Exploratory Research in Clinical and Social Pharmacy 9 (2023) 100224

Contents lists available at ScienceDirect

Exploratory Research in Clinical and Social Pharmacy

journal homepage: www.elsevier.com/locate/rcsop

Community pharmacy is the key to improving vitamin D levels

F. Lopez-Carmona [a], A. Toro-Ruiz [a], M. Gomez-Guzman [b], M.I. Valverde-Merino [a], C. Piquer-Martinez [a], M.J. Zarzuelo [a,*]

[a] Pharmaceutical Care Research Group CTS-131, Faculty of Pharmacy, University of Granada, Spain
[b] Department of Pharmacology, Faculty of Pharmacy, University of Granada, Spain

ARTICLE INFO

Keywords:
Community pharmacy
Pharmacists
Dietary habits
Vitamin D
Dietary supplementation
Vitamin D deficiency

ABSTRACT

Introduction: Vitamin D is an essential micronutrient that participates in the body's fundamental physiological processes. The pharmacist should involve the patient in his medication adherence, leading to a change in the patient's attitude towards his medication and towards his health problem, in order to achieve the pharmacological objective set.
Methods: Quasi-experimental multicenter study design with non-probabilistic convenience sampling. A pharmacist-led intervention in health education was carried out, divided in two groups, face-to-face interview and on-line survey, and the results were evaluated 3 months later to observe if there was any change in the patient's health status or in their vitamin D levels.
Results: The study was conducted in four pharmacies through face-to-face interviews ($n = 49$ patients) and online surveys ($n = 23$). Pharmaceutical intervention improved habits of exercise (0.81 ± 1.44 days/week face-to-face interviews vs −0.09 ± 2.35 days/week online surveys ($p = 0.048$)). In face-to-face interviews, consumption of vitamin D-rich foods was increased (0.55 unit of tuna/week; $p = 0.035$ and 0.56 unit of avocado/week; $p = 0.001$) and was improved correct intake of vitamin D supplements (32.5% baseline to 69.8% at 3 months). The increase in 25-hydroxyvitamin D levels (11.5 ng/mL after 3 months ($p = 0.021$)) was correlated to salmon consumption (0.951; $p = 0.013$) and the improvement of quality of life was correlated to avocado consumption (1; $p < 0.001$).
Conclusion: There are habits that improve vitamin D production such as increased physical activity, the correct use of vitamin D supplements and the consumption of foods with high vitamin D levels. The role of the pharmacist is crucial, involving the patient in the treatment making aware of the benefits for his/her health status of increasing vitamin D levels.

1. Introduction

Vitamins are a group of essential micronutrients as they participate in fundamental physiological processes of the organism.[1] Vitamin D is a fat-soluble vitamin that is synthesized by ultraviolet B irradiation. Vitamin D is considered not only a vitamin, but also a prohormone implicated in bone mineralization and the functioning of the cardiovascular, endocrine, immune and respiratory systems.[2]

1,25-dihydroxyvitamin D (1,25(OH)2D) is the active form of vitamin D, formed by the action of the mitochondrial enzyme 1α-hydroxylase.[3] Through diet and supplementation, vitamin D has two forms that increase serum concentration 25(OH)D levels: vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol).[4] Vitamin D3 seems to be more effective than vitamin D2 in increasing and maintaining higher serum concentration of 25(OH)D.[5]

The main source of vitamin D is obtained through exposure to sunlight (between 70 and 90% of the total). In the Caucasian population, a daily sun exposure of 15 min on the face and arms is recommended between March and October, with a protection factor between 15 and 30, depending on the latitude and intensity of the radiation. In the elderly population and in patients with osteoporosis, the recommended daily sun exposure should be 30 min.[6] But there are many factors that can prevent the adequate absorption of this prohormone, from enzymatic defects (a field of pharmacogenetic studies in recent years), to the action of drugs such as antituberculosis drugs, or diseases as liver cirrhosis, etc[2]

There is currently some controversy about the optimal values of vitamin D in the body. Historically, the range of 30–75 ng/mL has been accepted as normal values, and values below 20 ng/mL have been considered pathological.[7] Today, scientific societies such as the Institute of Medicine of the USA (IOM), the Scientific Advisory Committee on Nutrition (SACN) and the National Institute for Health and care Excellence (NICE) consider that a concentration close to 20 ng/mL would be adequate to ensure proper bone health; on the other hand, endocrinology societies such as The Endocrine Society of the USA, the Spanish Society of Endocrinology and

