ORIGINAL RESEARCH

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SEASONAL VITAMIN D VARIATIONS IN OSTEOPOROSIS PATIENTS

Objective: To study the seasonal variations of 25(OH) vit D in patients with osteoporosis.

Materials and methods. We observed 396 patients diagnosed with osteoporosis/osteopenia aged 24 to 93 years. The diagnosis of OP was based on the clinical recommendations of Osteoporosis-2021 approved by the Ministry of Health of the Russian Federation. All patients underwent dual-energy X-ray absorptiometry using the Lunar DPX apparatus. Vitamin 25(OH)D3 levels were determined using the commercial 25-OH Vitamin D ELISA kit. For statistical data processing, the software packages "STATISTICA 10.0 for Windows" were used.

Results. We have found that during the year most patients have significant seasonal changes in the 25(OH) vit D level. The minimum value was recorded in January and December (respectively, 50.85 and 55.83 nmol/l). We found significant differences in the concentration of 25(OH) vit D between patients who were observed in June and patients who were examined in the remaining months ($p<0.001$); as well as between patients examined in August and patients observed in the spring months ($p<0.05$). Similar significance was observed between July and April ($p=0.037$). It was found that the highest percentage of patients with vitamin D deficiency was observed in April and reached 16.67%. In the period from June to September, the frequency of hypovitaminosis was significantly lower and amounted to 1.92–3.7%. It was found that with increasing age of patients there is a gradual decrease in the level of 25(OH) vit D blood ($r = - 0.099$, $p = 0.049$).

Findings. Based on the data obtained, it is recommended to carry out the prevention of vitamin D deficiency for the population of the Volgograd region. Prevention should be carried out from September to May, in accordance with international recommendations. These recommendations are especially relevant for older people.

Keywords: vitamin D, osteoporosis, cholecalciferol, vitamin D.

Introduction. Currently, there are many publications in the scientific medical literature on the possible role of vitamin D metabolic disorders in various human pathologies [1, 2, 3, 5, 9]. Vitamin D3 (cholecalciferol) is a key player in human bone metabolism [7]. It is generally accepted that the required amount of the vitamin is synthesized by skin cells under the influence of UV rays. Later, cholecalciferol is hydroxylated in the liver, followed by the formation of 25(OH) D3 - calcidiol, which is a deposited and transport form of the vitamin. The tendency to study only one metabolite, 25(OH) vit D, is due to the fact that it is associated with indicators that reflect the state of the bone tissue. An analysis of the associations of serum vitamin D metabolites with bone mineral density (BMD) showed that only 25(OH) vit D was associated with higher BMD [6].

In many countries of the world, vitamin D deficiency is widespread, determined by the level of 25(OH) vit D less than 75 nmol/l, sometimes reaching values below 50 nmol/l [7]. This problem also exists in Russia, which is confirmed by various studies that have been carried out throughout the country. Worldwide, there is vitamin D deficiency in all age groups.

Osteoporosis (OP) is a metabolic disease of the skeleton, which is characterized by a decrease in bone mass, a violation of the microarchitectonics of bone tissue, which can lead to an increase in bone fragility, and, as a result, fractures with minor injuries [4]. All over the world there is a trend towards an increase in the incidence of fractures associated with osteoporosis, this is especially true for older people [4, 8, 10].

Considering the important protective role of vitamin D, it is important to study seasonal fluctuations in the level of vitamin D in blood serum in order to optimize schemes for the prevention of deficiency of this factor.

Objective: study the seasonal fluctuation of 25(OH) vit D in patients with osteoporosis.

