup with low PTH level is 8.03 (± 3.74) mg/dl. Calcium in the subgroup with increased PTH reaches the values from 7.91 to 12.1 mg/dl, with an average value of 9.62 (± 0.78) mg/dl.

Regarding vitamin D concentration, we noticed that in the group with low PTH value, the values range from 13 to 48.8 ng/ml, with an average value of 19.02 (± 11.28) ng/ml, while in the group with increased PTH, vitamin D has a range of 7.8-35.4 ng/ml, with an average value of 20.96 (± 5.49) ng/ml. Considering the reference values of vitamin D, concentrations lower than 30 ng/ml are considered insufficient. In many recent studies, various authors find that the concentration of vitamin D in the serum is insufficient at levels lower than 30 ng/ml (Arnold J. et al., 2007; Dawson-Hughes B et al 2005).

From the examination of the control group, we noticed that parathyroid problems are present in the asymptomatic population and their diagnosis is randomly performed during routine analyzes. This is also seen in studies conducted in other countries, highlighting the large number of randomly diagnosed cases during routine analysis.

Parathyroid Problems Group

In this group with parathyroid problems, we analysed three main groups, suffering from primary hyperparathyroidism, secondary parathyroidism and hypoparathyroidism. There is a strong correlation as we will see between parathyroid problems, PTH and vitamin D concentration in these groups.

A total number of 290 individuals suffering with primary hyperparathyroidism, was observed and evaluated for PTH and vitamin D levels. Analysis of PTH, resulted in very high values, ranging from 60.51 to 1845 pg/ml and an average of 272.23 (± 330.289). On the other hand analysis of vitamin D, resulted in low levels of vitamin D with an average of 18.15 (± 8.75) ng/ml, ranging from 3.56 to 39.10 ng/ml. Low levels of phosphates in the blood and high levels of calcium are present in this group. The age of these individuals varies from 18 to 85 years old, with an average of 46.7 (± 10.97). Most of these individuals are presented to the physician with bone disorders, in 75-80% of cases, fatigue and weakness, as well as muscle pain in 65-70% of cases. Other problems faced in these individuals are nephrocalcinosis in 14% of cases and renal calculi in 42% of cases.

Analyzing the distribution of PTH values, we noticed a higher frequency for PTH values from 60.5 pg/ml to 200 pg/ml. These individuals manifest the first signs of hyperparathyroidism. Most of them manifest high calcium values and normal PTH levels, or vice versa with high levels of PTH and normal calcium concentration, which is explained with two different stages of the disease development, as well as with the bifunctional calcium relationship, where calcium and PTH interact to regulate each other's concentration (Arnold J. et al., 2007).

Vitamin D concentration, is higher in this group compared to a group characterized by secondary hyperparathyroidism or hypoparathyroidism. It is explained with the certain relationship of parathyroid hormone and vitamin D, where PTH promotes the maturation of vitamin D and its conversion into biologically active form, in the proximal tubule of nephrons. The main function of vitamin D, is to increase calcium absorption from the intestine, through interaction with vitamin D receptor (VDR), expressed in the distal as well as in the proximal intestine (Veldurthy V. et al 2016).

Taking into consideration the age groups, most of the cases, (116 cases, of which 80 are female and 36 males) suffering from primary hyperparathyroidism problems are encountered in the age group from 40-50 years old. In this study and other studies also, it is observed that women in this group of age, are almost twice affected compared to the men of the same age (G. Pryia et al 2008, Dina M Elaraj, MD Orlo H Clark, MD, 2008, Ghada El et al., 2012).

The correlation between variables: PTH level, sex, age, calcium level, phosphorus level and vitamin D level is expressed by Spearman correlation coefficient, which indicates a highly significant correlation between PTH level and calcium, phosphorus, vitamin D, age ($p < 0.01$) and sex ($p < 0.05$). There is a poor correlation between PTH level and vitamin D concentration ($r = -0.275$, $p < 0.000$), which confirms that with the increase in PTH level there is a decrease in vitamin D concentration. It is theoretically expected that the high levels of PTH will affect and stimulate the maturation of vitamin D in the kidney. There is an exceptions to the case when primary hyperparathyroidism has not been treated for a long time and nephrocalcinosis or renal calculi, gradually lead to chronic renal failure, a condition which subsequently leads to vitamin D deficiency in these individuals due to the dysfunction of this mechanism. Results comparable to those of our work were also obtained from other studies performed on primary hyperparathyroidism and its relation to vitamin D (Ghada El. et al 2013; Shoni J.S. 2013).