* Corresponding author at: Pharmaceutical Care Research Group CTS-131, Campus de Cartuja sn Faculty of Pharmacy, University of Granada, Spain.
E-mail addresses: mgguzman@ugr.es (M. Gomez-Guzman), celiapiquer@correo.ugr.es (C. Piquer-Martinez), mjzarzuelo@ugr.es (M.J. Zarzuelo).

http://dx.doi.org/10.1016/j.rcsop.2023.100224
Received 7 November 2022; Accepted 17 January 2023

Nutrition (SEEN), the World Medical Association (WMA) and the Spanish Society for Bone and Mineral Metabolism Research have established optimal plasma vitamin D levels of ≥ 30 ng/mL.[8,9]

The recommended vitamin D intake has varied considerably over the last decades and is still under debate. In large part, the difference in criteria existing between different societies is due to the target population: general population or patients with special needs. The daily reference intake recommended by the European Union is 600 IU/day.[10] However, there are special situations, both physiological and pathological, in which an extra intake of vitamin D should be considered. The efficiency of vitamin D production by the skin decreases with age. Both intestinal absorption and hepatic hydroxylation are adequate; however, renal 1-α-hydroxylase activity usually decreases with age in parallel with declining renal function.[11] There are also a multitude of drugs that interfere with the absorption and/or metabolism of vitamin D; the most characteristic are carbamazepine, cimetidine, cholestyramine, colestipol, thiazide diuretics, phenytoin, phenobarbital and valproate.[12–16]

The pharmacist's professional practice must be modified to respond to a new social need. Pharmacists must focus their activity on the patient-medicine binomial.[18] From this need, the term pharmaceutical care is born, being the active participation of the pharmacist in assisting the patient in the dispensing and monitoring of a pharmacotherapeutic treatment, thus cooperating with the physician and other health professionals in order to achieve results that improve the patient's quality of life. It also entails the pharmacist's involvement in activities that provide good health and prevent disease.[19,20]

For all these reasons, the pharmacist should not only dispense medication to patients, but should also follow up to evaluate the results of their medication and thus be able to prevent and solve possible associated problems. In addition, the pharmacist, in his integration with the multidisciplinary team together with medicine and nursing, are the main links in a chain where the aim is to involve the patient in his medication, making him participate in the important decisions about his therapy (as long as the arsenal of available drugs allows it).[21,22] This activity substantially improves the patient's medication adherence, thus making it easier to achieve the pharmacological objective set, leading to a change in the patient's attitude towards his medication and, in short, towards his health problem.[23] This ability to generate this change, as well as the analytical capacity of the pharmacist, are the pillars on which we rely to carry out this study.

2. Methods

2.1. Study design

A quasi-experimental multicenter design of non-probabilistic convenience sampling was undertaken in Spanish community pharmacies from four locations (Granada center, Granada costa, Granada rural and Madrid center) for a period of three months (March to June 2022).

The study was divided into two groups:

a) Face-to-face group: four pharmacies were selected in which the pharmacists identified the potential patient beneficiaries, offered the service and provided health education in addition with a survey and supporting material. Three months later, pharmacist met with the patient by telephone to evaluate the new situation.

b) On-line group: the same survey with a short informative video was used in Google Forms® format to reach a larger and more diverse population. A valid email address was required to complete both the baseline and three-month surveys. By this, it was intended to compare the impact of a face-to-face pharmacist's intervention vs an online video-based pharmacist's intervention.

2.2. Survey design

The survey questions were taken from the form of the 2020 version of the "European Health Survey in Spain"[24]; due to the length of this survey, the questions that were most appropriate were selected. In the section on diet, questions were asked concerning the intake of products with high vitamin D content, to evaluate whether this intake could be increased and this would lead to an increase in vitamin D levels and an increase in the quality of life.

The survey initially consisted of 25 questions, including 5 key aspects: sociodemographic characteristics (4 questions), physical activity (4 questions), diet (8 questions), medication (8 questions), and health status (1 question). It was designed to be self-administered, using a language as simple and concise as possible to avoid misinterpretation, and to allow the patient to complete the survey at home or in the pharmacy without feeling pressured, to avoid possible interviewer bias, and to collect data from previous vitamin D tests, if available.

Before finalizing the design, the survey was tested to 6 people of different age ranges to get their opinion about the clarity of the survey concepts. Due to the length of the survey and in order to speed up the completion process, six questions were definitely eliminated, leaving a self-administered questionnaire of 19 items in total, with an average response time of 5 min. Once consensus was reached, the survey design was finalized.

