Vitamin D Role in Primary Dysmenorrhea

Primer Dismenorede D Vitaminin Rolü

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Öz

Primer dismenore, pelvik hastalık olmaksızın menstrüasyon sırasında veya öncesinde ortaya çıkan ve suprapubik ağrıya neden olan uterus kramplarıdır. Dismenore nedenlerini araştırırken, birkaç çalışma D vitamini (vit D) eksikliğinin rolünü vurgulamıştır. Vit D, ağrıya neden olan prostaglandinlerin sentezini baskılayarak etki eder. Çalışmamızın amacı D vitamini düzeyinin primer dismenoreyi etkileyip etkilemediğini araştırmaktır. Bu amaçla primer dismenoresi olan hastalarda ve dismenoresi olmayan kontrol grubunda vit D 3 düzeyi çalışılacaktır. Bu retrospektif, randomize, vaka kontrollü çalışma, Ocak 2020 ile Ağustos 2021 arasında iki farklı merkezde gerçekleştirildi. Etik kurul tarafından onaylandı. Bilgi, çalışma için uygun deneklerle görüşülerek elde edildi ve bilgilendirilmiş onam alındı. Araştırmaya katılan merkezlerin jinekoloji bölümlerine 750 kadın başvurdu. 16-35 yaş arası araştırmaya dahil edilmiştir. Pediatri kliniklerinden benzer semptomlarla 18 yaş altı hasta sevk edildi. 325 kadın dismenore grubuna atandı. Tüm hastalarda düzenli bir adet döngüsü ve adetten bir gün önce başlayan ağrı vardı. Dismenore ile ilgisi olmayan 325 hasta kontrol grubu olarak rastgele seçildi. Çalışmamızdaki katılımcılar dismenore grubu ve kontrol grubu olarak rastgele seçilmiş ve klinik özellikleri Tablo 1 ve 2'de karşılaştırılmıştır. Dismenore hastaları ile sağlıklı kontrol grupları karşılaştırıldığında anlamlılık dikkat çekiciydi. 25-hidroksivitamin D3 eksikliği olan dismenore hastalarının süt ürünlerini önemli ölçüde daha az tükettiği görülmüştür.Bu gurupta VAS değerleri daha yüksekti ve yetersiz eğitim ve işsizlik de önemli ölçüde daha yaygındı. Düşük serum D vitamini seviyeleri ve dismenore güçlü bir şekilde ilişkilidir. D vitamini düzeyleri, VAS skoru ve primer dismenore arasında anlamlı bir ilişki olduğu açıktır. Primer dismenorede vit D'nin etkinliğinin altını çizmek için daha büyük ölçeklerde daha fazla çalışmaya ihtiyaç vardır.

Anahtar Kelimeler: D Vitamini, Primer Dismenore, Süt Ürünleri

Abstract

Primary dysmenorrhea is uterine cramping that occurs during or before menstruation without pelvic disease and causes suprapubic pain. In researching the causes of dysmenorrhea, several studies have highlighted the role of lacking vitamin D (vit D). Vit D acts by suppressing the synthesis of prostaglandins that cause pain. Our study aims to investigate whether vit D level affects primary dysmenorrhea. For this purpose, vit D 3 level will be studied in patients with primary dysmenorrhea and a control group without dysmenorrhea. This retrospective, randomized, case-controlled study was conducted between January 2020 and August 2021 at two different centers. It was approved by the ethics committee. Information was obtained by interviewing eligible subjects for the study, and informed consent was obtained. 750 women presented to the gynecology departments of the participating centers involved in the study. Ages between 16-35 are included in the study. Under 18 patients were referred from pediatric clinics with similar symptoms. 325 women were assigned to the dysmenorrhea group. All patients had a regular menstrual cycle and pain that began the day before menstruation. 325 patients unrelated to dysmenorrhea were selected randomly as a control group. The participants in our study were randomly selected into the dysmenorrhea group and the control group, and their clinical characteristics were compared in Tables 1 and 2. Significance was remarkable comparing the dysmenorrhea patients with the healthy control groups. That dysmenorrhea patients with 25-hydroxyvitamin D3 deficiency had significantly less consumption of dairy products. VAS values were higher, and undereducation and unemployment were also significantly more common. Low serum vit D levels and dysmenorrhea are strongly related. It is obvious that there is a significant relationship between vit D levels, VAS score, and primary dysmenorrhea. More studies at larger scales are needed to underline the efficiency of vit D in primary dysmenorrhea.

