ORIGINAL ARTICLE

Relationship between Serum Level of Vitamin D in patients with BPH compared to healthy people in age group over 45

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ABSTRACT

Background: men older in neoplasm benign common most the is Hyperplasia Prostate Benign. the to According play candeficiencyD vitamin that seems it men, Iranian older in Hyperplasia Prostate Benign of prevalence high .BPH of development the in role important an

Materials and Methods: This study was performed as a case control atKamkarArabnia Educational and Medical Hospital, Qom in 2018. In this study, participants were divided into 2 groups of people with BPH and the control group (healthy people). All these people were tested for vitamin D by HPLC and their results were analyzed.

Results: The average age of the patients with BPH and in the control group was 67and 57 years, respectively. Most of the participants had free jobs (n= 77, 47.8%). 101 out of the 161 (62.7%) were underdiploma. 153 out of the 161 (95%) were urban. 89 out of the 161 (55.3%) had no underlying disease and 72 out of the 161 (44.7%) had underlying disease. 89 out of the 161 (55.3%) were smokers. Eighty patients (49.7% of total participants) had BPH. Although there was no significant relationship between smoking and BPH in the participants, however there was a significant association between serum levels of vitamin D and BPH in the subjects (P = 0.001). Most people with BPH had a freelance job, but no statistically significant association was found between job status and BPH (P = 0.92). In addition, there was no significant relationship between BPH and education level of individuals (P= 0.412).

Conclusion: According to the results of the present study, it can be concluded that there is a significant association between vitamin D level and prostate volume. Therefore, it is recommendedthat patients with BPH be tested for vitamin D levels and if needed vitamin D supplements be prescribed.

Keywords: Hyperplasia Prostate Benign, Vitamin D.

INTRODUCTION

Benign Prostate Hyperplasia (BPH) is the most common benign neoplasm and a chronic disease whichoften occursin the in older men. Histological prevalence in autopsy is 50% in men between the ages of 50-60 and 90% in men over 80 years old[1]. This disease is considered as a complex and multifactorial disease from a scientific and pathophysiological point of view. According to AUA guidelines, the incidence of BPH has raised public health concerns worldwide, especially in Asian countries[2]. BPH can cause LUTS (lower urinary track symptoms) associated with benign enlargement of the prostate, leading to obstruction of bladder output[3]. BPH causes excessive protein synthesis of stromal and epithelial cells in the prostate due to complex cellular changes, including changes in proliferation, differentiation, apoptosis, and aging[4]. Many epidemiological studies have been conducted around the world over the past few decades, but the prevalence of clinical BPH is difficult to determine. There is evidence that indicates vitamin D may play a role in the progression of BPH symptoms. Vitamin D_3 as a form of vitamin D and some of its analogues can be used as strong regulators of cell growth and prostate cell differentiation[5]). Sincethe vitamin D_3 binds to vitamin D receptor (VDR, which is a nuclear receptor, it modulates a variety of biological functions[6]. Vitamin D is produced in the skin by enzymatic changes in cholesterol after exposure to ultraviolet B radiation. 1α, 25-Dihydroxyvitamin D3 (1, 25 (OH) 2D3), the active form of vitamin D in the kidneys, is produced by hydroxylation its precursor, 25-hydroxyvitamin D3 (25 (OH) D3) and has animportant role in hemostasisof calcium and bone regeneration [7].

Biological effects of 1, 25 (OH) 2D3 are expressed by its receptor (vitamin D receptor (VDR)), which the VDR gene is located on chromosome 12 in humans[8]. In previous studies, multiple polymorphisms in the VDR gene, as well as the importance of its function and potential effects on disease susceptibility, have been investigated[9]. The expression of VDR is beneficial in various types of inflammatory and chronic diseases, on the other hand, recent epidemiological studies have reported that autoimmune disorders are associated with low serum levels of 25 (OH) D_3[10]. Since the super-physiological doses of 1 α, 25 (OH) $2D_3$ may cause hypercalcemia, vitamin D analogues are available to enhance the anti-inflammatory properties of VDR agonists[11]. In addition to bones, intestines, and kidneys, VDR is expressed in many other tissues, including the prostate and bladder[12]. Multiple genes with a VDR response directly or indirectly affect the cell cycle, proliferation, differentiation, and apoptosis, and the polytrophic effects are greater than its traditional role in calcium homeostasis[13].

