Middle East Fertility Society Journal xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Middle East Fertility Society Journal

journal homepage: www.sciencedirect.com

Original Article

The effect of vitamin D3 on improving lipid profile, fasting glucose and insulin resistance in polycystic ovary syndrome women with vitamin D deficiency

Homeira Rashidi *, Seyed Bahman Ghaderian, Leila Moradi

Health Research Institute, Diabetes Research Center, Ahvaz Jundishapur of Medical Sciences, Ahvaz, Iran

ARTICLE INFO

Article history:
Received 21 October 2017
Accepted 6 November 2017
Available online xxxx

Keywords:
Polycystic ovary syndrome
Vitamin D

ABSTRACT

Introduction: Metabolic disturbances are common in women with PCOS. Some studies have suggested that vitamin D deficiency may play a role in metabolic disorders and insulin resistance, although limited clinical trials on this subject have been published with contradictory findings. Therefore, the aim of this study was to investigate the effects of vitamin D on metabolic disorders in women with PCOS and vitamin D deficiency.

Methods: This study was a randomized-blinded clinical trial. Eighty-six women diagnosed with PCOS and vitamin D deficiency aged between 18 and 45 were enrolled. They were randomly divided into two groups of interventional (44 women) and control (42 women). In each group, patient assignment was done using randomized blocks of four. Based on the block combination, vitamin D at a dose of 50,000 unit per week (Interventional group) and a dose of 50,000 units per month (Control group) and elemental calcium at a dose of 1000 mg per day were administered by a nurse. Metabolic parameters (i.e., LDL, HDL, total cholesterol, HOMA-IR, serum insulin, FBS, TG) and serum vitamin D were measured at baseline and 2 months after treatment.

Results: In vitamin D group, serum levels of 25 (OH) D increased. There was no significant difference in the metabolic parameters before and after treatment in each group ($P > .05$). At the end of the study, the metabolic parameters and HOMA-IR did not show a significant difference.

Conclusion: This study showed that vitamin D replacement in women with PCOS and vitamin D deficiency has no effect on the improvement of metabolic parameters and HOMA-IR.

1. Introduction

Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder among women in their reproductive age, with a relative prevalence of 6–10% in the general population [1]. According to a cohort study conducted based on the criteria of the National Institutes of Health, the prevalence rate is 8.7% while in accordance with the criteria of Rotterdam, the prevalence is 11.2% [2] and this number seems to decrease as the person gets older, especially from the age of 35 onwards [3]. Definition and diagnosis of PCOS is based on criteria including clinical or paraclinical evidence of hyperandrogenism, ovarian dysfunction such as oligo-ovulation, and the exclusion of other causes of hyperandrogenism such as adrenal hyperplasia, hyperprolactinemia, and thyroid disorders [1]. PCOS is associated with insulin resistance, hypertension, central lipidemia and central venous dysfunction, all of which are risk factors for metabolic syndrome, type 2 diabetes, and coronary artery disease [1]. Metabolic disturbances are common in PCOS women: 30–40% have glucose tolerance disorder, 60–80% are resistant to insulin, and 10% have type 2 diabetes in their thirties or forties. Evidence suggests the pivotal role of insulin resistance in PCOS pathogenicity [5]. Obesity is common in PCOS, and over 50% of people affected are overweight [4]. Obesity is associated with insulin resistance, absence of glucose tolerance and dyslipidemia in PCOS women [4]. Dyslipidemia is also common in PCOS and includes high levels of total cholesterol and LDL, triglycerides and low HDL. Lipid disorders are seen in about 65–81% of these women [4]. Metabolic syndrome, which involves abnormalities in the metabolism of sugar, fat, protein, and maintenance of blood pressure, is an important complication of PCOS. The prevalence of this

Peer review under responsibility of Middle East Fertility Society.

* Corresponding author.
E-mail addresses: hrashidi2002@gmail.com, hrashidi@ajums.ac.ir (H. Rashidi), bahmanint@yahoo.com, ghaderian-B@ajums.ac.ir (S.B. Ghaderian), Lmoradi16@yahoo.com, moradi-L@ajums.ac.ir (L. Moradi).

https://doi.org/10.1016/j.mefs.2017.11.002
1110-5690/

disorder has been reported differently in different studies. A study reported its prevalence to be in 46% of women with PCOS, while an estimated 4–8% prevalence was reported in another study based on the National Institutes of Health criteria [6]. In a therapeutic approach to changing the pattern of life, weight control and reduced insulin resistance play an important role in treating the disease [7]. Another aspect of PCOS is its association with vitamin D. A possible theory to justify a metabolic disorder in this disease is the polymorphism in vitamin D receptor and the genes involved in its level regulation, which is associated with lipid, glucose, and hypotension [8]. It is estimated that 37% of these women have vitamin D deficiency [9]. Several studies have shown the role of vitamin D deficiency in the pathogenesis of insulin resistance, diabetes mellitus and metabolic syndrome [4]. In PCOS women, vitamin D deficiency is associated with insulin resistance, presence of beta cells, and metabolic syndrome [4]. A retrospective study recently revealed a reverse relationship between the level of 25 (OH) D and a ten-year risk of hyperglycemia and insulin resistance [5]. In some studies, the use of vitamin D in PCOS women led to improved insulin resistance and lipid profile, but these data are small and uncontrolled, and more studies are needed to prove these results [10]. Due to the 54.2% prevalence of vitamin D deficiency in women under 50 [11], the 14.6% prevalence of PCOS in Iran based on Rotterdam criteria [12], the hot weather conditions of Khuzestan, south-west of Iran where this study was conducted, the presence of food sources containing vitamin D, and the special clothing of the people of the region, we decided to study the effect of vitamin D on metabolic disorders of this population. Therefore, this study examined the effectiveness of vitamin D3 in the improvement of lipid profile, fasting glucose and resistance to insulin in PCOS women with vitamin D deficiency (see Diagram 1).