Keywords: Vitamin D, Primary Dysmenorrhea, Dairy Products

Introduction

Primary dysmenorrhea is uterine cramping that occurs during or before menstruation without pelvic disease and causes suprapubic pain. Primary dysmenorrhea occurs in at least 50% of menstruating women and disrupts social life and psychological effects (1). Although the pathogenesis of primary dysmenorrhea is not clearly understood, uterine contractions and pelvic pain are thought to be caused by excessive prostaglandin secretion (2).

In researching the causes of dysmenorrhea, several studies have highlighted the role of lacking vitamin D (vit D) (3). Vit D acts by suppressing the synthesis of prostaglandins that cause pain (4). Our study aims to investigate whether vit D level affects primary dysmenorrhea. For this purpose, vit D 3 level will be studied in patients with primary dysmenorrhea and a control group without dysmenorrhea (5).

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Başvuru Tarihi / Received: 26.07.2022
Kabul Tarihi / Accepted : 15.11.2022

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Material and Method

This retrospective, randomized, case-controlled study was conducted between April 2020 and August 2021 at two different centers. Ethics committee in Afyon approved our study with the code 2030-KAEK-2/ 04.03.2020 and 2020/3 meeting number. Information was obtained by

interviewing eligible subjects for the study, and informed consent was obtained. 750 women presented to the gynecology departments of the participating centers involved in the study. Ages between 16-35 are included in the study. Under 18 patients were referred from pediatric clinics with similar symptoms.

In our study, according to our exclusion criteria, 38 women with abdominal pathology, 19 women with additional diseases such as diabetes and hypertension, 21 women with a high white blood cell count in blood tests, and 13 women who took vit D supplements in their dietary routine and 9 women who did not volunteer for the study were not included. 325 women were assigned to the dysmenorrhea group. All patients had a regular menstrual cycle and pain that began the day before menstruation (6). 325 patients unrelated to dysmenorrhea were selected randomly as a control group. Participants were contacted by telephone and completed a questionnaire asking them to report their demographic characteristics and the pattern and characteristics of their menstrual cycle. The amount of milk intake in the diets of those who volunteered to participate in the study was examined (3,7). The intake of dairy products was determined on daily basis as less than 1, 1 to 2 and more than 2 servings per day. Individuals who volunteered to participate in the study were asked 10 questions about the physical and psychological symptoms they experienced before menstruation. Symptoms included depression, irritability, social withdrawal, increase or decrease in appetite, weakness, headache, nausea, and breast tenderness (8). Pain during menstruation was rated by participants using the visual analog scale (VAS).

Laboratory Studies

To determine serum levels of parathyroid hormone and D3, participants diagnosed with dysmenorrhea registered at the obstetric clinic or had parathyroid hormone and D3 tested at any outpatient clinic 2 months before the registration date. We used lower and upper margins as <11.5 ng/ml for vit D and >65 pg/ml for parathyroid hormone.

Statistical analysis

Collected data were analyzed by Statistical Package for Social Sciences version 19.0 (SPSS-IBM Inc., Armonk, NY, USA). Continuous variables were expressed as mean±standard deviation (range: minimum maximum) whereas categorical variables were denoted as numbers or percentages. Student t-test, chi-square test and Mann Whitney U-test were used for the comparisons. Spearman correlation test was used to detect the correlations among the variables. Two-tailed p values less than 0.05 were accepted to be statistically significant.

Results

The participants in our study were randomly selected into the dysmenorrhea group and the control group, and their clinical characteristics were compared in Tables 1 and 2. Significance was remarkable comparing the dysmenorrhea patients with the healthy control groups.

