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Research Article

Improvement of Primary Dysmenorrhea with Oral Dose of Vitamin D: A Pilot Study

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Abstract

Primary dysmenorrhea is a common disorder characterized by painful uterine cramping, just before or during menstruation, in the absence of any pelvic pathologic conditions. It is frequently accompanied by other symptoms such as nausea, vomiting, diarrhea, asthenia, and insomnia.

An excessive uterine production of prostaglandins (PGs) is the pathogenetic trigger of dysmenorrhea. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the currently accepted drugs for the management of this disorder.

Because the vitamin D receptor is widespread and the mitochondrial cytochrome P450 enzyme 25-hydroxyvitamin D_3 (25[OH] D)-1α-hydroxylase (1α-OHase), which catalyzes the synthesis of 1α,25-dihydroxyvitamin D_3 ($1,25[OH]_2D$) from its precursor 25(OH) D, is expressed in the human uterus and in immune system cells, and because vitamin D reduces the synthesis of PGs, a beneficial effect of vitamin D in the uterus pathophysiology is possible.

We evaluated the effect of vitamin D supplementation on individuals in 3 categories: individuals with mild dysmenorrhea; moderate dysmenorrhea and severe dysmenorrhea.

The aim of this intervention study was to evaluate the effect of oral dose of cholecalciferol (2 000 IU) on primary dysmenorrhea

Keywords: Vitamin D; Dysmenorrhea

Introduction

Dysmenorrhea is one of the frequent pathologies of gynecological origin. Despite the high prevalence between 45-90%, its pathophysiology is unknown. It is divided into primary and secondary depending on the existence of an organic cause such as fibroids, polyps, endometriosis.

Dysmenorrhea characterized by spasmodic cramping pain in the lower abdomen, in the absence of pelvic problems, often happens just pre or at the onset of menstrual bleeding and persists for 8-72 h. The pathogenic mechanism behind dysmenorrhea are not been fully understood, but may be because of the increase in the generation of prostaglandins and leukotrienes [1-3].

Several factors have been related to the origin of dysmenorrhea, such as family history, age at menarche, BMI, caffeine intake [4].

Several studies have analyzed the role of prostaglandins in the origin of dysmenorrhea, determining an increase in their production in the myometrium. In the final stage of ovulation, there is an accumulation of fatty acids in the cell membrane. Subsequently,

with the end of the menstrual cycle, there is a decrease in progesterone levels, which leads to the release of fatty acids and subsequent synthesis of prostaglandins PGE2 and PG2alpha and leukotrienes that cause contractions of the myometrium.

Vitamin D is a steroid hormone which has a key action in the metabolism of calcium in the bones, but in turn has a large number of target organs such as the uterus within the female reproductive system [2-5].

Vitamin D is a prohormone synthesized in the skin in response to ultraviolet UVB rays, which converts cholesterol into inactive cholecalciferol and is activated by 2 hydroxylations in the kidney and liver. The active form of vitamin D performs its functions in target organs by acting through the vitamin D receptor (VDR)5. In this way, vitamin D modulates various processes such as progression, apoptosis, differentiation and angiogenesis [6].

The latest published population studies point to vitamin D deficiency as a true pandemic.

Objective

To determine if vitamin D levels correlate with the intensity of dysmenorrhea and if the improvement of these parameters improves the quality of life of these patients.

Material and Methods

Study design

Type of study

An observational study has been designed, that is, using the medication in the of the same in the study conditions of habitual use, in accordance with the indication established in its technical data sheet approved.

Patients had to meet all the inclusion criteria and not meet any of the Exclusion criteria.

The Investigator obtained the Informed Consent of the patients prior to inclusion

Inclusion criteria

- Women 18-50 years (both included).
- Women with dysmenorrhea
- Patients with confirmed hypovitaminosis D; understanding by hypovitaminosis levels less than 30 ng/ml
- Patients who agree to participate in the study and have signed the Consent Informed.

Exclusion criteria

- Women < 18 years.
- Women > 50 years.
- Patients for whom treatment with vitamin D is contraindicated.
- Patients who cannot comply with the study visits.

Criteria for discontinuation or premature withdrawal

The patients were considered included in the study once the consent was signed informed. Discontinuation was defined as the fact that a patient included in the study, for any reason, leave it at any time, before it is meet the conditions indicated in the protocol, without having to offer any explanation or justification. Study patients could also discontinue at any time at the discretion of the investigator or sponsor for safety or other reasons.

