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Vitamin D supplementation has no effect on insulin resistance assessment in women with polycystic ovary syndrome and vitamin D deficiency

Hania R. Ardabili [a], Bahram P. Gargari [b,*], Laya Farzadi [c]

[a] Department of Biochemistry and Diet Therapy, Faculty of Health and Nutrition, Students' Research Committee, Tabriz University of Medical Sciences, Tabriz 5166614711, Iran

[b] Nutritional Research Center, Department of Biochemistry and Diet Therapy, Faculty of Health and Nutrition, Tabriz University of Medical Sciences, Tabriz 5166614711, Iran

[c] Department of Obstetrics and Gynecology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz 5166614711, Iran

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Abstract

Insulin resistance is one of the most common features of polycystic ovary syndrome (PCOS). Some studies suggest that vitamin D deficiency may have a role in insulin resistance; thus, the aim of the current study was to determine the effect of vitamin D supplementation on insulin resistance in women with PCOS and a vitamin D deficiency. We hypothesized that vitamin D supplementation would lower the glucose level and insulin resistance in women with PCOS and a vitamin D deficiency. The current study was a randomized, placebo-controlled, double-blinded trial with 50 women with PCOS and a vitamin D deficiency, 20 to 40 years old, assigned to receive 3 oral treatments consisting of 50 000 IU of vitamin D_3 or a placebo (1 every 20 days) for 2 months (vitamin D, n = 24; placebo, n = 26). The fasting blood glucose, insulin, 25-hydroxyvitamin D, and parathyroid hormone levels, as well as the homeostasis model assessment of insulin resistance and quantitative insulin sensitivity check index were measured at baseline and after treatment. In the vitamin D group, the serum level of 25-hydroxyvitamin D increased (6.9 ± 2.8 to 23.4 ± 6.1 ng/mL, $P < .0001$), and the parathyroid hormone level decreased (70.02 ± 43.04 to 50.33 ± 21.99 μIU/mL, $P = .02$). There were no significant changes in the placebo group. There was a significant increase in insulin secretion in the vitamin D group ($P = .01$), but this was not significant compared with the placebo group. The fasting serum insulin and glucose levels and the insulin sensitivity and homeostasis model assessment of insulin resistance did not change significantly by the end of the study. We were not able to demonstrate the effect of vitamin D supplementation on insulin sensitivity and insulin resistance in women with PCOS and vitamin D deficiency.

Keywords: Polycystic ovary syndrome; Vitamin D deficiency; Insulin resistance; 25-hydroxyvitamin D; Women

Abbreviations: 25 (OH) D, 25-hydroxyvitamin D; BMI, body mass index; HOMA-B, homeostasis model assessment of beta cell function; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-S, homeostasis model assessment of insulin sensitivity; PTH, parathyroid hormone; PCOS, polycystic ovary syndrome; QUICKI, insulin sensitivity by quantitative insulin sensitivity check index; SD, standard deviation.

1. Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age. Polycystic ovary syndrome is characterized by hyperandrogenism and chronic anovulation [1]. The prevalence of PCOS in women of reproductive age is estimated to be 6.4% to 6.8%

* Corresponding author. Department of Biochemistry and Diet Therapy, Nutritional Research Center, Faculty of Health and Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran. Tel.: +98 4113357581x270 or 09143165247; fax: +98 4113340634.

E-mail addresses: bahrampg@yahoo.com, pourghassemb@tbzmed.ac.ir (B.P. Gargari).

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worldwide [2]. Currently, PCOS is defined by the presence of having at least 2 of the following criteria: irregular or absent ovulation, elevated levels of androgenic hormones, and enlarged ovaries containing at least 12 follicles each [3]. Of women with PCOS, 50% to 70% are insulin resistant [4]. Current evidence shows that insulin resistance has a central role in the etiology of PCOS [1]. It appears that insulin resistance and compensatory hyperinsulinemia cause hyperandrogenism [5] and obesity [6], and in addition, insulin resistance is a risk factor for impaired glucose tolerance and type 2 diabetes mellitus [7].

