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Serum vitamin D concentrations among 609 patients of Endocrine Outpatient Clinic – preliminary report

Ocena zaopatrzenia w witaminę D 609 pacjentów Poradni Endokrynologicznej – doniesienie wstępne

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Summary

Introduction. Only scarce data have been published regarding serum vitamin D status in adult population in Poland. The preliminary results of the retrospective assessment of vitamin D status in adult patients of our outpatient Clinic, based on records from the databases of Central Laboratory, Bielański Hospital are presented.

Material and methods. From the database of the Central Laboratory of Bielański Hospital, Warsaw, we selected 908 records of serum 25OHD measurements made in years 2007-2009 for the 609 normocalcemic patients: men and women, in wide range of age.

Results. The mean vitamin D concentration was 19.86 ± 16.08 ng/ml in the whole examined population. Vitamin D levels above 30 ng/ml were found only in 52 patient (8.54% of subjects). Vitamin D insufficiency (20-30 ng/ml) was found in 23.8%, moderate vitamin D deficiency (10-20 ng/ml) was found in 44.9%, and overt hypovitaminosis D (> 10 ng/ml) in 21.8% of subjects. Vitamin D concentrations was highest in the younger patients, significantly higher in group < 50 years vs. > 70 years of age (adequately 18.43 ± 10.31 ng/ml vs. 15.93 ± 9.00 ng/ml, $p = 0.02$). A linear regression analysis shown a slight significant association between age and serum vitamin D concentrations. Serum 25OHD concentrations in fractured patients was found to be significantly lower than in non-fractured subjects. In patients taking several OTS preparations of vitamin D, the serum levels of 25OHD after 6-18 months of such as treatment did not differ significantly from basal results and still were low.

Conclusions. The prevalence of low vitamin D concentration in Poland is very high and is associated with aging. Uncontrolled vitamin D supplementation from OTS sources (dietary supplements, multivitamins) is not effective.

Key words: vitamin D, age, fractures

Streszczenie

Wstęp. Jedynie pojedyncze publikacje oceniają stężenie witaminy D u osób dorosłych w Polsce. Przedstawiono wstępne wyniki retrospektywnego badania oceniającego stan zaopatrzenia w witaminę D u pacjentów Poradni Endokrynologicznej przy Klinice Endokrynologii CMKP w Warszawie, oparte o archiwalne wyniki oznaczeń 25OHD w surowicy pochodzące z laboratoryjnej bazy danych Laboratorium Centralnego Szpitala Bielańskiego w Warszawie.

Materiał i metody. Analizowano 908 wyników oznaczeń 25OHD w surowicy wykonanych w latach 2007-2009 u 609 pacjentów z normokalcemią, mężczyzn i kobiet, w szerokim przedziale wieku.

Wyniki. W badanej populacji średnie stężenie witaminy D wynosiło $19,86 \pm 16,08$ ng/ml. Stężenie witaminy powyżej 30 ng/ml stwierdzono jedynie u 52 osób (8,54% badanych). Niewielki niedobór witaminy D (20-30 ng/ml) stwierdzono u 23,8%, umiarkowany niedobór (10-20 ng/ml) u 44,9%, zaś jawną hipowitaminozę D (> 10 ng/ml) u 21,8% badanych. Stężenia witaminy D były wyższe u młodszych pacjentów, znamienne pomiędzy grupą wiekową poniżej 50 roku i powyżej 70 r.ż. (odpowiednio $18,43 \pm 10,31$ ng/ml vs. $15,93 \pm 9,00$ ng/ml, $p = 0,02$). Wykazano słabą, jednak znamienne odwrotną korelację pomiędzy wiekiem a stężeniem witaminy D. U osób po przebytych złamaniach osteoporotycznych stężenia 25OHD były znamienne niższe, niż u osób bez złamań. Stosowanie dostępnych bez recepty preparatów zawierających witaminę D nie powodowało po 6-18 miesiącach wzrostu stężenia 25OHD w surowicy.

Wnioski. Częstość występowania niedoboru witaminy D w Polsce jest bardzo wysoka i wiąże się z postępowaniem wieku. Stosowanie powszechnie dostępnych preparatów zawierających witaminę D (suplementy diety, multiwitaminy) nie powoduje istotnej poprawy zaopatrzenia w 25OHD.

