VİTAMİN D VE UTERİN PROLAPSUS ARASINDAKİ İLİŞKİ

The Association Between Vitamin D and Uterine Prolapse

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ÖZET

Amaç: Pelvik organ prolapsusu pelvik organların vajinal duvarlara veya ötesine herniasyonu olarak tanımlanır. Vitamin D eksikliğinin pelvik taban kas güçsüzlüğüne sebep olduğu düşünülmektedir. Çalışmamızın amacı uterin prolapsusu olan hastalarda vitamin D eksikliğini ve incelemektir.

Gereç ve Yöntemler: İzmir Tepecik Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Kliniği'nde Şubat 2015-2016 arasında peri- ve postmenapozal yaşta vajinal değerlendirmede evre 3-4 uterin prolapsusu saptanan ve opere olan hastalar; kontrol grubu olarak da aynı yaş grubunda herhangi bir jinekolojik durum nedeniyle opere olan hastalar retrospektif olarak incelendi. Vitamin D metabolizmasını etkileyecek hastalık veya fekal inkontinans sebebi olabilecek evre 3 kronik böbrek yetmezliği, kronik karaciğer hastalığı, gastric bypass, kolovajinal fistül ve pelvik radyasyon öyküsü olan kişiler çalışmadan çıkarıldı.olan kişiler çalışmadan çıkarıldı. Dahil edilen kişilerin yaş, gravida parite, doğum şekli ve 25 (OH) vitamin D, ICS prolapsus evreleri kaydedildi.

Bulgular: Çalışma kriterlerine uygun 40 hasta ve 40 kişi kontrol olarak kaydedildi. Hasta grubunun 25-OH D vitamini düzeyleri (9,5±14,0 ng/ml) kontrol grubundan (15,3 ± 20,3 ng/ml) düşük olarak saptandı (p=0,140). Hasta grubunun 95,0%'i ve kontrol grubunun 77,5%'inde 25-OH D vitamini eksikliği (<20 ng/mL) saptandı (p=0,024). 25-OH D vitamini eksikliği uterin prolapsus için bağımız risk faktörü olarak saptandı (OR=5.8, 95% CI=1.0 – 33,3).

Sonuç: Vitamin D eksikliği uterin prolapsus gelişimi için risk faktörü olabilir.

Anahtar Kelimeler: *Pelvik organ prolapsusu; Vitamin D; Risk faktörü*

ABSTRACT

Aim: Pelvic organ prolapse, the hernniation of the pelvic organs or beyond the vaginal walls. Vitamin D deficiency appears to be cause for pelvic muscle weakness. The aim of this study is to investigate the lack of vitamin D in patients with uterine prolapse.

Methods: The records of patients were evaluated retrospectively in peri- and postmenopausal age group who were diagnosed with ICS stage 3-4 uterine prolapse based on vaginal examination and operated between February 2015-2016 in Izmir Tepecik Education and Research Hospital Gyneology and Obstetrics clinic. The files of 40 patients with ICS stage 0 in the peri- and postmenopausal period, whose 25 (OH) vitamin D were measured at the same time with the patient group and who underwent surgery due to any gynecologic indication, were evaluated as control group. Women were excluded if they had any medical conditions known to impair absorption or metabolism of vitamin D, or to be a major cause of fecal incontinence including Stage ≥3 chronic kidney disease, chronic liver disease, gastric bypass, colovaginal fistula, and pelvic irradiation.

Results: 40 patients' and 40 control cases' data who met the study criteria were recorded. The patient group had a lower level of 25 (OH) vitamin D (9,5 ± 14,0 ng/ml) than the control group (15,3 ± 20,3 ng/ml). Furthermore, 25 (OH) vitamin D deficiency (25 [OH] vitamin D level <20 ng/mL) was found in 95,0% of the patient group and 77,5% of the control group (p=0,024). A 25 (OH) vitamin D level of <20 ng/mL was found to be the independent risk factor for uterine prolapse (OR=5,8, 95% CI=1,0 – 33,3).