Table 1. Demographics of all patients

	Patients (n = 325)	Control group (n = 325)	p
Age	24.4±1.8	24.5±1.9	0.932
Weight (kg)	54.6±4.0	55.2±4.2	0.854
Height (m)	1.57±0.10	1.56±0.15	0.677

Table 2. Vit D levels and VAS score

	Patients (n=325)	Control group (n = 325)	p
25-hydroxyvitamin D (ng/ml)	8.2±2.7	15.1±1.9	0.001
25-hydroxyvitamin D "deficiency	260 (80%)	37 (11.0%)	0.001
Parathyroid hormone (pg/ml)	69.1±13.5	51.1±11.0	0.001
Visual analog scale score	8.6±1.5	1.9±1.7	0.001

The consumption of dairy products was lower in the dysmenorrhea group than in the control group (p=0.001). Serum D3 level was lower in the dysmenorrhea group (p=0.001), and serum parathyroid hormone was higher in the dysmenorrhea group (p= 0.001). Menstrual bleeding (p=0.004) and VAS score (p=0.001) were also higher in the dysmenorrhea group. Calcium levels were lower in the dysmenorrhea group (p=0.001).

Positive family history was more frequent in the dysmenorrhea group than in the control group (p=0.001).

Nervousness, headache, depression, fatigue, and breast tenderness were more frequent in the dysmenorrhea group comparing the control group. Appetite changes that may cause weight gain was also more frequent in the dysmenorrhea group (9).

The menstrual cycle and menstrual bleeding were longer in the subjects diagnosed with dysmenorrhea who also had low serum vit D levels (5, 6, 9). In the same group, the amount of menstrual bleeding was less and the average height of the group was lower. Undereducation and unemployment were also significantly more common (10). In addition,

headache, irritability, fatigue, and depression were more common in the serum vit D deficient group (all $p<0.05$).

Discussion

Primary dysmenorrhea occurs in about half of women of childbearing age. (11) The pain of dysmenorrhea is caused by prostaglandins (11). Prostaglandins cause contraction of the uterus. NSAIDs reduce prostaglandin synthesis and decrease pain. Taking vit D reduces the use of medications in women with dysmenorrhea (12). Vit D is a biological molecule, with low levels of vit D, and the absorption of calcium is also affected. In a feedback loop, low calcium levels increase the secretion of parathyroid hormones (13). There are many causes of dysmenorrhea. If we look at the causes, smoking, early menarche, and family history are the most important ones (14). Our study shows that family history is significantly higher. In our study, vit D levels in the dysmenorrhea group comparing the control group were lower.

In a similar study, vit D deficiency was 50.4% in 258 healthy Turkish women (29), whereas in a study on 368 young women aged 18-25 years in Turkiye, the prevalence of vit D deficiency was 44.5% (5, 6). In our study, vit D deficiency and hyperparathyroidism in 325 women with dysmenorrhea were 80% and 46.1%, respectively. In other studies, the results are close to our values (15). In our study, 73.8% of 325 women in the dysmenorrhea group consumed dairy products once a day (16). Only 7% of their dairy product consumption is more than once daily. In our study and other studies, socioeconomic level plays a minor role in considering vit D level (17). Premenstrual symptoms observed in our study, irritability (51.7%), fatigue (49.7%), mood swings (41.5%), depression (46.6%), and headache (43.8%) were noted (18). There is a correlation between premenstrual symptoms and calcium. Previously it is shown that low vit D intake leads to premenstrual symptoms. Dietary supplementation with vit D and calcium reduces premenstrual symptoms. In our study, individuals with low vit D (19) levels have dysmenorrhea and they also have complaints about premenstrual symptoms. Adding Vit D supplementation may be helpful in these symptoms (20). Therefore, problems in vit D metabolism may cause dysmenorrhea as well as psychological and gastrointestinal symptoms (21). Low serum vit D levels and dysmenorrhea are strongly related (5,6,21). It is obvious that there is a significant relationship between vit D levels, VAS score, and primary dysmenorrhea. More studies at larger scales are needed to underline the efficiency of vit D in primary dysmenorrhea.

Table 3. Patients diet regime and Dysmenorea

	25-hydroxyvitamin D_3 deficiency (n=275)	25-hydroxyvitamin D_3 normal (n=50)	p
Consumption of dairy products			0.001
<1 serving/day	248 (90.2%)	6 (12.0%)	0.001
1-2 servings/day	24 (8.7%)	26 (52.0%)	0.001
>2 servings/day	3 (1.1%)	18 (36.0%)	0.001
Visual analogue scale score	7.3±1.2	5.5±0.7	0.002

Ethics Committee Approval: Ethics committee in Afyon approved our study with the code 2030-KAEK-2/ 04.03.2020 and 2020/3 meeting number.