Treatments and products under study

The drug used in this study is vitamin D. It was administered cholecalciferol 2000 IU daily for 4 weeks. The treatment carried out has been based on the correction of hypovitaminosis D according to the guidelines of the endocrinology society. Timely controls and treatment and duration schemes are endorsed by these entities. In the article by Brakta., *et al*. he mentions the non-toxic levels of vitamin D, these being 30 ng/dl, which are obtained with an intake of 2000 IU/vit D, per day. Chronic administration of vitamin D can be toxic, causing hypercalcemia and hypoparathyroidism; Therefore, it is not indicated in patients with optimal levels of vitamin D. The American Endocrine Society recommends a weekly dose of 50,000 IU of vitamin D for adults with vitamin D deficiency vitamin, for 6-8 weeks to reach target numbers; or their equivalents in daily or monthly doses; and later a maintenance guideline variable between 800 and 2000 IU/day; never exceeding 500,000 IU/year, for risk of toxicity.

Considerations regarding information to subjects and informed consent

All patients received detailed information from the investigator about the nature of the study, its purposes, procedures, estimated

duration, potential risks and benefits associated with participation in the study, as well as any inconvenience that this could entail and the voluntary nature of their participation and the option to abandon the treatment at any time, without this affecting your treatment subsequent doctor, nor to the relationship with the doctor who treated her.

Research ethics committee

The protocol, patient information sheet, consent form proposed informed and any other information for the patients, were reviewed by a CEI/CEIm. Any modification to the protocol, other than changes administrative, would require an amendment to the protocol that should be approved by this Committee.

Practical considerations

Participation in this study included 2 visits that coincided with the visits planned by the specialist physician in his usual clinical practice. On these visits they collected all the data from the patient's medical history.

The research was carried out in the Gynecological Unit of the García Orcoyen Hospital.

A validated questionnaire was used to assess the degree of dysmenorrhea pain [28]. The VAS is a subjective evaluation of the pain on a point of 0 (no painful symptoms) to 10 (most severe pain possible), measurable in millimeters on a linear scale. Dysmenorrhea pain was classified on VAS as none (point: 0), mild (point: 1-3), moderate (point: 4-7), or worst imaginable pain (point: 8-10) [29].

Vitamin D measurement

Laboratory measurement. An electrochemiluminescence (ECL) method was used for the measurement of serum 25 (OH) vitamin D. Serum 25 (OH) vitamin D was categorized based on the accepted cutoff values (nmol/L): serum 25 (OH) vitamin D levels <50 deficiency, 50-74.9 insufficiency and >75 sufficiency [].

Statistical analysis

McNemar or Cochran's Q tests and paired sample t-test were used to compare variables before and after supplementation. All data are expressed as frequency, percent and mean ± SD. $P < 0.05$ was considered statistically significant. Statistical analyses were conducted with SPSS version 17 (SPSSInc, Chicago, Ill., USA).

Serum Vit D (25-hydroxyvitamin D) was determined using an enzyme-linked immunosorbent assay (ELISA kit, Diazist, Tehran, Iran) based on the manufacturer's protocol. Vit D status was categorized based on serum concentrations of 25(OH) D as follows: Vit D deficiency (< 20 ng/ml), and insufficiency (20-30 ng/ml) and suffi- ciency (> 30 ng/ml) [31].

Results

The mean age of the patients was 29.37 years with a minimum age of 19 and a maximum of 45 years.

The prevalence of deficiency, insufficient and sufficient serum levels of 25OH vitamin D was 31,8%, 22.7% and 54.5% in participants at the baseline, respectively.

Vas					
		Frequency	**Percentage**	**valid percentage**	**Accumulated percentage**
Valid	0-3	10	45.5	45.5	45.5
	4-7	5	22.7	22.7	68.2
	8-10	7	31.8	31.8	100.0
	Total	22	100.0	100.0	

Table 1: Shows the number of patients based on pain intensity. Visual Analogic Scala (VAS).

Dysmenorrhea pain was classified on VAS as none (point: 0), mild (point: 1-3), moderate (point: 4-7), or worst imaginable pain (point: 8-10).

Descriptive					
				Statistical	Dev . Mistake
vit1	0-3	Media		30.00	2,737
		95% confidence interval for the mean	Lower limit	23.81	
			Upper limit	36.19	
		Average trimmed to 5%		29.72	
		Median		29.50	
		Variance		74,889	
		Dev . Deviation		8,654	
		Minimum		twenty	
		Maximum		Four. Five	
		Range		25	
		Interquartile range		fifteen	
		Asymmetry		.395	.687
		kurtosis		-1,138	1,334
	4-7	Media		16.80	,800
		95% confidence interval for the mean	Lower limit	14.58	
			Upper limit	19.02	
		Average trimmed at 5%		16.89	
		Median		18.00	
		Variance		3,200	
		Dev . Deviation		1,789	
		Minimum		14	
		Maximum		18	
		Range		4	
		Interquartile Range		3	
		Asymmetry		-1,258	.913
		Kurtosis		.313	2,000
	8-10	Media		9.71	,892
		95% confidence interval for the mean	Lower limit	7.53	
			Upper limit	11.90	
		Average trimmed at 5%		9.74	
		Median		10.00	
		Variance		5,571	
		Dev. Deviation		2,360	
		Minimum		6	
		Maximum		13	
		Range		7	
		Interquartile Range		4	
		Asymmetry		-.163	,794
		Kurtosis		-.242	1,587

Table 2: Shows the classification of patients based on the level of vitamin D and the intensity of dysmenorrhea.