The presence of VDR in the human prostate was first reported in 1992[14]. Subsequent studies have shown that VDR was found in a variety of stromal and epithelial cells, normal cells, cancer cells, and BPH, and its presence was confirmed in prostate cancer cells[15]. According to Immunohistochemical data, there is a significant difference in the amount of VDR in patients' prostate samples[16]. Calcitriol has been shown to increase the level of VDR

protein in the prostate, possibly by stabilizing the VDR ligand by destroying the proteasome[17]. Vitamin D metabolites prevent the growth of normal and malignant prostate cells[18]. The balance between planned cell death and cell proliferation suggests that prostate growth is regulated by both androgens and growth factors in coordination with several other factors. Changes in the molecular mechanisms of these two processes can lead to BPH due to abnormal prostate growth. Therapeutic approaches to BPH management can be broadly divided into anti-adrenergic and anti-androgenic therapies[19]. α1-adrenoceptor antagonists of and α5-reductase inhibitors are suitable treatment strategies for BPH. However, long-term use of these drugs can lead to unpleasant side effects. Due to the deficiency of preventive medications for asymptomatic BPH, which inhibits the progression of LUTS, new treatments have shifted more toward static molecules, including metabolic factors such as hexokinase inhibitors, growth factors (vitamin D3 analogues), and treatments based on Gi agonists. VDR agonists appear to be suitable for reducing symptoms compared to prostate volume reduction in BPH[20]. Elocalcitol is an artificial derivative of vitamin D_3 that regulates cell proliferation and apoptosis. Previous reports have shown that BPH cell proliferation associated with cancer cells and suppressed by elocalcitolis more than finasteride (5 α -reductase inhibitor).

In a study, elocalcitol reduced the prostate volume significantly in patients with BPH compared with the placebo group[21]. Calcitriol has the potential to treat BPH and prostate cancer. Therefore, calcitriol analogues possibly maintainantiproliferative properties but do not cause hypercalcemia side effects in vivo[22]. VDR has emerged as a vital factor in BPH whose autocrine functions are very different from its classical performance in mineral homeostasis. Therefore, ignoring the potential impact of VDR is effective in the mortality of patients with BPH. In general, vitamin D or its analogues may have the best effects as chemotherapeutic agents in BPH. Studies in animal models also show that vitamin D agonists are effective in prevention before the initial onset of BPH. Based on the evidence presented, we believe that vitamin D and its analogues are evaluated in clinical trials of BPH patients with different stages of the disease. Finally, combination therapy with 1α, 25(OH) $2D_3$compounds should be considered for better and more effective treatment of BPH. These observations emphasized on the need for better awareness among researchers, physicians, and patients of high prevalence of vitamin D disability and further screening for vitamin D / VDR, especially among high-risk populations such as elderly patients and patients with BPH. The aim of this study was to determine the serum level of vitamin D in patients with BPH in comparison with healthy individuals in the age group over 45 years in Kamkar Arabnia Educational and Medical Center at Qom in 2018.

MATERIALS AND METHODS

This study was conducted as a case control study between individuals with BPH and healthy people (control) in the age group over 45 years at Kamkar Arabnia Educational and Medical Center during the quarterly period in 2018.According to the following formula, the number of samples in each group was 71. The amount of standard deviation of vitamin D in prostate patients and healthy individuals as well as the accuracy of the experiment were considered according to a similar study by Caretta et al[29].

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 (S_1^2 + S_2^2)}{d^2}$$

$\alpha = 0.05$

$\beta = 0.2$

$S_1 = 22.8,$

$S_2 = 14.6$

$d = 9$

In this study the sampling method was available sampling. The data collection tool was a researcher-made checklist. After approving the proposal in the Research Council of the Faculty of Medicine and after obtaining the code of ethics for this study, the researcher referred to Kamkar Medical Education Center and after the necessary coordination, started sampling. Then, after sampling of the studied individuals and after obtaining conscious consent of the patients, the individuals were divided into two groups of patients (people with BPH) and control (healthy people) and the matching of individuals was based on the age of the patients. Then, serum levels of vitamin D were measured in all of these individuals and the results were included in the checklist. The criteria for entering to this study included men over the age of 45 years old, consent to study, no underlying diseases such as kidney problems, liver problems, vitamin D malabsorption, malignancy, hyperparathyroidism, osteogenic and osteoprotective diseases, as well as those without the prostate cancer. Exit criteria in this study can be mentioned as follows: dissatisfaction with participating in the study and the existence of any factor that affects the amount of serum levels of vitamin D. All questionnaires used in the study were anonymous and identified by code. The results of the diagnostic tests were communicated to the patients.

Statistical analysis: Quantitative variables were described using mean and standard deviation and qualitative variables were described using absolute and relative frequency. T-test was usedto compare quantitative data in two groups and chi-square or fisher test was used for qualitative variables. Pearson correlation test was used to investigate the relationship between quantitative variables. Data analysis was performed using SPSS statistical software version 22. Significant levels were considered below 0.05.