2. Method

After obtaining permission from the Ethics Committee of Ahwaz Jundishapur University of Medical Sciences, in a randomized-blinded clinical trial, we studied women with polycystic ovary syndrome referring to the clinics of endocrine diseases at Golestan and Imam Khomeini hospitals of Ahwaz. IRCT registeration number is IRCT2015100824426N1.In this study, the aim of the project was first explained to all women, and if they were willing, informed consent was obtained. Non-probabilistic sampling involved women aged 18–45 based on inclusion criteria. The women were homogenized for their vitamin D and BMI and then divided into four groups by the specialist physician as follows (see Table 1):

BMI < 30 25 (OH) D $\leq$ 20
BMI < 30 20<25 (OH) D <3020
BMI $\geq$ 30 25 (OH) D $\leq$ 20
BMI $\geq$ 30 30>25 (OH) D>20

Then a nurse was assigned to administer vitamin D. The nurse distributing the medication and the women themselves were unaware of the treatment used.

In each group, patient assignment was done using randomized blocks of four. Then the six combinations of these blocks were written, and we randomly selected the number of samples needed from these blocks. Based on the block combinations, vitamin D at a dose of 50,000 unit per week (Code A) and a dose of 50,000 units per month (Code B) and calcium alumina at a dose of 1000 mg per day were distributed among the women by the nurse.

In this study, the first method involved administering vitamin D at 50,000 units weekly for 8 consecutive weeks while in the second method, vitamin D was administered at 50,000 units daily for 2 consecutive months (the minimum dose of vitamin D morally recommended). In each of the two procedures, calcium carbonate tablets were administered twice a day for the entire period of treatment. After recording the patient's basic information including age, BMI and W/H ratio, we recorded serum triglyceride levels, LDL, HDL, total cholesterol, fasting blood glucose, non-insulin levels, vitamin D, in the information form (See the Appendix) before starting the treatment and after the end of the treatment in the eighth week.

2.1. Inclusion criteria

- Age 45 to 18 years.
- not being pregnant or lactating.
- No use of drugs affecting metabolic parameters such as metformin, corticosteroid three months prior to the experiment, vitamin D and calcium, and multivitamin six months before the experiment.
- Meeting at least 2 items of the Rotterdam criteria for PCOS diagnosis including:
  A: oligo-ovulation or Anovulation characterized by oligomanure or amenorrhea
  B: Hyperndrogenesis with a clinical or laboratory diagnosis characterized by hirsutism or alopecia or increased blood testosterone levels.
  C: Polycystic ovary characterized by ultrasound that means at least 12 follicles per ovary, or 9–2 mm in size, or ovarian enlargement of more than 10 ml (obtained from the formula [0.5 $\times$ length $\times$ width $\times$ thickness]) in Ultrasound [12].
- Vitamin D less than 30 ng/ml.

2.2. Exclusion criteria

- Chronic diseases such as acute dexamethasone, chronic renal failure, cirrhosis, pancreatitis, nephrotic syndrome and malignancy.
- Having hyperprolactinemia, Cushing's syndrome, congenital adrenal hyperplasia, and androgen secretion tumors.

2.3. Measurement methods

Body Mass Index: By measuring body weight in kilograms using a digital scale and dividing it into squared height in meters at the beginning and end of the study.

The level of fasting blood glucose was measured by Alisun 3000, triglyceride and cholesterol total blood count using an enzyme kit of Pars Azma and measured with the BT-3000 Auto-Analyzer. HDL was measured by measuring the enzymatic levels of cholesterol and the BT-3000 auto-analyzer. Calculation of LDL was done using Friedewald formula. Insulin resistance: Measured by the HOMA index, which includes the following formula.

Level 25 (OH) D and fasting insulin levels were measured by Liusun using Eliza method.

It should be noted that all trials were conducted at the Laboratory of the Diabetes Research Center. The women' laboratory data were also re-measured two months after the start of the treatment (pretest 1 and post-test 1). In the end, descriptive statistics were used to provide statistical indices, tables and charts, and analytical statistics were used for testing the normality of the variables (the Kolmogrov-Smirnov test), paired *t*-test for intra-group comparison and independent *t*-test for inter-group comparisons with $P < .05$. Data analysis was done using SPSS version 20.

Please cite this article in press as: H. Rashidi et al., The effect of vitamin D3 on improving lipid profile, fasting glucose and insulin resistance in polycystic ovary syndrome women with vitamin D deficiency, Middle East Fertil Soc J (2017), https://doi.org/10.1016/j.mefs.2017.11.002