Conclusion: Vitamin D deficiency may be a risk factor in the development of uterine prolapse.

Key words: Pelvic organ prolapse; Vitamin D; Risk factor

INTRODUCTION

International Continence Society (ICS) as the downward displacement of the female reproductive organs during Valsalva maneuver (1). The risk of surgery due to pelvic organ disorders (POP or stress urinary incontinence) for a woman is 11%, and it is the third most common indication for hysterectomy (2). The incidence of POP stage 2 and 3 in women presenting to gynecology outpatient clinics is 51% according to the ICS staging (3). But prevalence of stage 3 and 4 could only reach 2,6% (3).

Risk factors for the development of POP are hysterectomy, ethnic origin, age, the number of parities and births, myopathy, neuropathy, smoking, constipation, menopause, and body mass index (4,5). The modification of risk factors such as obesity, smoking, chronic constipation may reduce the likelihood of prolapse. Although the increase in the number of parities is a risk factor for prolapse, Hendrix et al. (6) detected different stages of prolapse in one in five nulliparous women. In addition, POP risk increases by 100% for every 10 years of age. Menopause is not an independent risk factor.

Vitamin D has the most significant effects on calcium and phosphorus metabolism and bone mineralization. Vitamin D deficiency and insufficiency have been found to be associated with many chronic diseases including rickets, osteoporosis, osteomalacia, common cancers, cardiovascular diseases, metabolic syndrome, infectious and autoimmune diseases. It has been thought that vitamin D directly and indirectly, by the effect on calcium, affects muscle contraction (7). Immunohistochemical staining of the muscle biopsies of women has shown that vitamin D receptors in muscle cells decrease with aging (7). There are also several studies showing that vitamin D deficiency causes pelvic floor muscle weakness, which makes it a risk factor for overactive bladder and urinary incontinence (8-10).

In the present study, we aimed to investigate the lack of vitamin D in patients with uterine prolapse.

MATERIALS AND METHOD

The records of 40 patients were evaluated retrospectively in peri- and postmenopausal age group who were diagnosed with ICS stage 3-4 uterine prolapse (desensus uteri) based on vaginal examination and who underwent surgery between February 2015 and February 2016 at Tepecik Training and Research Hospital Gynecology and Obstetrics Clinic. The age, gravida, parity, vaginal birth, and cesarean birth rates of the patients were analyzed. Levels of 25 (OH) vitamin D and ICS prolapse stages were recorded.

Terminology of female pelvic organ prolapse and pelvic floor dysfunction was classification according to study of Bump et al (1). The examination of pelvic organ prolapsus was performed by standing and Valsalva maneuver. At ICS stage 0, prolapse was not. At ICS stage 3, the distal portion of the prolapsus is less than 1 cm below the hymen. At ICS stage 4, there was total eversion of total vaginal length. The files of 40 patients with ICS stage 0 in the peri- and postmenopausal period, whose 25 (OH) vitamin D were measured at the same time with the patient group and who underwent surgery due to any gynecologic indication, were evaluated as control group. There was not 2, 3. or 4. stage cystocele or rectocele at control group. At population of control, point of C was -7 or -8, point of D was -9 or -10, point of Ba was -3 or -4 and point of Bp was -3 or -4. The control group comprised the patients who underwent surgery due to reasons such as a leiomyoma, benign adnexal mass, and endometrial hyperplasia. For the case group, 40 appropriate patients were available during the study time. The case and control group planned to match 1-1. So, the patients who control groups were selected by the simple random sampling method among patients who underwent gynecology operation between the same time. Patients (for case and control group) who were previously treated with vitamin D therapy, multivitamin supplementation, calcium supplementation for any indication, fatty fish ≥2×/week, smoking and those with malignancy were excluded from the study. Season of blood sampling of 20 patients at case and control group was summer. Season of blood sampling of 20 patients at case and control group was winter. All of the patients have the same ethnicity.