Subsequently, a second survey was designed to be completed at 3 months to assess whether there had been any changes in lifestyle or nutrition habits and whether these changes were significant for vitamin D levels and perception of health status. This survey consisted of the same questions and included a new question to assess the patient's perception of vitamin D deficiency symptomatology at this time; this item was evaluated by the same 6 persons, giving their agreement without objections.

2.3. Supporting material

For the face-to-face interviews, to support the pharmacist's intervention and to ensure a better follow-up of the recommendations, an informative leaflet was designed for the patient to take home and post it on a visible place. The brochure consisted of 5 main recommendations to improve D levels with a brief description of each one. It was designed in warm colors resembling the action of the sun and was written in first person to involve the patient in their habits and in their treatment.

In case of the on-line group, it was initially proposed to link the supporting brochure to the survey so that it could be downloaded and printed by the participants. Due to the low availability of printers and the possible lack of commitment of the study participants, this idea was discarded, and instead an informative 3:25 min video was recorded in which the study leader briefly explained the main recommendations for increasing vitamin D levels. In order to assess the maximum comprehension of the video, it was shown to 4 people of different age ranges and each person was asked a battery of 4 questions, observing that there was a decrease in attention after the first minute and a half of the video. Therefore, the video was redesigned and shortened to 1 min and 25 s, testing again to the four people who got all the answers correct, thus concluding the design of the video.

2.4. Study population

Patients were recruited when the pharmacist detected any of the possible symptoms associated with a vitamin D deficiency.

Patient inclusion criteria were: 14 years of age or older; signature of informed consent and authorization from parent or guardian if applicable; diagnosis of vitamin D deficiency or insufficiency or, failing that, habits and/or symptomatology compatible with vitamin D deficiency or insufficiency; patients treated with drugs that interfere with the absorption and/or metabolism of vitamin D: carbamazepine, cimetidine, cholestyramine, colestipol, thiazide diuretics, phenytoin, phenobarbital and valproate.

The exclusion criteria for patients were: hepatic, biliary, renal or cardiac insufficiency; hypoparathyroidism; kidney stones; patients who do not speak Spanish; patients who cannot read or write Spanish; caregivers or persons in charge of a patient with vitamin D deficiency; patients who do not want to fill out the informed consent form; patients without a valid telephone number/e-mail address.

2.5. Sample size calculation

In the face-to-face group, it was estimated that each pharmacist could take on a recruitment and follow-up of 15 patients, considering a possible loss to follow-up of 20%. Therefore, it was estimated that 60 patients were needed from the 4 pharmacies.

In the online group, it was estimated that it could reach to the same size of face-to-face group.

2.6. Description of the first intervention

Patients with possible vitamin D deficiency were detected during the pharmacist's routine activity by different methods:

- The information on the patient's electronic health card at the time of dispensing.
- After a conversation with the patient in which he/she referred to any of the symptoms associated with vitamin D deficiency.
- After a conversation with the patient in which the pharmacist detected lifestyle habits compatible with vitamin D deficiency.

Once the patient was identified to be at risk of suffering from vitamin D deficiency, each pharmacist offered the possibility of participating in the study; patients who accepted signed the informed consent form.

A different intervention is carried out according to the type of patient detected:

a) Patient already taking vitamin D supplementation: the patient is briefly explained the functions of vitamin D as well as the main ways of obtaining it, with special emphasis on habits in which a deficiency of vitamin D is detected. The patient is also asked how he/she takes vitamin D in order to improve its absorption with the pharmacist's recommendation.

b) Patient who does not take a vitamin D supplement: the patient is explained the functions of vitamin D and the main ways of obtaining it, and the patient's lifestyle/food habits to be improved are emphasized as they may be the cause of a possible deficit of this molecule. The patient is also told about the most frequent symptoms associated with vitamin D deficiency so that he/she may or may not be affected by one or more of them.

Next, each patient was given the survey, which could be filled in the Personalized Care Zone (PCZ) of pharmacy or at home, and the support material, emphasizing that it was very important for them to have this booklet at home in sight most of the time. Also, the pharmacist insisted that the patient should be as sincere as possible, and to remind them to fill in the telephone number field correctly, since within a month they will receive a telephone call to continue with the next part of the study.

In the on-line group, the pharmacist's intervention was carried out through the designed video and later the survey was passed. To ensure that all the people visualized the video, until the was not reproduced, the survey could not be finished and the data could not be sent.

2.7. Follow-up intervention

A month later, for the face-to-face group, the pharmacist in charge was responsible for contacting the study participants by telephone, in chronological order, to complete the second survey, with up to a maximum of four call attempts.

