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Seasonal variation in vitamin D levels in patients attending in Basic Healthcare Center

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Summary
Background: Previous reports have shown a high prevalence of vitamin D deficiency among different populations in our country. However fewer longitudinal studies about seasonal changes in serum vitamin D have been published. The aim of the present study was to determine seasonal variation in serum vitamin D in patients attending in Basic Healthcare Center.

Patients and method. Prospective longitudinal cohort study of 82 patients attending in Basic Healthcare Center. In all cases, serum levels of calcium, 25OHD and PTH were determined during January, February and March (Period 1) and September and October (Period 2).

Results: Serum calcium levels did not differ between Period 1 and Period 2. During Period 1, 50.6% presented 25OHD levels < 15 ng/ml and 3.65% presented 25OHD levels > 30 ng/ml. During Period 2, 25OHD levels increased (31.88 vs 15.75 ng/ml, p < 0.001). Prevalence of patients with 25OHD levels < 15 ng/ml decreased (2.7 vs 50.6%, p < 0.001) and prevalence of patients with 25OHD levels > 30 ng/ml increased (50.68 vs 3.65%, p< 0.001). Negative correlation between 25OHD and PTH concentrations during both periods was observed.

Conclusions: These results show vitamin D deficiency during winter months in the majority of patients attending in Basic Healthcare Center. The prevalence of patients with vitamin D deficiency decreased after summer, however only half of the patients reached optimal vitamin D levels. Based on our results, to guarantee optimum vitamin D levels in the general population, the promotion of sanitary policies is recommended.

Key words: vitamin D deficiency, secondary hyperparathyroidism, sunlight.
Introduction
At the end of the 1930s the chemical structure of vitamin D was described. Humans obtain vitamin D naturally through the diet and by exposure to the sun. Ultraviolet B solar radiation penetrates the skin and converts 7-dehydrocholesterol into previtamin D3, which is rapidly transformed into vitamin D3. The vitamin D3 in the skin, and that originating from the diet, are metabolised in the liver into 25-hydroxy-vitamin D–25(OH)D–which determines the best index for the evaluation of vitamin D reserves in the organism. The 25(OH)D is metabolised in the kidneys by the action of the enzyme 25-hydroxy-vitamin D–1 α–hydroxylase into its active form, 1,25-dihydroxy-vitamin D–1,25(OH)2D–

In recent decades there has been a notable increase in the understanding of the role of vitamin D in the pathology of some diseases, and it has been confirmed that its deficit is extraordinarily common in many sections of the population, which has led some to suggest an almost “epidemic” character to this deficiency. In addition, the confirmation of the presence of vitamin D receptors in numerous tissues and cells of the organism suggests that vitamin D may play a role in the pathology of various cardiovascular and autoimmune diseases.

The estimated prevalence of vitamin D deficiency in the general population of the US is 96%. In Europe, where, differently from the US, only a few foods are enriched with vitamin D, the general population would have a higher risk of suffering this deficiency, in the region of around 40%, with a lower prevalence in the Scandinavian countries, while the estimated prevalence in other continents varies between 30% and 94%.

In those studies published in our country, the prevalence varies between 30% and 70% for independent people of an advanced age, and is even higher (70-100%) in people who are institutionalised or with multiple pathologies. In other sectors of the population, such as postmenopausal women, patients with bone fractures, and individuals with risk of osteoporosis, the prevalence varies between 39 and 70%. Lastly, studies in the young healthy population show different degrees of vitamin D deficit with a prevalence which varies between 27 and 50%.

Exposure to sun plays a fundamental role in vitamin D concentrations. Various studies show significant differences in the values of 25(OH)D according to the season of the year in which the determination of the concentration of vitamin D was carried out.

In our country, most of the works concerning vitamin D deficiency previously published are transversal, and study this deficiency in certain sectors of the population, such as institutionalised older people, postmenopausal women or patients with osteoarticular pathology. While, on the other hand, studies carried out in a healthy population, of prospective and longitudinal design, are scarce. The objective of this work was to understand the influence of exposure to sun, according to the season of the year, on blood concentrations of vitamin D in a cohort of subjects being treated at a primary healthcare clinic.

Material and method

Design and ambit
Observational, analytical, longitudinal and prospective study of a cohort of mobile adults aged between 18 and 80 years, treated at a primary healthcare clinic of the Orcasitas Health Centre pertaining to the Primary Care Area 11 of Madrid, over two periods: Period 1, in the months of January, February and March, and Period 2, in the months of September and October.