Słowa kluczowe: witamina D, wiek, złamania

INTRODUCTION

Once supplementation in vitamin D started to be common and rickets appeared to have been conquered, many health care professionals thought the major health problems resulting from vitamin D deficiency had been resolved. However, rickets can be considered the tip of the vitamin D – deficiency iceberg. In fact, vitamin D deficiency remains common in children and adults. Vitamin D deficiency in adults can precipitate or exacerbate osteopenia and osteoporosis, cause osteomalacia and muscle weakness, and increase the risk of fracture. However, in the past several years, attention has turned to nonskeletal effects of vitamin D insufficiency, particularly in relation to cardiovascular disease, diabetes mellitus, cancer, and immune dysfunction. Vitamin D deficiency could also increase mortality. These and other consequences of vitamin D inadequacy may result in poorer public health (1).

Although there is no consensus on optimal levels of 25-hydroxyvitamin D (25OHD) as measured in serum, vitamin D deficiency is defined by most experts as a serum 25OHD level of less than 20 ng/ml (50 nmol/L). A level of 25OHD of 21 to 29 ng per milliliter (52 to 72 nmol/L) can be considered as a relative insufficiency of vitamin D, and a level of 30 ng/ml or greater can be considered to indicate sufficient vitamin D (2, 3). With the use of such definitions, it has been estimated that 1 billion people worldwide have vitamin D deficiency or insufficiency (1). According to several studies, 40 to 100% of U.S. and European elderly men and women still living in the community (not in nursing homes) are deficient in vitamin D (4-8).

Data on serum vitamin D concentration in the Polish population are scarce. The only available findings were derived from the MORE (Multiple Outcomes of Raloxifene Evaluation) study. The study showed that in 12.5% of women vitamin D concentration was lower than 10 ng/ml, and in 45.4% it was between 10 and 20 ng/ml (9). Therefore, vitamin D deficiency was found in almost 60% of the examined women. In 2009 Napiórkowska et al. in 274 randomly selected Warsaw women aged 60-90 years found the mean 25OHD concentration of 13.6 ng/ml in the whole examined population. Moreover, vitamin D levels above 30 ng/ml were detected only in 4% of subjects (10).

In August, 2013 we started to assess retrospectively vitamin D status in adult, normocalcemic patients of our outpatient Clinic, based on records from the databases of Central Laboratory, Bielański Hospital (supported in years 2007-2010 by dr. med. Teresa Fryda Laboratorium Medyczne Sp. z o. o.; and in years 2011-2013 by Diagnostyka Sp. z o. o.). Detailed questionnaire was

developed to collect information about subjects general health conditions, medications, and previous fractures. Here we present the very preliminary results of this study, concerning vitamin D concentration.

MATERIAL AND METHODS

From the database of the Central Laboratory of Bielański Hospital, Warsaw, we selected 908 records of serum 25OHD measurements made in years 2007-2009 for the 609 normocalcemic patients of the our outpatient Clinic (mainly Thyroid Diseases Unit and Osteoporosis Unit). In 132 patients, serum 25OHD measurements were repeated at least twice. Patients were next identified by their national identification number (pol. *Powszechny Elektroniczny System Ewidencji Ludności – PESEL*) and detailed information about their health status, including vitamin D supplementation, fractures, cardiovascular events and metabolic disorders was collected by telephone interviews, based on previously developed questionnaire. Up to today, data from 232 patients were collected.

A serum 25-hydroxyvitamin D concentration was assessed by a chemiluminescence immunoassay, by an automated method on the Elecsys 2010 apparatus (Roche Diagnostics, Mannheim, Germany; intra-assay precision 1.5-4.1%, interassay precision 2.6-6.5%). Other biochemical parameters in blood were assessed using routine laboratory methods.

Statistical was performed using STATISTICA software (StatSoft Inc., Tulsa, United States). Analysis of variance (Kruskal-Wallis ANOVA) was used primarily to compare data between age groups. Linear regression analysis was performed to assess independent associations between vitamin D levels and age.

RESULTS

The presented preliminary analysis comprised 609 women and men (mean age 53.03 ± 18.16 years, median age 55.00 years, range 18-85 years). The population was divided into 3 groups: under 50 years, 50-70 years and over 70 years of age.