A venous sample was taken in a clotted tube for

serum vitamin D analysis at the time of recruitment and 25-hydroxy vitamin D levels were measured by electro chemiluminescent immunoassay (ECLIA, Roche Diagnostic, Basel, Switzerland). Before all gynecologic surgery the level of vitamin D is measured routinely in our center. To increase the external validity and generalizability of our data, women were excluded if they had any medical conditions known to impair absorption or metabolism of vitamin D, or to be a major cause of fecal incontinence including Stage ≥3 chronic kidney disease, chronic liver disease, gastric bypass, colovaginal fistula, and pelvic irradiation. Vitamin D deficiency was defined as a total serum vitamin D level of ≤20 ng/mL (8). The patients with total serum vitamin D levels of ≥30 ng/mL were classified as vitamin D sufficient (8). The patients with serum levels between 21 and 29 ng/mL were classified as vitamin D insufficient (8).

This study was approved by the institutional Ethics Committee A written informed consent was obtained from each patient.

Statistical analysis was performed using the Statistical Package for Social Science (SPSS) for Windows version 21.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean and standard deviation (SD), and number and percentage. The chi-square (χ2) test and Student's t-test were used to analyze unpaired data. Univariate and multivariate logistic regression analyses were conducted to identify the factors affecting formation of a uterine prolapse, and the results were presented in odds ratios (OR) with 95% confidence interval (CI). A p value of <0.05 was considered statistically significant.

Table 1. Demographic data and clinical characteristics of case and control groups

	Case group (n=40)	**Control group (n=40)**	**p**
Age, mean ± SD (years) (median)	58.6 ± 11.1 (59)	54.8 ± 7.2 (54)	0.076*
Postmenopause, n (%)	32 (80.0)	33 (82.5)	0.500**
Gravida, mean ± SD (median)	4.6 ± 2.6 (3,5)	3.7 ± 3.2 (3,0)	0.159*
Body mass index, mean ± SD, (kg/cm2) (median)	28.1 ± 5.2 (27,5)	27.5 ± 3.9 (28,0)	0.613*
25 (OH) vitamin D, mean ± SD (ng/ml) (median)	9.5 ± 14.0 (5,28)	15.3 ± 20.3 (5,36)	0.140*
Vitamin D deficiency, n (%)	38 (95.0)	31 (77.5)	0.024**
Stress Urinary Incontinence, n (%)	9 (22.5)	6 (15.0)	0.284**

(SD = Standart Deviation, Vitamin D deficiency = 25 (OH) vitamin D < 20 ng/ml, POP = Pelvic organ prolapse, * = According to student's t-test, ** = According to χ2 test)

Tablo 2. Results of univariate and multivariate analyses of odds ratios using the logistic regression model, with desensus uteri as the dependent variable

	Univariate analyses			Multivariate analyses		
Number of vaginal births (≥ 4)	%95 CI	OR	p	**%95 CI**	OR	p
Menopause age (menopause for ≥ 10 years)	1.1-8.8	3.1	0.030	0.7–7.3	2.3	0.140
Age (≥ 60)	0.9-5.5	2.2	0.076	0.5–10.0	2.2	0.306
25 (OH) vitamin D (<20ng/ml)	1.1-6.9	2.7	0.039	0.3–6.4	1.3	0.742
Body mass index (>25) (kg/cm2)	1.1-27.4	5.5	0.037	1.1–33.3	5.8	0.043
Vitamin D deficiency, n (%)	0.3-2.0	0.8	0.626	0.6–5.2	1.8	0.284

(CI = Confidence Intervals , OR = Odds Ratios)

RESULTS

Demographic data and clinical characteristics of uterine prolapse patients with the patient (ICS stage 3 and 4) and control groups (ICS stage 0) are shown in Table 1. There was no statistically significant difference in the age (p=0.076) and the number of postmenopausal patients (p=0.500) between the groups. Also, there was no statistically significant difference in the mean gravity (P=0.159) between the groups. The patient group had a lower level of 25 (OH) vitamin D (9.5 ± 14.0) than the control group (15.3 ± 20.3); however, it did not reach statistical significance (p=0.140). Furthermore, 25 (OH) vitamin D deficiency (25 (OH) vitamin D level <20 ng/mL) was found in 95.0% of the patient group and 77.5% of the control group (p=0.024).