In the group with secondary hyperparathyroidism, the level of vitamin D, due to chronic renal impairment comes down to 4.65 (a value considered absent) up to 34.20 ng/mL with an average value of 15.72 (± 4.454) ng/ml, which, according to some studies, is considered inadequate (Arnold J. et al., 2007).

The chronic renal impairment function, on the other hand, causes these patients to be hypocalcemic in most cases. In these individuals, the low level of vitamin D has a direct impact on the reduction of serum calcium (Arnold et al., 2007; Malberti F. et al 1999). Reduced vitamin D levels also decrease the absorption of calcium into the intestine.

Received data show a modest correlation between PTH level and vitamin D concentration ($r = -0.479$, $p < 0.01$), which proves that PTH level increase is associated with decreased vitamin D. Possibly this is caused by the decrease of the activity of the α -1 hydroxylase enzyme in the kidney, which is responsible for the maturation of vitamin D in the kidneys.

In the group with hypoparathyroidism, the low values up to the absence of PTH (from 0.50 to 14.98 pg/ml, with an average value of 9.52 (± 4.03)), are associated with hypocalcemia, with an average of serum calcium of 7.28 (± 0.60) mg/dl, hyperphosphatemia, with mean serum phosphates of 5.04 (1.03) mg/dl and low vitamin D levels, average 15.8 (± 9.31) ng/ml. Taking into consideration the total number of cases diagnosed with hypoparathyroidism in this study, we notice that women are more affected than men, 36 in total compared to males 28 in total.

Mostly, these individuals visit the doctor due to a variety of symptoms, like weakness and different neuromuscular disorders such as: muscular cramps, tremors and muscular spasms, mainly as a result of hypocalcemia. After measuring PTH concentration in the serum of all these individuals, it resulted in low PTH values below 15 mg/dl.

The correlation between PTH, calcium, phosphorus and vitamin D in the group of individuals with secondary hyperparathyroidism, expressed by the Pearson correlation coefficient, indicates a highly significant correlation between these parameters. We found a modest correlation between PTH level and vitamin D concentrations ($r = 0.494$, $p = 0.000$), indicating that increased PTH levels are associated with increased vitamin D concentration. This as a result of the direct impact of PTH on α -1 hydroxylase enzyme activity in the kidneys.

Significant correlation exist between the vitamin D level and the calcium level ($r = 0.520$, $p = 0.000$), which proves that increased vitamin D concentration, causes the increase of calcium in serum.

We found also a poor correlation ($r = -0.313$, $p < 0.05$) between increased vitamin D level and low phosphorus concentration. It can happen due to the insufficiency of PTH, which increases the excretion of kidney phosphorus but also due to the low concentration (insufficiency) of vitamin D, which stimulates the absorption of phosphorus from the nephrons.

Insufficiency of vitamin D results more problematic in secondary hyperparathyroidism and hypoparathyroidism compared with primary hyperparathyroidism. In secondary hyperparathyroidism it comes as a result of the chronic fall in renal function and in the hypoparathyroidism group it is a result of PTH insufficiency. According to other studies, there is a high prevalence of vitamin D deficiency in other populations around the globe, including countries with a sunny environment (Ning Z. et al 2016., Cashman K. D. 2016., Holick M. F. and Chen T. C., 2008).

Conclusion

This study demonstrated a high vitamin D insufficiency level in the group with parathyroid problems as well as in the control group. We found parathyroid problems even in the control group, accompanied by low levels of vitamin D or insufficiency and high levels of PTH and more rarely low levels of PTH. Insufficiency of vitamin D and high values of PTH are characteristic for primary hyperparathyroidism, accompanied by hypercalcemia and hypophosphatemia in general. Low levels of vitamin D and very high values of PTH (10-100 times higher than the reference value) characterize secondary hyperparathyroidism. Hypocalcemia and hyperphosphatemia must be considered too in this group. There are met low levels of vitamin D, low levels of PTH, hypocalcemia and high levels of phosphates in hypoparathyroidism also. The clinical spectrum of individuals with parathyroid problems varies between the subgroups involved in the study, but also within the group depending on their age or their life style.

Recommendations

We recommend regular blood tests, in order to prevent parathyroid problems and other diseases linked to low levels or insufficiency of vitamin D.

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