Serum vitamin D concentrations in the examined population are shown in figure 1. The mean serum concentration was 19.86 ± 16.08 ng/ml (range 3.53-63.6 ng/ml). Adequate vitamin D status, defined as serum 25OHD concentration higher than 30 ng/ml, was detected only in 52 patient (8.54% of subjects). Vitamin D insufficiency (20-30 ng/ml) was found in 23.8%, moderate vitamin D deficiency (10-20 ng/ml) was found in 44.9%, and overt hypovitaminosis D (> 10 ng/ml) in 21.8% of subjects.

Vitamin D concentrations was highest in the younger patients, significantly higher in group < 50 years vs.

> 70 years of age (respectively 18.43 ± 10.31 ng/ml vs. 15.93 ± 9.00 ng/ml, $p = 0.02$), as shown in figure 2. A linear regression analysis shown a slight but significant inverse association between age and serum vitamin D concentrations (fig. 3).

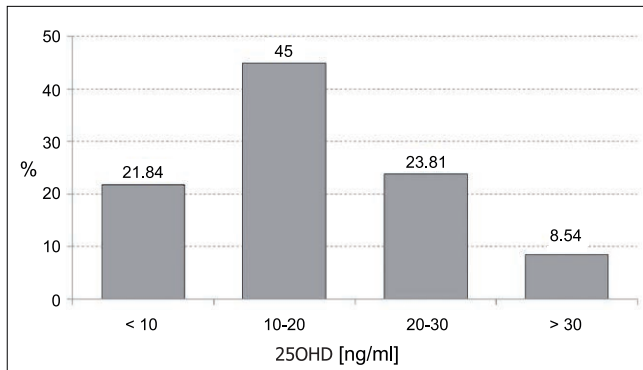


Fig. 1. Prevalence of vitamin D adequacy, insufficiency and deficiency in examined population.

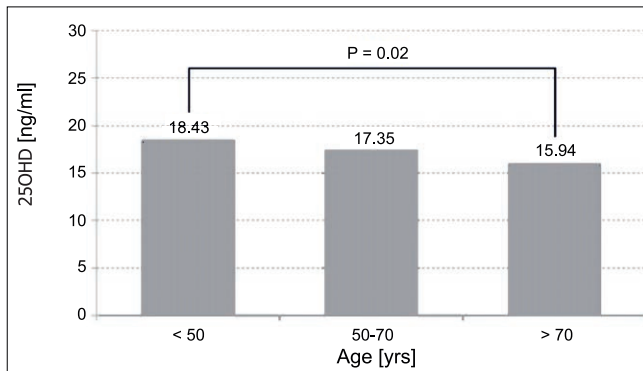


Fig. 2. Mean vitamin D concentration in age groups.

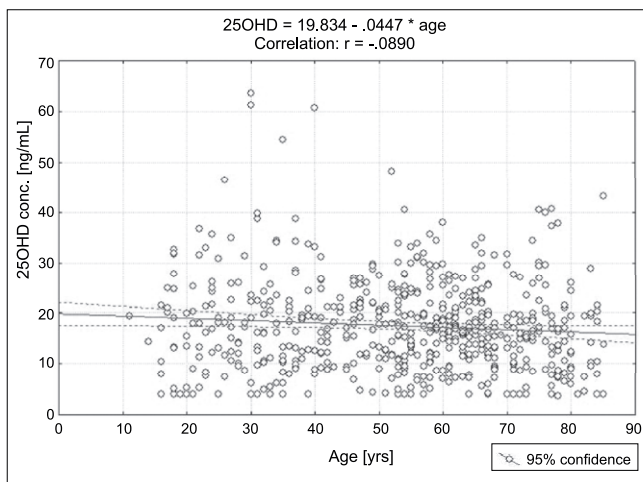


Fig. 3. Correlation between age and serum vitamin D concentration.

Fractures

In 232 interviewed patients, 75 subjects reported previous low-trauma fracture(s). Serum 25OHD concentrations in fractured patients was found to be significantly lower than in non-fractured subjects (15.49 ± 9.60 ng/ml vs. 18.11 ± 8.81 ng/ml respective-

ly, $p = 0.04$). However, these difference was significant only in patients aged 50-70 years (14.88 ± 7.36 ng/ml vs. 18.28 ± 8.21 ng/ml, $p = 0.03$) (tab. 1).

Table 1. Mean 25OHD in fractured vs non-fractured patients.