RESULTS

The results of this study showed that the medianage in the group with BPH and in the control group was 67 and 57 years, respectively. There was a significant relationship between the two groups (P= 0.045). In the evaluation of the job status of the participants in this study, most of the participants had free jobs 77(47.8%). 101 out of the 161(62.7%) were under diploma. 153 out of the 161(95%)

were urban. 89 out of the 161(55.3%) had no underlying disease and 72 out of the 161(44.7%) had underlying disease. 89 out of the 161(55.3%) were smokers. 80 patients (49.7% of total participants) had BPH. There was no significant relationship between smoking and BPH in the individuals under study.

Table 1: The relationship between smoking and BPH

		BPH		Total	P value
		Yes	No		
Cigarette	Yes	41	48	89	0.307
	No	39	33	72	
Total		80	81	161	

As shown in table 1, there was no significant relationship between smoking and BPH in the individualsof this study (P=0.307).

Table 2: The relationship between the level of vitamin D and BPH

	BPH	N	Mean	SD	P value
Vitamin D	Yes	80	25.18	17.32	0.001
	No	81	34.51	18.21	

Table2, show that there was a significant relationship between vitamin D levels and BPH in the patients with BPHand healthy people (P=0.001).

Table 3: Relationship between BPH and people's occupation

		Job				Total	P value
		Freelance	Employee	Worker	Unemployed		
BPH	Yes	38	22	15	5	80	0.92
	No	39	20	18	4	81	
Total		77	42	33	9	161	

This table indicate that most people with BPH had a freelance job (n=38) and no statistically significant association was found between the job and BPH (P = 0.92).

Table 4: The relationship between BPH and literacy level (education)

		Education level			Total	P value
		Undergraduate	Diploma	Higher diploma		
BPH	Yes	52	23	5	80	
	No	49	22	10	81	0.412
Total		101	45	15	161	

As can be seen in the table above, there was no significant relationship between BPH and the education level of individuals (P = 0.412).

DISCUSSION

In terms of job status, most of the participantsin this research had free lance job 77(47.8%). 101 out of the 161(62.7%) were undergraduates. 153 out of the 161(95%) were urban. 89 out of the 161(55.3%) had no underlying disease and 72 out of the 161(44.7%) had underlying disease. 89 out of the 161(55.3%) were smokers. 80 out of the 161(49.7%) had BPH. There was no significant relationship between smoking and BPH in the subjects. There was a significant relationship between vitamin D levels and BPH in the individuals.Zhang et al. (2016) in a case control study using 322 Chinese menevaluated the prostate volume and urine flow by transrectal ultrasound and urinary flowmetry, respectively. Two hundred and thirty-one (71%) were defined as vitamin D deficiency.The vitamin D deficiency group had a significantly higher prostate volume. This study suggests that vitamin D deficiency may be a marker of BPH. Thus, it may be used as a future therapeutic target in patients with BPH[23].

In another study, Haghsheno et al. (2013) studied the relationship between vitamin D levels, sex hormones, globulin binding to sex hormones, albumin related to calcium and the level of lipid in people with BPH.Results indicated that the mean volume of prostate was 40ml which this volume affected by 4 factors. These factors to increase the prostate volume were: vitamin D deficiency, serum level of calcium, globulin bindingto sex hormones, increased density of cholesterol and body lipoprotein mass[24]. Pauletta et al (2014), considering that vitamin D deficiency and prostate cancer in black men are more common than other people,they reported that by increasing vitamin D supplementation, there was no significant difference in free and total PSA levels. Therefore, vitamin D treatment cannot have a significant effect on changes in free PSA and total in serum[25,26]. A study by Murphy et al. (2016) examined the relationship between vitamin D and prostate volume. They concluded that serum levels of 25(OH) Dwere inversely and significantly related to increase the prostate volume and size, especially in men with BPH. Therefore, this study suggests that the need to use of vitamin D supplements in these people can be further investigated[27] .Espinosa et al. (2013) stated that BPH is due to the overgrowth of stromal and epithelial cells in the prostate. Their study indicated that increase vitamin D intake by diet and supplements is associated with a reduction in the prevalence of BPH. Vitamin D analogues up to 6,000 IU per day can reduce prostate volume in patients with BPH. The authors report that vitamin D can reduce the prostate volume in people with BPH, and vitamin D deficiency in serum can be directly correlatedwith the prevalence of BPH[28].

CONCLUSION

Based on the results of our study and the findings of other studies, it can be concluded that there is a significant relationship between vitamin D levels and its relationship with prostate volume in patients. Therefore, it is recommended that for patients with BPH, the serum level of vitamin D should be checked and if needed vitamin D supplementation should be prescribed.

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