In the on-line group, an e-mail was enabled to contact the participants and send them the second questionnaire. The e-mails were sent in blocks of 10 to avoid entering anti-spam lists and a protocol was established for resending the questionnaires to the participants who had not responded.

2.8. Data collection

On March 2022, all pharmacies were recruited, and pharmacists were duly trained. For the face-to-face group, pharmacies had until April 2022 as deadline to collect the questionnaires and until June 2022 to send them all together to the responsible pharmacist. For the on-line group, the survey was sent to various groups through social networks, Whatsapp® groups, e-mail, Facebook® and Instagram®, starting in March 2022 and collecting the data obtained in June 2022.

2.9. Outcome variables

The outcome variables that were measured and evaluated in the surveys were as follows: Sociodemographic data, Foods with vitamin D, Vitamin D blood levels, Quality of life (measured by means of Visual Analogical Scale), Days of physical exercise, Way of taking vitamin D and vitamin D blood levels, Perception of symptoms associated with vitamin D deficiency.

2.10. Data analysis

Data were analyzed using the software package SPSS statistics (V.26.0, SPSS). A descriptive analysis was performed; continuous variables were described using the mean and standard deviation and percentiles depending on the distribution of the variable. Categorical variables were described using percentages. For the comparison of continuous variables, Student's *t*-test or ANOVA test was used if there was a normal distribution and Kruskal-Wallis otherwise. Comparison of categorical variables was performed using the $\chi 2$ test, Fisher exact test or Yates chi-square test if necessary. To determine the relationship between the dependent variables and the independent variables, Pearson correlation models were performed. The level of significance was set at $p < 0.05$.

3. Results

In the face-to-face group, initially fifty-four patients were recruited from the 4 pharmacies that participated in the study. After attempting to contact all patients by telephone for the second survey, there were 5 patients who did not respond to the telephone, leaving a final sample of 49 patients. In the online group, after sending the e-mails to the patients who completed the first part of the study, a total of 23 responses were obtained (Table 1).

As it is shown in Table 1, the largest number of patients participating in the face-to-face group were recruited from the central Granada pharmacy ($n = 17$) and fewer from the rural pharmacy ($n = 6$). Most patients recruited were female ($n = 37$ face-to-face; n = 17 Online), and the age range was mostly between 41 and 65 years ($n = 23$ face-to-face; $n = 10$ Online). With the weight and height measurements, the body mass index (BMI) of all the patients was calculated, obtaining that more than half of the patients were normal weight, although in a range very similar to

Table 1
Baseline characteristics of patients.

Variables	Face-to-face (total N = 49) n (%)	Online (total N = 23) n (%)
Pharmacy Location		
Granada Center	17 (34.7)	
Granada Costa	14 (28.6)	
Granada Rural	6 (12.2)	
Madrid Center	12 (24.5)	
Gender		
Male	12 (24.5)	6 (26.1)
Female	37 (75.5)	17 (73.9)
Age		
14–40 years	13 (26.5)	4 (17.4)
41–65 years	23 (46.9)	10 (43.5)
66–100 years	13 (26.5)	9 (39.1)
IMC		
Low weight (>18.5)	1 (2.0)	1 (4.3)
Normal weight (18.5–24.9)	26 (53.1)	9 (39.1)
Overweight (25.0–29.9)	22 (44.9)	13 (56.5)
Education		
No studies	3 (6.1)	0 (0)
Primary	2 (4.1)	0 (0)
High school	8 (16.3)	3 (13.0)
Vocation degree	11 (22.4)	7 (30.4)
University	25 (51.0)	13 (56.5)

those who were overweight ($n = 26$) in the on-site study; however, in the online study, the majority were overweight ($n = 13$) (Table 1).

According to the survey question: "How many days do you walk at least 10 minutes a day to get around?" and comparing the two groups, it was observed that the improvement of life habits in relation to physical exercise was significantly greater ($p = 0.048$) in the face-to-face group, with a significant increase of 0.81 ± 1.44 more days of exercise per week on average, compared to the on-line group, in which the mobility data of the participants even worsened -0.09 ± 2.35 (Table 2).

Table 2 shows that in general there was an increase in the number of foods consumed rich in vitamin D weekly, being significant in the case of tuna for the face-to-face group (0.55; $p = 0.035$), and in the case of avocado in the online group (0.56; $p = 0.001$).

The face-to-face interview analysis verified that the increased of salmon consumption per week is correlated to the increase in vitamin D levels. This increase was statistically significant (0.951; $p = 0.013$). On the other hand, when analyzing the patients in the face-to-face group who had increased their avocado intake during this period, a positive correlation was obtained with the VAS value (1; $p < 0.001$). Therefore, the greater the increase in the intake of this fruit, the better the data on the perception of quality of life obtained with respect to the first survey.