Age (yrs)	N	Fractured	N	Non-fractured	P
		mean \pm SD		mean \pm SD	
< 50	19	17.98 \pm 12.96	56	18.71 \pm 9.36	NS
50-70	39	14.89 \pm 7.37	65	18.38 \pm 8.21	0.03
> 70	16	14.20 \pm 10.22	34	17.01 \pm 9.27	NS
Total	74	15.49 \pm 9.60	155	18.11 \pm 8.82	0.04

Effect of supplementation

132 from 232 interviewed patients reported to be treated with various vitamin D supplements (mainly as multivitamin preparations, alimentary supplements or OTC – calcium/vitamin D preparations) after the first 25OHD measurement reflecting vitamin D insufficiency or deficiency. In this patients, after 6 months to 18 months of the treatment, the mean vitamin D concentration, was 19.51 ± 15.19 ng/ml and did not differ from basal values.

DISCUSSION

Mean serum vitamin D concentration in the examined population was low. It was similar to the mean 25OHD concentration for 152 Polis women aged 65 years or older, who participated in the MORE study (21 ng/ml) (9), and higher than the mean concentration found in 274 Warsaw random women by Napiórkowska et al. (10). This difference may be caused, at least in part, by the fact that in our study the blood samples were taken in all year, while in the study they were also collected in winter. Therefore, the prevalence of vitamin D deficiency that has been shown in this study may more accurately reflect the actual value observed in the general population in Poland.

We have found a weak, however significant inverse association between age and vitamin D concentrations. Such correlation was observed in some other studies (11, 12), whose authors also have observed an inverse relationship between vitamin D and age.

The lower concentrations of vitamin D found in previously fractured patient are in agreement with many former reports, indicating the low vitamin D status as a modest risk factor for osteoporotic (especially hip) fracture (13-16). The association between serum 25OHD and hip fracture (as the main outcome) has been studied in three prospective studies from the US: the NHANES III (17), the MrOS study in men (18), and the Women’s Health Initiative (19), the latter being the largest prospective study we are aware of with vitamin D status in blood determined at baseline and hip fracture as outcome, including 400 cases. They observed a statistically significant trend of increasing risk of hip fracture through decreasing quartiles of 25OHD. Of the interest is our founding, that this difference was significant for the age group 50-70 years, but not significant in the oldest (> 70 years) age group. It may reflects the role of vitamin D deficiency in the development of low bone strength in early period of osteoporosis.

Much more important are data of inadequacy of uncontrolled vitamin D supplementation from OTS sources. In patients taking several OTS preparations of vitamin D, the serum levels of 25OHD after 6-18 months of such as treatment did not differ significantly from basal results and still were low. In various studies, more than 50% of postmenopausal women taking medication for osteoporosis had suboptimal levels of 25-hydroxyvitamin D – below 30 ng per milliliter (75 nmol per liter) (8, 20). There is a growing evidence of the bad quality of vitamin D supplements as well as multivitamin compounds. Neither US Food and Drug Administration (FDA), nor EMEA or any local pharmaceutical authorities does not regulate vitamin D supplements, so their potency may not be well evaluated. In a recent trial examining vitamin D in menopausal women, there was found that compounded vitamin D₃ (cholecalciferol) supplements varied significantly in potency. Only one-third of studied compounded calcium/vitamin D pills met US Pharmacopeial (USP) Convention standards, which require that compounded pills contain 90 to 110% of the active ingredient (21). This variability in compounded cholecalciferol pills led authors to additionally investigate over-the-counter (OTC) cholecalciferol pills, in which they also found significant variability. Its also

worth to say about generally very poor adherence to uncontrolled, OTC regimens of treatment. In consequence, it seems rationale to prescribe only those preparations of vitamin D, registered as drugs, and carefully monitor the effects on serum 25OHD levels.

The main limitation of our study is the fact that the examined population did not fulfill criteria for representativeness of the population and is far from rigorous rules of random, epidemiological trial. Most of patients referred to our Osteoporosis Unit for some reasons: back pains, x-ray suspicion of osteoporosis or osteoporotic fractures, and some patients of Thyroid Diseases Unit suffered from thyrotoxicosis. However, the vast majority was observed in fact for neutral goiter. Therefore, the prevalence of vitamin D deficiency observed in our study probably reflects the true figure for the general population more accurately than the results from studies on only osteoporotic women.

CONCLUSIONS

In conclusion, it can be stated that the prevalence of low vitamin D concentration in Poland is very high. Lower vitamin D levels are associated with aging. Uncontrolled vitamin D supplementation from OTS sources (dietary supplements, multivitamins) is not effective.

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