Materials and methods. We observed 396 patients diagnosed with OP/osteopenia aged 24 to 93 years, of which 376 (94.95%) women and 20 (5.05%) men. The study lasted from January to December 2017 inclusive. The patients were examined at the Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborowski". All patients lived in the Volgograd region. The diagnosis of OP was based on the clinical recommendations of Osteoporosis-2021 approved by the Ministry of Health of the Russian Federation. There were 245 patients with a history of fractures, 151 without fractures. All patients underwent dual-energy x-ray absorptiometry using the Lunar DPX apparatus. Vitamin 25(OH)D3 levels were determined using the commercial 25-OH Vitamin D ELISA kit. Statistical data processing was carried out using software packages "STATISTICA 10.0 for Windows." Using the standard deviation (σ), we determined how much the 25(OH) vit D values deviated on average from the average in each month. Significance of differences between groups were compared by methods of variation statistics (ANOVA). The results were considered statistically significant at $p<0.05$.

Results. We have found that most patients have significant seasonal changes in 25(OH) vit D during the year. The maximum average values of the level of 25(OH) vit D were observed in residents of the Volgograd region in June (90.38 nmol/l), and the minimum value was recorded in January and December (respectively, 50.85 and 55.83 nmol/l). The results are shown in table 1.

We compared the significance of differences in the level of 25(OH) vit D depending on the month in which the patients were examined. The results are presented in table 2.

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Table 1

Variation in 25(OH) vit D depending on the month

Month	Number of observations	Mean 25(OH) vit D (μ)	Standard deviation 25(OH) vit D (σ)
January	10	50.85	10.56
February	16	65.55	32.25
March	54	57.02	27.67
April	36	53.51	37.18
May	49	57.71	34.18
June	43	90.38	56.65
July	48	69.71	30.93
August	52	73.89	37.97
September	27	70.53	24.97
October	19	65.94	18.95
November	34	67.59	34.18
December	8	55.83	16.3
Total	396	66.58	36.44

From the data presented in Table 2, it can be seen that there were significant differences in the concentration of 25(OH) vit D between patients who were observed in June and patients who were examined in the remaining months ($p<0.001$); as well as between patients examined in August and patients observed in the spring months ($p<0.05$). Similar significance was observed between July and April ($p=0.037$).

In order to identify the number of patients in need of drug prevention of hypovitaminosis D, we calculated the number of patients with vitamin D deficiency.

Although January and December have the lowest mean 25(OH) vit D values, there were no patients deficient in that month (table 3).

From the data presented in Table 2, it can be seen that the highest percentage of patients with vitamin D deficiency was observed in April and reached 16.67%. In the period from June to September, the frequency of hypovitaminosis was significantly lower and amounted to 1.92–3.7%.

We also studied the relationship of 25(OH) vit D with gender and age of patients. We found that with increasing age of patients, there is a gradual decrease in the level of 25(OH) vit D in the blood ($r = - 0.099$, $p = 0.049$), see Figure 1.

We did not find significant differences between the sex of patients and the value of vitamin D (the level of 25(OH) vit D in men 62.1 ± σ, in women 66.8 ± σ).

We have studied the relationship between the level of 25(OH) vit D and the presence of bone fractures. The results are presented in table 4.

Table 4 shows that there are no significant differences in the level of 25(OH)

Table 2

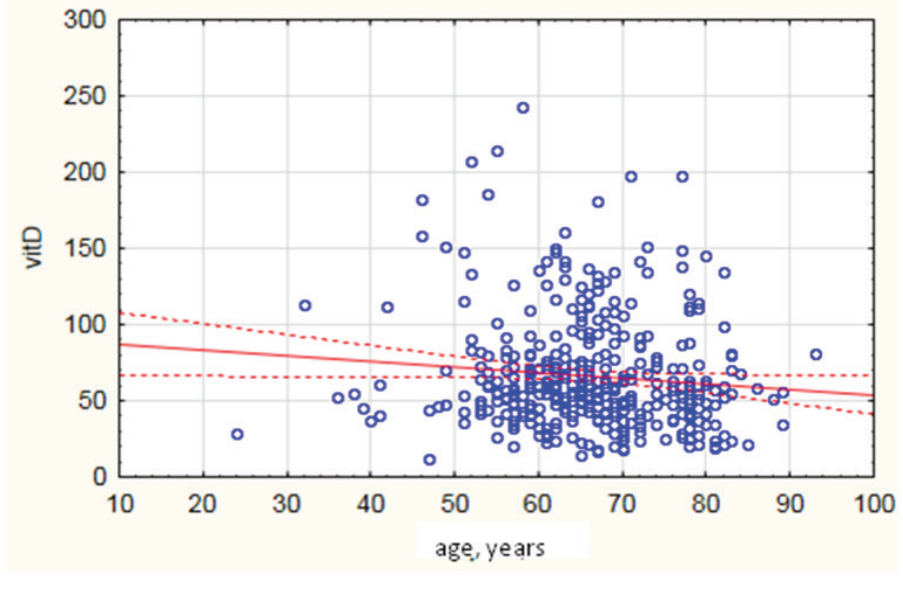
Reliability of differences in the level of 25(OH) vit D among residents of the Volgograd region, depending on the month of the survey