References

1. Pakniat H, Chegini V, Ranjkesh F, et al. Comparison of the effect of vitamin E, vitamin D and ginger on the severity of primary dysmenorrhea: a single-blind clinical trial. Obstet Gynecol Sci. 2019;62(6):462-8.
2. Abdi F, Amjadi MA, Zaheri F, et al. Role of vitamin D and calcium in the relief of primary dysmenorrhea: a systematic review. Obstet Gynecol Sci. 2021;64(1):13-26.
3. Abdul-Razzak KK, Ayoub NM, Abu-Taleb AA, et al. Influence of dietary intake of dairy products on dysmenorrhea. J. Obstet. Gynaecol. Res. 2010;36(2):377-83.
4. Roy S. A review on the efficacy of fish oil and its components in alleviating the symptoms of primary dysmenorrhea. BLDE Univ J Health Sci. 2022;7(1):19.
5. Karacin O, Mutlu I, Kose M, et al. Serum vitamin D concentrations in young Turkish women with primary dysmenorrhea: a randomized controlled study. Taiwan J Obstet Gynecol. 2018;57(1):58-63.
6. Ayşegül Ö, Seda A, Şevket O, et al. A randomized controlled study of vitamin D in the treatment of primary dysmenorrhea. Duzce Med J. 2019;21(1):32-6.
7. Yu A. Complementary and alternative treatments for primary dysmenorrhea in adolescents. Nurse Pract. 2014;39(11):1-12.
8. Zarei S, Mohammad-Alizadeh-Charandabi S, Mirghafourvand M, et al. Effects of calcium-Vitamin D and calcium-alone on pain intensity and menstrual blood loss in women with primary dysmenorrhea: A randomized controlled trial. Pain Med. 2017;18(1):3-13.
9. Naz MSG, Kiani Z, Fakari FR, et al. The effect of micronutrients on pain management of primary dysmenorrhea: a systematic review and meta-analysis. J. Caring Sci. 2020;9(1):47.
10. Dawood MY. Primary dysmenorrhea: advances in pathogenesis and management. Obstet Gynecol. 2006;108(2):428-41.
11. Charandabi SMA, Mirghafourvand M, Nezamivand-Chegini S, et al. Calcium with and without magnesium for primary dysmenorrhea: a double-blind randomized placebo controlled trial. Int J Women's Health Repro Sci. 2017;5(4):332-8.
12. Ferries-Rowe E, Corey E, Archer JS. Primary dysmenorrhea: diagnosis and therapy. Obstet Gynecol. 2020;136(5):1047-58.
13. Abdul-Razzak KK, Obeidat BA, Al-Farras MI, et al. Vitamin D and PTH status among adolescent and young females with severe dysmenorrhea. J Pediatr Adolesc Gynecol. 2014;27(2):78-82.
14. Bahrami A, Avan A, Sadeghnia HR, et al. High dose vitamin D supplementation can improve menstrual problems,

dysmenorrhea, and premenstrual syndrome in adolescents. Gynecol Endocrinol. 2018;34(8):659-63.
15. Kulzhanova D, Amanzholkyzy A, Saparbaev S, et al. Vitamin D status in adolescent girls with primary dysmenorrhea. Issued since 1920. 2021;57(2):17.
16. Nasehi M, Sehhatie F, Zamanzadeh V, et al. Comparison of the effectiveness of combination of fennel extract/vitamin E with ibuprofen on the pain intensity in students with primary dysmenorrhea. Iran J Nurs Midwifery Res. 2013;18(5):355.
17. Kannan P, Cheung K-K, Lau BW-M. Does aerobic exercise induced-analgesia occur through hormone and inflammatory cytokine-mediated mechanisms in primary dysmenorrhea? Med Hypotheses. 2019;123:50-4.
18. Rajput V. An overview on dysmenorrhea. Int. J. Nurs. Educ. 2021;9(3):381-4.
19. Zarei S, Mohammad-Alizadeh-Charandabi S, Mirghafourvand M, et al. Effects of calcium-vitamin D and calcium alone on pain intensity in women with primary dysmenorrhea: a randomized controlled trial. Pain Med. 2017;18(1):3-13.
20. Durain D. Primary dysmenorrhea: assessment and management update. J Midwifery Womens Health. 2004;49(6):520-8.
21. Núñez-Troconis J, Carvallo D, Martínez-Núñez E. Primary Dysmenorrhea: pathophysiology. Investig Clin. 2021(4):378-406.