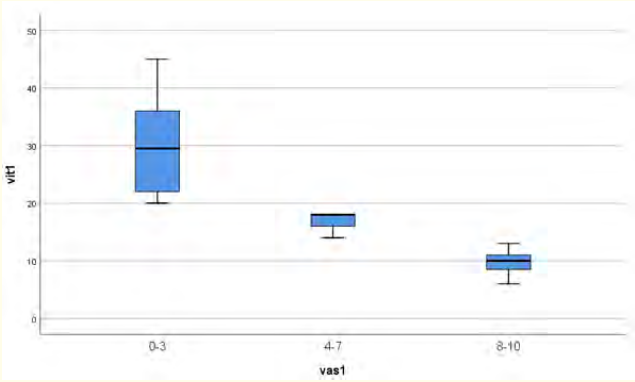

Figure 1

Correlation between pelvic pain and vitamin D serum levels.

Correlations			
		vit1	**go1**
vit1	Pearson correlation	1	-.836 **
	Next (bilateral)		,000
	No.	22	22
VAS1	Pearson correlation	-.836 **	1
	Next (bilateral)	,000	
	No.	22	22
**. The correlation is significant at the 0.01 level (bilateral).			

Table 3: Shows the vitamin D values before and after the intervention.

Statistics of paired samples					
		Half	No.	Dev . Deviation	Dev . average error
pair 1	vit1	20.55	22	10,923	2,329
	vit¡4	26.68	22	8,968	1,912
Paired sample correlations					
		No.	Corre-lation	Next.	
pair 1	vit1 and vit¡4	22	.887	,000	

Table 4

Discussion

Data from our pilot study show a clear association between blood vitamin D levels and intensity of dysmenorrhea. There are several studies that have tried to corroborate the correlation between vitamin D and dysmenorrhea with mixed results [8-10]. Our data agrees with the reports that find a correlation, although we have the limitation of being a pilot study.

If this correlation exists, it has been hypothesized that correcting vitamin D levels would improve the symptoms of dysmenorrhea in patients. In the pilot group, we have seen that when vitamin D levels improve after oral administration of 2000UI daily for 4 weeks, the intensity of dysmenorrhea decreases. It was decided to use cholecalciferol on a daily basis to avoid the possibility of toxicity. The recovery regimes of the optimal level of vitamin D can be carried out on a daily, weekly or monthly basis. In this study, it was carried out daily so that the assessment of dysmenorrhea was uniform, that is, when faced with shock therapy regimens, dysmenorrhea can suddenly improve and then reappear. The use of daily regime allows to avoid. that confusion factor [11-13].

Vitamin D reduce dysmenorrhea through different mechanisms. At the endometrium,, it reduces the expression of cyclooxygenase 2, which reduces the levels of prostaglandin production. In addition, it regulates the expression of the enzyme 15 hydroxyprostaglandin dehydrogenase, causing a greater inactivation of prostaglandins. Another route of action would be the anti-inflammatory effect, blocking the TNF signal and increasing the activity of the protein. kinase. The increase in the production of the p38 cytokine would be directly related to a decrease in the intensity of dysmenorrhea [11].

This investigation is limited by the number of patients recruited, but the hypothesis analyzed is confirmed in subsequent studies. dysmenorrhea could be effectively treated if patients acquire optimal levels of vitamin D. The way to reach these levels is through the consumption of supplements in patients at risk of hypovitaminosis D that ensure a contribution of 600 IU/day. The determination of vitamin D levels is not done systematically today, but from here we advocate that it be carried out on people at high risk of hypovitaminosis. Only knowing the real levels We will determine which is the best way to correct the degree of hypovitaminosis, either through foods rich in vitamin D or the administration of vitamin D preparations [14-16].

Conclusion

This pilot study demonstrates the existence of a correlation between the intensity of dysmenorrhea and serum vitamin D levels. Daily cholecalciferol supplementation with 2000 IU improves serum vitamin D levels, causes an improvement in the intensity of dysmenorrhea. With these data we consider it necessary to determine the levels of vitamin D in situations of pelvic pain associated with dysmenorrhea in order to correct the blood levels, achieving an improvement in the symptoms of the patients.

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