Month	January	Febrjuary	March	April	May	June	July	August	September	October	November	December
January (n=10)		0.302	0.611	0.833	0.575	**0.001**	0.124	0.059	0.132	0.274	0.187	0.766
Febrjuary (n=16)	0.302		0.396	0.256	0.440	**0.016**	0.682	0.409	0.654	0.974	0.848	0.525
March (n=54)	0.611	0.396		0.643	0.921	**<0.001**	0.070	**0.014**	0.105	0.344	0.171	0.928
April (n=36)	0.833	0.256	0.643		0.587	**<0.001**	**0.037**	**0.008**	0.058	0.214	0.095	0.866
May (n=49)	0.575	0.440	0.921	0.587		**<0.001**	0.094	**0.021**	0.130	0.388	0.210	0.889
June (n=43)	**0.001**	**0.016**	**<0.001**	**<0.001**	**<0.001**		**0.005**	**0.023**	**0.022**	**0.012**	**0.005**	**0.011**
July (n=48)	0.124	0.682	0.070	**0.037**	0.094	**0.005**		0.555	0.923	0.693	0.788	0.303
August (n=52)	0.059	0.409	**0.014**	**0.008**	**0.021**	**0.023**	0.555		0.688	0.401	0.419	0.178
September (n=27)	0.132	0.654	0.105	0.058	0.130	**0.022**	0.923	0.688		0.664	0.746	0.301
October (n=19)	0.274	0.974	0.344	0.214	0.388	**0.012**	0.693	0.401	0.664		0.869	0.497
November (n=34)	0.187	0.848	0.171	0.095	0.210	**0.005**	0.788	0.419	0.746	0.869		0.396
December (n=8)	0.766	0.525	0.928	0.866	0.889	**0.011**	0.303	0.178	0.301	0.497	0.396	

Table 3

The number of patients with vitamin D deficiency depending on the month of observation

Month	Total Patients	Number of patients with vitamin D deficiency	Percentage of patients with vitamin D deficiency
January	10	0	0.00
February	16	2	12.50
March	54	3	5.56
April	36	6	16.67
May	49	6	12.24
June	43	1	2.33
July	48	1	2.08
August	52	1	1.92
September	27	1	3.70
October	19	1	5.26
November	34	1	2.94
December	8	0	0.00
Total	396	23	



Correlation between patient age and 25(OH) vit D levels

Table 4

Significance of differences between patients with a history of fractures and vitamin D levels

In patients with a history of	n	25(OH) vit D (nmol/l)		Reliability
		M	σ	
Persons with a history of fracture	245	67.85	39.39	F=0.043 p= 0.834
No fracture history	151	65.80	34.55	

vit D depending on the presence of bone fractures. These results may be explained by the fact that some patients received medical treatment, including calcium and vitamin D supplements.

Findings. According to the literature, 25(OH) vit D deficiency is currently a pandemic that affects virtually all age groups. We have identified significant seasonal fluctuations in 25(OH) vit D in the examined group of patients. With the help of statistical methods of analysis, the influence of the seasonal factor on the level of 25(OH) vit D was proved. Despite the southern geographic location and the high level of insolation in the summer months, according to the data obtained, we can conclude that there is a lack of vitamin D among residents who live in the Volgograd region.