The increase in serum vitamin D levels was significant for patients who received a face-to-face pharmacy interview (11.5 ng/mL; $p = 0.021$) vs those who only received Online training (-0.65 ng/mL; $p = 0.200$) (Table 2).

Finally, with respect to each patient's perception of their health status, all patients in the on-site study, after completing the visual analog scale (VAS), showed an increase in mean health status of 4.63 points ($p = 0.205$), with the lowest score at 3 months being 15 and the highest being 100 (Table 2); however, although not significant, in the online group only an increase of 1.82 points ($p = 0.817$) was observed (Table 2).

Moreover, in the first interview of the study, we evaluated how patients took vitamin D and we found that 32.5% ($n = 13$) of the patients did so correctly. After the pharmacist's intervention, 69.8% ($n = 30$) of the patients took vitamin D with a meal, the preferred option being breakfast (Table 3). When pharmacist gave advice on how patients should take vitamin D, we found that depending on the pharmacy where the recommendation was made, patients improved to a greater or lesser extent the administration of this drug in a statistically significant way (-0.298; $p = 0.038$) in favor of the pharmacies of central Granada and the coast and to the detriment of the rural pharmacy. Likewise, the optimal administration of this drug was compared with the increase in vitamin D-rich foods by the patients, again obtaining a positive correlation in which patients who increased their consumption of vitamin D-rich foods also improved their dosage (0.302; $p = 0.035$).

During the study, a total of 9 referrals were made to the physician for patients whose symptoms, lifestyle or dietary habits suggested a vitamin D deficiency. Of these, 5 were diagnosed with vitamin D deficiency and were prescribed a supplement, and 4 of them were sent for a confirmatory analysis.

Table 3
Correct intake of vitamin D in face-to-face study.

	N (%) Baseline	N (%) 3 months
At any time of the day	14 (35.0)	6 (14.0)
With food	13 (32.5)	30 (69.8)
In the morning on an empty stomach	10 (25.0)	5 (11.6)
Before going to sleep	3 (7.5)	2 (4.7)
Total	40 (100)	43 (100)

The patients' perception of the most frequent symptoms associated with vitamin D deficiency and insufficiency was evaluated in a question added to the questionnaire. The results of this study show that when asked if they associated vitamin D deficiency with any of the following situations, the most frequently chosen answer in all cases was "never"; only in the case of fatigue were the percentages somewhat equal, with 26.5% ($n = 13$) and 16.3% ($n = 8$) of the respondents choosing "very frequently" and "always", respectively in face-to-face study, however in online study, most participants (47.8%) rarely associated fatigue with vitamin D deficiency ($n = 11$) (Table 4).

A negative correlation with statistical significance was found between the sex of the patient and muscle pain associated with vitamin D deficiency (-0.286; $p = 0.046$), and the female respondents were much more aware of this symptom than the male participants in the study.

4. Discussion

There are presentations of vitamin D supplement in doses of 600 to 800 IU, administered daily. The long time elapsed between doses, as well as the sensation of innocuousness perceived by the population about these treatments, can generate problems of non-adherence. This is where pharmaceutical action is crucial, as health agents, whose task will be to inform, raise awareness and involve the patient in the monitoring of his or her 25-hydroxyvitamin D levels. The pharmacist should detect possible cases of vitamin D deficiency, and try to generate a change towards more effective lifestyle habits in the eyes of the absorption of this molecule and therefore, an improvement in the quality of life of patients.

The question of the survey "How many days do you walk at least 10 minutes a day to get around?" has helped to measure the capacity for change that the pharmacist can generate when giving some type of recommendation to the patient, due to the increase in the number of days in the face-to-face study (0.81 ± 1.44), thanks to the pharmaceutical intervention versus the online one (-0.09 ± 2.35) ($p = 0.048$) where the patient only watched a video to improve their vitamin D levels through good habits. Similar results were seen in the study by Walker et al. (2019) where face-to-face education of different healthcare professionals for the

Table 2
Variables related to vitamin D.