Sample and inclusion criteria
The minimum sample size, according to an α risk of 5%, an absolute precision of 10%, an expected proportion of 0.25 and 10% of losses, was 77 people for each group, who were selected by simple random sampling. Pregnant women, subjects with limited mobility, patients with chronic systemic diseases (nephropathies, hepatopathies, neoplastic disease and malabsorption syndromes) endocrinopathies (thyroid, parathyroid and suprarenal disease) and/or in treatment with drugs which affect calcium metabolism, such as vitamin D, bisphosphonates, calcitonin, calcium supplements, multivitamins, glucocorticoids, theophylline, lithium, diuretics, statins, anti-convulsives, isoniazide or oral anticoagulants.

The participants were informed of the objectives of the study, gave their verbal consent in all cases and the approval of the Ethics and Research Committee of the Primary Healthcare Area 11 region was given. With the aim of avoiding the influence of variables other than seasonal exposure to sun, the subjects received instructions not to modify their dietary habits or their normal degree of exposure to sun during the period of the study.

Biochemical determinations
Venous blood samples were extracted, in fasting, for the biochemical study. The following determinations were carried out: haemogram, basic biochemistry, total calcium, phosphorus, calcium corrected according to blood albumin, albumin, magnesium, thyrotropin (TSH), intact parathyroid hormone (PTH) and 25(OH)D.

The figures for calcemia were corrected according to the albuminemia with the following formula: total calcemia + [0.8 (4 – total albuminemia)].

The concentrations of 25(OH)D were quantified by chemiluminescent immunoanalysis with the Immulite 2000 autoanalyser (reference values 14 – 75 ng/ml), with intra-trial and extra-trial coefficients of variation of 3% and 4.6% respectively. The concentrations of intact PTH were measured by chemiluminescent immunoanalysis, with the Immulite 2000 autoanalyser (Siemens) (reference values 7 – 57 pg/ml) with intra-trial and extra-trial coefficients of variation of 4.1% and 5.9% respectively.
Definition of vitamin D deficit
The cut off point was established at 15 ng/ml in our study, according to earlier publications which showed an increase in the values of PTH in subjects with concentrations of 25(OH)D equal to or less than this value. The optimum level of vitamin D was established at values of 25(OH)D higher than 30 ng/ml.

Statistical analysis
The quantitative continuous variables are expressed as the mean, with the confidence interval (CI) at 95%, and qualitative variables as relative frequencies or percentages.

To compare the qualitative variables between the two periods the Student’s t test was used for paired data and the chi-squared test for qualitative variables.

To study the relationship between variables the Pearson correlation coefficient was used.

In all cases the test was considered to be statistically significant when p < 0.05. The statistical study was carried out using a social science statistics software package (SPSS 9.0.1).

Results
In Period 1 82 subjects were included, 52% women, with an average age of 54.93 years (CI 95%: 50.94 – 58.91). The average concentrations of corrected calcium, 25(OH)D and PTH are shown in Table 1. 50.6% of the subjects showed values of 25(OH)D lower than 15 ng/ml, and 2.4% values of PTH above the upper limit of the normal range.

In Period 2 73 subjects were included (9.88% losses compared with Period 1), 52.3% women with an average age of 53.89 years (CI 95%: 51.37 – 57.20). The values of corrected calcium were similar to those obtained in Period 1. A significant increase was seen in the values of 25(OH)D compared with Period 1, along with a decrease in the percentage of subjects with values lower than 15 ng/ml. The percentage of subjects with values of 25(OH)D higher than 30 ng/ml was increased significantly during Period 2 (50.68% vs 3.65%, p<0.001). The values of PTH in Period 2 fell significantly (Table 1). In both periods there was a significant inverse correlation between the values of PTH and those of 25(OH)D (Figures 1 and 2).

Discussion
The results of our study show that more than half of the population treated at a primary healthcare clinic had vitamin D deficiency during the winter months. While there are different classifications of the degrees of hypovitaminosis D, in our study we established vitamin D deficiency as being a concentration of 25(OH)D equal to or less than 15 ng/ml, the value above which a compensatory secretion of PTH is initiated. Given this cut off point, the prevalence of vitamin D deficit of our population is higher than that described in our country in a population at risk of osteoporosis and in women of a fertile age, and lower than that in a group of postmenopausal women from a rheumatology clinic. However, the use of other criteria for vitamin D deficiency, the absence of a
precise definition of the season in which the samples were taken, and the presence of pathologies and circumstances which predispose a person to vitamin D deficiency in these earlier works, are circumstances which limit comparison with our results.

Although, obviously, the prevalence of vitamin D deficit recorded in our study cannot be extrapolated to the general population, it approximates to that outlined in McKenna’s review, in which more than 40% of adults from western and central Europe had vitamin D deficiency during the winter months.

