Complementary Therapies in Clinical Practice 26 (2017) 53–60

Contents lists available at ScienceDirect

Complementary Therapies in Clinical Practice

journal homepage: www.elsevier.com/locate/ctcp

Effect of vitamin D supplementation on polycystic ovary syndrome: A systematic review and meta-analysis of randomized controlled trials

Fang Fang [a], Ke Ni [b], Yiting Cai [a], Jin Shang [a], Xiaoke Zhang [a], Chengliang Xiong [a, c, *]

[a] Family Planning Research Institute, Center of Reproductive Medicine, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, People's Republic of China
[b] Department of Anesthesiology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, People's Republic of China
[c] Wuhan Tongji Reproductive Medicine Hospital, Wuhan, People's Republic of China

ARTICLE INFO

Article history:
Received 21 October 2016
Accepted 21 November 2016

Keywords:
PCOS
Vitamin D
RCTs
Meta-analysis

ABSTRACT

Objective: To evaluate the effect of vitamin D supplementation on patients with PCOS.
Methods: We performed a literature search in database and identified all of the RCTs published before December 2015 that compared the effect of vitamin D supplementation with placebo or metformin in PCOS patients.
Main results: Nine out of 463 identified studies were included, involving 502 women presenting with PCOS. Vitamin D supplementation had significant effect on the improvement of follicular development with a higher number of dominant follicles (OR, 2.34; 95% CI, 1.39 to 3.92). Differences in regular menstrual cycles were also observed when metformin plus vitamin D was compared with metformin alone (OR, 1.85; 95% CI, 1.01 to 3.39).
Conclusions: Evidence from available RCTs suggests vitamin D supplementation may be beneficial for follicular development and menstrual cycle regulation in patients with PCOS. Additional high-quality RCTs are required to confirm the effectiveness of vitamin D on PCOS.

Contents

* Corresponding author. Family Planning Research Institute, Center of Reproductive Medicine, Tongji Medical College, Huazhong University of Science and Technology, No.13 Hangkong Road, Wuhan 430030, People's Republic of China.
E-mail address: clxiong951@sina.com (C. Xiong).

http://dx.doi.org/10.1016/j.ctcp.2016.11.008
1744-3881/

1. Introduction

Polycystic ovary syndrome (PCOS) is recognized as the most common endocrine disorder that affects 5–21% of women at reproductive age [1]. PCOS is a heterogeneous disease characterized by symptoms of menstrual irregularity, anovulatory infertility, hirsutism as well as other metabolic manifestations, including hyperandrogenemia, dyslipidemia, and insulin resistance. Nevertheless, the treatment of PCOS is not determined and surrounded by controversies. First-line medication therapy for PCOS can control symptoms to some extent, but may not be completely effective in preventing complications. There is a growing need to develop pharmacologic interventions to improve the management of PCOS.

Recently there has been a focus on vitamin D supplementation as an adjuvant treatment of PCOS. Indeed, women with PCOS have been found to have a high prevalence of vitamin D deficiency, and correlations of serum vitamin D level with several metabolic symptoms have also been demonstrated in PCOS patients, which both support that vitamin D deficiency is associated with multiple metabolic risk factors in PCOS women [2–5]. It has been suggested that vitamin D may play a role in the pathogenesis of PCOS [6,7]. The primary physiologic role of vitamin D is to regulate calcium and phosphorus homeostasis and bone metabolism. Vitamin D receptors (VDRs) are distributed across various human tissues including ovary and endometrium suggesting an active role of vitamin D in female reproductive tissues [8]. PCOS is also related to abnormal calcium and phosphate metabolism and the patients are characterized by elevated levels of phosphorus and parathyroid hormone (PTH) and decreased levels of vitamin D, which may be associated with obesity [9].

Since vitamin D deficiency may play a role in exacerbating PCOS, there may be a place for vitamin D supplementation in the management of this syndrome. To date, several clinical trials have evaluated effects of vitamin D on women with PCOS. There is some, but limited, evidence for beneficial effects of vitamin D supplementation on insulin resistance, ovarian follicles maturation, ovulation and menstrual regularity in women with PCOS [10–12]. However, previous studies have yielded conflicting results regarding this topic, partly because of the relatively small sample sizes and the variability in the markers and assays used. Thus, we conducted a quantitative meta-analysis of currently available randomized controlled trials (RCTs) to evaluate the potential role of vitamin D supplementation in the treatment of PCOS.

2. Materials and methods

2.1. Search strategy and engines

We searched MEDLINE, OVID Embase and Web of Science from their inception to December 2015 and systematically identified studies that evaluated the effect of vitamin D supplementation in the treatment of PCOS. The search strategy included the terms *polycystic ovary syndrome, polycystic ovary disease, PCOS, calcitriol and vitamin D.* In addition to the electronic search, we also scanned the reference lists of retrieved articles to identify any additional relevant studies.

2.2. Inclusion and exclusion criteria

Inclusion criteria were: (1) RCTs; (2) studies that compared vitamin D supplementation with placebo or metformin, the most commonly used agent in PCOS treatment; (3) studies that enrolled women with strict diagnosis of PCOS using Rotterdam European Society of Human Reproduction and Embryology (ESHRE)/American Society of Reproductive Medicine (ASRM) or National Institute of Child Health and Human Development (NICHD) criteria [13,14]; and (4) articles published in English. Patients were not limited by age, body weight, or race. Doses of vitamin D and duration of treatment were not limited.

Exclusion criteria were: (1) studies reporting other diseases, such as type 1 or 2 diabetes mellitus, Cushing's syndrome, hyperthyroidism, metabolic syndrome, or other hormone-related disorders; (2) studies in which the diagnosis of PCOS was not strict and (3) articles not published in English.

2.3. Data extraction

Two of the authors independently evaluated the eligibility of all retrieved studies from the databases and extracted the relevant data from each included study. During the data abstraction process, no attempt was made to contact the authors for further information beyond what had been published. Disagreements were resolved by consensus or arbitration. We abstracted the following data from each study: the first author's name, year of publication, journal name, country, study design, sample size, diagnostic criteria for PCOS, full descriptions of participants enrolled (principal baseline characteristics such as age, weight, and BMI), the interventions they received (type and frequency), the control interventions, and the main outcomes. We extracted the outcomes of interest at the longest point of complete follow-up, which included serum vitamin D and PTH levels, glucose and lipid metabolic parameters (serum total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), high-density lipoprotein cholesterol (HDL-C), fasting plasma insulin, fasting plasma glucose, QUICK and HOMA-IR), dominant follicle numbers and regular menstrual cycles.

2.4. Assessment of risk of bias in included studies

To assess the methodological quality of the included RCTs, we used the Cochrane risk of bias assessment tool to evaluate randomization performance and methods, allocation concealment, extent of blinding (participants, data collectors, outcome assessors, and data analysts), incomplete outcome data, selective reporting and other bias. The evaluations were scaled as low, unclear, and high risk of bias, according to criteria for judging risk of bias provided by Cochrane handbook [15].

2.5. Statistical analysis

Dichotomous data were expressed as the odds ratios (ORs) with the 95% confidence interval (95% CI). Continuous data are presented as the mean differences and standard deviation for all included