Variables	Face-to-face (total N = 49)				On line (total N = 23)			
	Baseline	Month 3	Change	*p*-value	Baseline	Month 3	Change	p-value
Activity (days per week)	5.55	6.36	0.81	0.017*	4.7	4.6	−0.09	0.900
Weekle food								
Avocado	2,22	2,32	0,1	0,824	1,56	2,13	0,56	0,001*
Egg	3	3,06	0,06	0,834	2,56	2,6	0,04	0,879
Salmon	0,91	1,26	0,35	0,100	0,91	1	0,08	0,645
Tuna	1,73	2,28	0,55	0,035*	1,56	1,52	−0,04	0,862
Sardine	0,63	0,55	−0,08	0,703	0,434	0,434	0	1
Swordfish	0,14	0,12	−0,02	0,768	0,13	0,13	0	1
Mushrooms	0,98	1,34	0,36	0,099	0,95	0,82	−0,13	0,628
Dairy	2,78	3,3	0,52	0,532	4,21	3,65	−0,56	0,47
25-hydroxyvitamin D levels (ng/mL)	23,46	34,96	11.5	0.021*	22,14	21,49	−0,65	0.200
VAS	72,51	77,14	4,63	0.205	70,43	72,26	1,82	0.817

VAS: Visual Analogical Scale.

Table 4
Perception of symptoms associated with vitamin D deficiency.

	Fatigue N (%)	Muscle pain N (%)	Nervousness N (%)	Insomnia N (%)	Fragility N (%)	Getting sick easily N (%)
Never	17 (34.7)	33 (67.3)	40 (81.6)	39 (79.6)	33 (67.3)	37 (75.5)
Rarely	3 (6.1)	7 (14.3)	4 (8.2)	4 (8.2)	2 (4.1)	3 (6.1)
Often	8 (16.3)	5 (10.2)	2 (4.1)	2 (4.1)	3 (6.1)	3 (6.1)
Very often	13 (26.5)	1 (2.0)	2 (4.1)	2 (4.1)	9 (18.4)	3 (6.1)
Always	8 (16.3)	3 (6.1)	1 (2.0)	2 (4.1)	2 (4.1)	3 (6.1)
Total Face-to-face	**49 (100)**	**49 (100)**	**49 (100)**	**49 (100)**	**49 (100)**	**49 (100)**
Never	4 (17.4)	8 (34.8)	8 (34.8)	7 (30.4)	15 (65.2)	11 (47.8)
Rarely	11 (47.8)	10 (43.5)	8 (34.8)	10 (43.5)	2 (8.7)	9 (39.1)
Often	6 (26.1)	4 (17.4)	6 (26.1)	5 (21.7)	2 (8.7)	0 (0)
Very often	2 (8.7)	1 (4.3)	1 (4.3)	1 (4.3)	3 (13.0)	1 (4.3)
Always	0 (0)	0 (0)	0 (0)	0 (0)	1 (4.3)	2 (8.7)
Total Online	**23 (100)**	**23 (100)**	**23 (100)**	**23 (100)**	**23 (100)**	**23 (100)**

implementation of vitamin D supplement use improved knowledge and therefore, their health outcomes such as fall prevention in the elderly population.[25] In addition pharmacist intervention to improve vitamin D levels through exercise was key in the study conducted by Malaeb et al. (2017) (OR = 0.63; 95%CI = 0.167–1.377; $p = 0.04$).[26]

With respect to the recommendations on the weekly consumption of foods rich in vitamin D, it has been observed that thanks to the pharmaceutical intervention there is a significant increase in the case of tuna ($p = 0.035$) in the face-to-face study, and for avocado in the online study ($p = 0.001$). In addition, in the face-to-face study, there is a significant positive correlation between salmon consumption and the increase in 25-hydroxyvitamin D levels ($p = 0.013$). Similarly, a favorable correlation is also observed with increased avocado seminal consumption and improved quality of life (VAS) ($p < 0.001$), as observed in the study by Manoy et al. (2017), where vitamin D supplementation in patients with osteoarthritis improved their quality of life ($p = 0.002$).[27] Even the review by Dreher and Davenport (2013) found potential health effects following avocado consumption.[28]

The increase in serum 25-hydroxyvitamin D levels was significant for patients who received a face-to-face pharmacy intervention (11.5 ng/mL; $p = 0.021$) versus those who only received Online training (−0.65 ng/mL; $p = 0.200$). Yett et al. (2022) have proven that the role of the pharmacist through a protocol in patients with Cystic Fibrosis Clinic improved 25-hydroxyvitamin D levels ($p < 0.001$), increasing the value by 23.2 ng/mL at 6 months of study.[29]

Also, it was shown that the pharmacist's intervention helped the correct intake of vitamin D from 32.5% taking it with food to 69.8%, with a significant correlation in urban versus rural pharmacies ($p = 0.038$). As in the review by Awadh et al. (2021) in which they concluded that the pharmacist has an important role in patient education regarding the use of vitamin D supplements, recommending indications, dosing, adverse effects and drug interactions.[30] In addition, this pharmaceutical intervention to assist in the correct administration of vitamin D also led to an improvement in the consumption of vitamin D-rich foods ($p = 0.035$).