The exposure of the skin to sunlight represents the most important source of vitamin D (80-100% of requirements). Since the 1970s, the annual cyclical variation in blood concentrations of 25(OH)D, has been known, reaching maximum values in the final phases of the summer and minimum values in the winter. In parallel, bone mass falls during autumn and winter, while it improves or remains stable during the spring and summer.

The concentrations of 25(OH)D in the patients in our study determined during the months of September and October were double those obtained in the period January – March, with the prevalence vitamin D deficit dropping from 50% in the winter months to less than 3% at the end of the summer. Although various studies published in our country show the seasonal influence on values of vitamin D, our work highlights the magnitude of the change of status in vitamin D which happens after the summer months, similar to that in other longitudinal studies carried out in different European countries and in different states of North America.

The drop in concentrations of vitamin D and the subsequent reduction in blood levels of ionised calcium, detected by calcium sensors in the parathyroid glands, triggers an increase in the expression, synthesis and secretion of PTH. Hence, PTH values constitute a highly sensitive indicator of vitamin D deficit, increases in this hormone being caused even in situations of moderate deficiency. In addition, some studies have shown that the increase in concentrations of PTH bears a closer relationship to bone mineral density than that measured by the concentration of vitamin D, especially in older people, in whom secondary hyperparathyroidism is a determining factor in bone fragility. The negative correlation found between PTH and 25(OH)D in both periods of our study, the fall in concentrations of PTH and of the percentage of patients with blood PTH higher than the upper limit for normality recorded in the post-summer period confirm the improvement in vitamin D status in our population by the end of the summer months.

Exposure to sunlight is responsible for the maintenance of adequate levels of vitamin D in most of the world’s population. However, numerous circumstances may modify the cutaneous production of vitamin D. In addition to the seasonal changes already referred to, variations in latitude, daily hours of sunlight and the period of exposure to the sun, the area of the skin’s surface exposed to the sun, the type of skin and the person’s race, the percentage of body fat, and even the use of different types of clothes for cultural or religious reasons in individuals in the same zone, are factors which may alter considerably the synthesis of vitamin D. On the other hand, the intake of foods, natural, or artificially enriched, with a high vitamin D content, contributes moderately to the status of vitamin D in most of the countries studied.

The results of our work show that after the summer months, the values of 25(OH)D of the population studied doubled, reducing the percen-
tage of patients with vitamin D deficit and secondary hyperparathyroidism, changes undoubtedly related to the increase in the cutaneous synthesis of vitamin D due to a greater exposure to sunlight. However, in our study the influences of aforementioned factors which may modify the production of vitamin D, were not analysed, and neither were the variations in dietary intake of vitamin D which might have happened during the period of observation, facts which constitute limitations to our work. Although before embarking on the study the subjects received instructions not to change their dietary habits or their degree of normal exposure to sunlight, the possibility cannot be entirely discounted that some variations in these variables may have contributed to the change in status of vitamin D observed at the end of the summer. In fact, an observational study similar to ours did record spontaneous increases in the ingestion of vitamin D and calcium in the population studied, which contributed to the seasonal changes in bone mass and calcitropic hormones observed.

Even though the overall improvement in vitamin D status recorded after the summer months is notable, it must be highlighted that only half the subjects of our study reached levels of 25(OH)D higher than 30 ng/ml, a level which constitutes an optimum status for vitamin D8, ensuring bone health and prevent vitamin D deficiency during the winter months. Thus, the results of our study confirm the difficulty of achieving an optimum level of vitamin D only by exposure to sun, in accordance with that highlighted by Quesada and Sosa.

The emerging understanding of the involvement of vitamin D deficit in a predisposition to many neoplastic, inflammatory, autoimmune and metabolic diseases, in addition to the unequivocally demonstrated skeletal changes, reinforce the need to achieve an optimum level of vitamin D in the population of our country, which, as in other European populations, has a high prevalence of vitamin D deficit. Only the active promotion of public health policies which strengthen the development of food enriched with vitamin D, and even preventative use of pharmacological supplements of vitamin D, will allow the eradication of a deficiency which is already reaching almost pan
demic proportions.

In conclusion, more than half the patients treated in a primary care health centre had vitamin D deficiency during the winter months, a situation which improves notably by the end of the summer, even though only half of them reach optimum levels which guarantee an adequate vitamin D status. In the light of our results, and in accord with other authors, the promotion of health policies which optimise the nutritional status of vitamin D in the general population of our country would be recommended.

Conflicts of interest: the authors declare that they have no conflicts of interest.

Bibliography