The results of univariate and multivariate logistic regression analyses are summarized in Table 2. Vitamin D deficiency (25 (OH) vitamin D level <20 ng/mL), number of vaginal deliveries (≥4), menopause age (menopause for ≥10 years), age (≥60), and body mass index were found to be the risk factors for pelvic floor dysfunction. Our considerable result of a 25 (OH) vitamin D level of <20 ng/mL was found to be the independent risk factor for uterine prolapse (OR=5.8, 95% CI=1.0 – 33.3).

DISCUSSION

In this retrospective, case-control study, the deficiency of vitamin D was analyzed as a possible etiological risk factor for descensus uteri. Despite the reduction of POP stages and complaints by modifying risk factors for pelvic floor disorders, the outcomes were not satisfactory for the patients. It was thought that it might cause pelvic floor disorders indirectly by changing calcium levels and directly due to the presence of vitamin D receptors in pelvic floor muscle cells. In the literature, there is a limited number of studies investigating the relationship between vitamin D levels and pelvic floor disorder.

The mean age of the patients with pelvic floor disorder was found to be between 47.9 and 64.3 (10,11) in our study. Navaneethan et al. shown that 74.5% of the patients with pelvic floor disorders were at the age of 50 years and over, 72.9% of them delivered 4 or more infants, and 72.5% of them were in the menopause for at least five years (12). In our patient group, the mean age was 58.6±11.1 and the mean menopause period was 12.4±9.9 years. The mean gravida number of our patient group was found to be not difference.

The patients who had pelvic floor disorders were reported to have vitamin D deficiency more frequently than the control group (10,12). In the pelvic floor disorders group, the level of 25 (OH) vitamin D (29.3 ng/mL) was lower than the control group (35.0 ng/mL) (p<0.001) (11). There was no significant difference in the relationship between vitamin D levels and POP, according to the regression analysis of the study (12). However, risk factors for pelvic floor disorders were assessed using the multivariate logistic regression analysis in another study (10). The risk decreased by 6% for every 5 ng/mL increase in 25 (OH) vitamin D levels for all age groups, indicating statistical significance (p=0.043) (10). In our study, the 25 (OH) vitamin D level was found to be lower than 20 ng/mL in 95.0% of the patients with uterine prolapse, and there was a significant difference between the patient and control groups (p=0.024). In the patient group, the mean 25 (OH) vitamin D level was 9.5±14.0 ng/mL, whereas it was 15.3±20.3 ng/mL in the control groups (p=0.140). In the regression analysis which was conducted to identify the risk factors of uterine prolapse, D vitamini deficiency was statistically significant risk factor (95% CI=1.1–33.3, OR=5.8, p=0.043).

Another result of pelvic floor dysfunction is fecal incontinence, cystocele, rectocele, and stress urinary incontinence. In a study, the mean 25 (OH) vitamin D level of patients with fecal incontinence was lower than the control group (p=0.04) (13). The most common finding of vitamin D deficiency in postmenopausal women is osteoporosis.

Our study's retrospective design may have several selection and measuring biases, as retrospective cohort studies are subject to selection and may include unknown confounding variables, which may adversely affect the accuracy of the results. Despite this limitation, however, the similarity of demographic characteristics in the study population and the availability of follow-up

data increased the validity of our results and mitigated the weaknesses.

In conclusion, vitamin D deficiency may be a risk factor in the development of uterine prolapse. In the light of our study results and the literature data, we conclude that the administration of hormone therapy to patients with POP prevented postmenopausal osteoporosis-related fractures, which were as a consequence of vitamin D deficiency. However, further large-scale, long-term, prospective studies are required to confirm these findings and to investigate whether vitamin D replacement can be used to prevent POP. The possible effects of vitamin D treatment on postoperative recurrence and quality of life in patients who develop POP and are treated by surgical methods may also be other issues to be addressed.

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