The pharmacist has also contributed to referral to the physician in those cases where symptoms or lifestyle habits suggesting vitamin D deficiency were detected. The pharmacist's crucial collaboration with other health professionals can contribute to the prevention of vitamin D deficiency.[31]

The patient's perception of the symptoms associated with vitamin D deficiency was evaluated in our study, observing that most patients do not associate symptoms such as fatigue, insomnia, fragility, among others, to a vitamin D deficit or insufficiency, with only fatigue being the symptom most frequently associated by 42.8% very frequently or always in the face-to-face. The low percentages associated with theoretically characteristic symptoms such as muscular (and chronic) pain and bone fragility are striking. Therefore, we can affirm that the study participants are either mostly asymptomatic for almost all the symptoms of this deficit or they do not associate their symptoms to vitamin D deficiency and insufficiency and associate them to other pathologies. The third option is the lack of symptoms associated with this pathology in the general population. Thurfah et al. (2022) found that vitamin D supplementation improves the symptomatology of patients with depression.[32] The role of the pharmacist is important to improve knowledge on daily recommendations on improving vitamin D levels and consequently education on the diseases and drugs associated with vitamin D deficiency ($p < 0.001$).[26]

Nonetheless, women proved to be more aware than men of the symptoms of this pathology, as was the case with muscle pain (−0.286; $p = 0.046$).

Despite attempts to minimize bias, there were certain limitations in conducting this study. We consider that the follow-up time period is too short to improve 25-hydroxyvitamin D levels. A more long-term design with systematic vitamin D measurements every 2 to 3 months in all patients would be much more appropriate. In addition, the study started at a time when there were certain restrictions by COVID-19 and concluded at a time when many restrictions were lifted, so that mood and the ability to walk outside could improve, which could lead to a slight bias in this study.

The low participation in the on-line development was associated with the e-mail getting onto spam lists making the data obtained somewhat disparate and both an increase and a decrease in any one of the values greatly influencing the rest.

5. Conclusion

There are habits that improve vitamin D production such as increased physical activity, the correct use of vitamin D supplements and the consumption of foods with high levels of vitamin D, with salmon, tuna and avocado being those that have been shown to increase vitamin D levels or quality of life.

The work of the pharmacist is crucial, as a health agent, demonstrating a great ability to involve the patient in their treatment, making them aware of the benefits to their health status of increasing vitamin D levels, as well as helping them to better understand their pathology and strategies to address their treatment.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. van Schoor N, Lips P. Global overview of vitamin D status. Endocrinol Metab Clin N Am 2017;46(4):845–870.
2. Holick MF, Chen TC, Lu Z, Sauter E. Vitamin D and skin physiology: a D-lightful story. J Bone Miner Res Off J Am Soc Bone Miner Res 2007;22(suppl 2):V28–V33.
3. Fuleihan Gel H, Bouillon R, Clarke B, et al. Serum 25-Hydroxyvitamin D levels: variability, knowledge gaps, and the concept of a desirable range. J Bone Miner Res Off J Am Soc Bone Miner Res 2015;30(7):1119–1133.