Note that there were no statistically significant differences between the average values of vitamin D levels in the summer months, accompanied by high solar activity (July-August) and the average values in the autumn months (September-November). Perhaps this fact is explained by the short time spent outdoors on hot summer days, which does not contribute to sufficient production of endogenous 25(OH)D3.

In our opinion, when choosing how aggressive and preventive therapy tactics should be in patients with OP in order to compensate for a possible vitamin D deficiency, several facts should be taken into account. Firstly, practitioners do not in all cases have the opportunity to examine the level of cholecalciferol, and even more so to track it in dynamics (for example, due to financial reasons). Secondly, patients with OP are, for the most part, elderly patients, which means they have a high comorbidity. Given the huge role of vitamin D deficiency in the development and progression of a number of cardiological, rheumatological, bronchopulmonary and other diseases, in our opinion, patients with OP need earlier preventive therapy. Without laboratory confirmation of the normal content of vitamin D, relying only on the presence of sufficient insolation (summer months), it is unacceptable to draw conclusions about the sufficient level of vitamin D in patients with OP.

Based on the results, it is recommended to carry out the prevention of vitamin D deficiency for the population of the Volgograd region. Prevention should be carried out from September to May, in accordance with international recommendations. These recommendations are especially relevant for older people.

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DIFFERENTIAL INFORMATIVENESS OF SERUM ONCOMARKERS FOR DETECTION OF RARE FORMS OF UTERINE BODY CANCER

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Aim. The aim of the study was to conduct a comparative analysis of the preoperative level of the concentration of tumor markers CA-125, HE4 and DJ-1 in the blood serum in endometrial and non-endometrial cancer of the uterine body.

Materials and methods. 249 patients with endometrial carcinoma (EC), 33 patients with serous (SC) and 24 patients with clear cell carcinoma (CCC) of the uterine body of stages II-IV according to FIGO were examined. Prior to the start of specialized antitumor treatment, the concentration of CA-125, HE4 and DJ-1 proteins was determined in blood serum by enzyme immunoassay.

Results. In patients with EC, SC and CCC the blood levels of CA-125 and HE4 tumor markers were elevated relative to the reference normal range, but did not differ significantly between the groups (p>0,05). A comparative analysis showed that a statistically significant difference between the groups was found only for the DJ-1 marker. In patients with EC, the mean blood level of DJ-1 corresponded to 521,4±12,8 pg/ml and in rare forms of uterine body cancer it was higher. With CCC the concentration DJ-1 was 984,2±19,2 pg/ml and in SC – 998,5±23,7 pg/ml.

Conclusion. For the differential diagnosis of endometrial and non-endometrial cancer of the body of the uterus, preoperative measurement of the concentration of DJ-1 in the blood is informative.

Key words: uterine body cancer, endometrial carcinoma, serous uterine body cancer, clear cell uterine body cancer, tumor markers.

Introduction. In the practice of oncologists, the determination of serum levels of tumor markers CA-125 (Cancer Antigen-125) and HE4 is used in the screening and prognosis of uterine cancer. An elevated level of CA-125 before surgery is accompanied by a poor prognosis for patients with endometrial carcinoma, which requires a higher frequency of postoperative examination of patients [6]. The HE4 (Human epididymis protein 4) marker is highly sensitive and specific in detecting early forms of endometrial cancer; its level has been correlated with the lethality of patients with poorly differentiated RTM [5]. In recent years, there has been encouraging information about the promise of protein deglycase DJ-1, also known as PARK7 (Parkinson's disease-associated protein 7), for the diagnosis of uterine cancer. DJ-1 is a multifunctional protein that activates proliferative cell processes and plays an important role in the pathogenesis and progression of cancer by modulating the tumor suppressor PTEN. The association of the level of DJ-1 in the blood with the course of the disease is associated by the authors with an increase in the expression of genes encoding this