There is some evidence that vitamin D deficiency is related to impaired glucose clearance and insulin secretion in animal [8] and human models [9]. Vitamin D has different functions and potential effects in addition to calcium homeostasis. Vitamin D receptors exist in tissues, such as pancreatic islet cells and the ovaries. These findings show the complex effect of vitamin D on human metabolism [10]. Liu et al [11] showed that the plasma 25-hydroxyvitamin D (25 [OH] D) concentration is inversely associated with the fasting blood glucose level and insulin resistance. One recent prospective study demonstrated an inverse association between the baseline serum 25 (OH) D level and the 10-year risk for hyperglycemia and insulin resistance [12]. Pittas et al [13] confirmed that patients with impaired fasting glucose who used cholecalciferol plus calcium supplementation for 3 years had a lower increase in insulin resistance in comparison with a control group.

It has been suggested that a vitamin D deficiency is a problem in patients with PCOS [14,15]. A recent study confirmed that increased body weight has a negative effect on serum 25 (OH) D concentrations [16], as well as parathyroid hormone (PTH) levels [17], in women with PCOS.

It should be mentioned that there have only been 2 small intervention studies with vitamin D supplementation on glucose metabolism in PCOS patients [14,18]. With attention to the scarcity of the data on the subject, the aim of the current study was to determine the effect of oral cholecalciferol administration on insulin sensitivity and glucose metabolism indices in women with PCOS who are vitamin D deficient in a randomized, placebo-controlled, double-blinded model. We hypothesized that vitamin D supplementation would lower glucose levels and insulin resistance in women with PCOS who are vitamin D deficient. To test this hypothesis, we administered 3 doses of cholecalciferol to women with PCOS and vitamin D deficiency, and the serum glucose, insulin, PTH, and 25 (OH) D levels and insulin resistance were measured before and after supplementation.

2. Methods and materials

2.1. Study participants

Women with PCOS were recruited from the academic outpatient clinic at Alzahra Hospital of the Tabriz University of Medical Sciences. Of 170 patients with PCOS, 60 vitamin D–deficient women were selected for the study. The sample size calculation showed that 25 subjects would be required for each arm of the trial to detect a change of 1.2 in the homeostasis model assessment of insulin resistance (HOMA-IR) with 80% power and 5% significance. The standard deviation (SD) was assumed to be 1.48 [18]. The inclusion criteria were as follows: women who were between 20 and 40 years old, were vitamin D deficient, and had PCOS diagnosed by a gynecologist. Serum 25 (OH) D levels less than 20 ng/mL were considered to be indicative of a vitamin D deficiency [19]. The diagnosis of PCOS was based on the Rotterdam criteria, which necessitated 2 of the following 3 features: oligoovulation and anovulation, biochemical signs of hyperandrogenism, and polycystic ovaries on ultrasound examination (defined as the presence of 12 follicles measuring 2-9 mm in diameter and/or an ovarian volume >10 cm^3) [3]. Patients who were diagnosed with an androgen-secreting tumor, Cushing syndrome, congenital adrenal hyperplasia, hyperprolactinemia, and/or virilism were excluded from the study. Volunteers reported that they did not have impaired fasting glucose, diabetes, hypothyroidism, hyperthyroidism, liver disease, renal dysfunction, or cardiovascular disease or dysfunction. Study participants who took medications known to affect metabolic parameters, such as metformin and corticosteroid drugs, vitamin D, and serum calcium, were excluded. Patients were followed up for 2 months, and blood samples were obtained 20 days after the last treatment. The study protocol was approved by the Tabriz University of Medical Sciences Ethics Committee. All volunteers gave written informed consent to participate in the study. The trial was registered at IRCT.ir (IRCT138904113140N2).

2.2. Study design

The study was a randomized, placebo-controlled, double-blinded trial. Women were stratified based on age and body mass index (BMI) in blocks of 6 subjects then randomly assigned to the placebo or vitamin D group from computer-generated random number lists. Randomization and allocation were concealed from the researcher and participants until after the main analyses had been completed. The intervention was from March 2010 through June 2010, the time interval in which the vitamin D–effective ultraviolet radiation at 39° latitude (the city in which the study was conducted is located at 39° latitude) is similar [20]; therefore, ultraviolet radiation was deemed not to be a cofounder.

Patients were advised to maintain their usual diets and other lifestyle parameters, such as sunlight exposure and physical activity that could affect the level of vitamin D and metabolic factors, and to avoid taking vitamin D or calcium supplements during the study. Height and body weight were measured at baseline and at the end of the study. Weight was measured without shoes and in light clothing with a precision of 0.1 kg. Standing height was measured without shoes, and