4. Cranney A, Horsley T, O'Donnell S, et al. Effectiveness and safety of vitamin D in relation to bone health. Evidence Report/Technol Assess 2007;158:1-235.
5. Tripkovic L, Lambert H, Hart K, et al. Comparison of vitamin D2 and vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and meta-analysis. Am J Clin Nutr 2012;95(6):1357–1364.
6. Glendenning P, Chew GT, Inderjeeth CA, Taranto M, Fraser WD. Calculated free and bioavailable vitamin D metabolite concentrations in vitamin D-deficient hip fracture patients after supplementation with cholecalciferol and ergocalciferol. Bone 2013;56(2):271–275.
7. Oristrell J, Oliva JC, Casado E, et al. Vitamin D supplementation and COVID-19 risk: a population-based, cohort study. J Endocrinol Investig 2022;45(1):167–179.
8. Kimball SM, Holick MF. Official recommendations for vitamin D through the life stages in developed countries. Eur J Clin Nutr 2020;74(11):1514–1518.
9. Varsavsky M, Rozas Moreno P, Becerra Fernandez A, et al. Recommended vitamin D levels in the general population. Endocrinol diabetes y nutricion 2017;64(suppl 1):7-14.
10. Rudnicka A, Adoamnei E, Noguera-Velasco JA, et al. Vitamin D status is not associated with reproductive parameters in young Spanish men. Andrology 2020;8(2):323–331.
11. Alonso-Cabezas M, Pollan M, Alonso-Ledesma I, et al. Sociodemographic and lifestyle determinants of adherence to current dietary recommendations and diet quality in middle-aged Spanish premenopausal women. Front Nutr 2022;9, 904330.
12. Xu Z, Jing X, Li G, et al. Valproate decreases vitamin D levels in pediatric patients with epilepsy. Seizure 2019;71:60–65.
13. Sreedharan M, Devadathan K, Mohammed Kunju PA, et al. Vitamin D deficiency in ambulant children on carbamazepine or sodium valproate monotherapy. Indian Pediatr 2018;55(4):307–310.
14. Kennedy DA, Cooley K, Skidmore B, Fritz H, Campbell T, Seely D. Vitamin d: pharmacokinetics and safety when used in conjunction with the pharmaceutical drugs used in cancer patients: a systematic review. Cancers 2013;5(1):255–280.
15. Schmidt DR, Holmstrom SR, Fon Tacer K, Bookout AL, Kliewer SA, Mangelsdorf DJ. Regulation of bile acid synthesis by fat-soluble vitamins a and D. J Biol Chem 2010;285(19):14486–14494.
16. Nicoli F, Dito G, Guabello G, Longhi M, Corbetta S. Hypercalciuria in postmenopausal women with reduced bone mineral density is associated with different mineral metabolic profiles: effects of treatment with thiazides and anti-resorptives. Front Med 2021;8, 780087.
17. Gastelurrutia MA, Faus MJ, Martinez-Martinez F. Reply to the paper: defining professional pharmacy services in community pharmacy. Res Soc Admin Pharm: RSAP 2013;9(4):490–491.
18. Dualde E, Font G, Santonja FJ, Faus MJ. Impact of pharmacists' participation in a pharmacotherapy follow-up program. Am J Pharm Educ 2012;76(2):34.
19. Fikri-Benbrahim N, Garcia-Cardenas V, Saez-Benito L, et al. Adherence: a review of education, research, practice and policy in Spain. Pharm Pract 2009;7(3):125–138.
20. Gastelurrutia MA, Benrimoj SI, Castrillon CC, de Amezua MJ, Fernandez-Llimos F, Faus MJ. Facilitators for practice change in Spanish community pharmacy. Pharmacy World Sci PWS 2009;31(1):32–39.
21. Gastelurrutia MA, Faus MJ, Fernandez-Llimos F. Providing patient care in community pharmacies in Spain. Ann Pharmacother 2005;39(12):2105–2110.
22. Martin-Calero MJ, Machuca M, Murillo MD, Cansino J, Gastelurrutia MA, Faus MJ. Structural process and implementation programs of pharmaceutical care in different countries. Curr Pharm Des 2004;10(31):3969–3985.
23. INE. *European Health Survey in Spain*. 2020.
24. Walker P, Kifley A, Kurrle S, Cameron ID. Process outcomes of a multifaceted, interdisciplinary knowledge translation intervention in aged care: results from the vitamin D implementation (ViDAus) study. BMC Geriatr 2019;19(1):177.
25. Malaeb D, Hallit S, Salameh P. Assessment of vitamin D levels, awareness among Lebanese pharmacy students, and impact of pharmacist counseling. J Epidemiol Global Health 2017;7(1):55–62.
26. Manoy P, Yuktanandana P, Tanavalee A, et al. Vitamin D supplementation improves quality of life and physical performance in osteoarthritis patients. Nutrients 2017;9(8).
27. Dreher ML, Davenport AJ. Hass avocado composition and potential health effects. Crit Rev Food Sci Nutr 2013;53(7):738–750.
28. Yett ES, Phan H, Mills AR, et al. Development and evaluation of a pharmacist-driven vitamin D protocol for a cystic fibrosis clinic. J Pediatr Pharmacol Ther 2022;27(4):306–311.
29. Awadh AA, Hilleman DE, Knezevich E, Malesker MA, Gallagher JC. Vitamin D supplements: the pharmacists' perspective. J Am Pharm Assoc 2003;61(4):e191–e201.2021.
30. Broussard DL. Public health in pharmacy: improving vitamin D status in the U.S. population. J Am Pharm Assoc 2003;53(2):206–209.2013.
31. Thurfah JN, Christine Bagaskhara PP, Alfian SD, Puspitasari IM. Dietary supplementations and depression. J Multidiscip Healthc 2022;15:1121–1141.