



VITAMIN E AND POLYCYSTIC OVARY SYNDROME: A REVIEW ON THE REPORTED CLINICAL TRIALS

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ABSTRACT

Polycystic ovary syndrome is a major gynecological disorder in reproductive-aged women. It is due to the imbalance in the production of sex hormones. Vitamin E is known as the vitamin for reproduction but reports on its effects on reproductive health remain largely understudied. The health benefits of Vit. E on the other body systems, however, have been extensively reported including on its role as an antioxidant, anticancer, anti-proliferative, anti-angiogenic, anti-inflammatory agent, and many more. Since the reports on its benefits on reproductive system are scarce, hence the available reports on the intervention studies specifically on polycystic ovary syndrome (PCOS) are very limited. This paper intended to provide a review on the reported effects of Vit E on PCOS in clinical trials, which could possibly be extended on its importance in future clinical use.

The summary of papers showed that it is still a long way ahead before the mechanisms of actions and outcomes from vitamin E interventions against PCOS could be understood in detail, and yet to suggest the use of vitamin E as one of the natural-based treatment options in the future clinical use.

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Introduction

Polycystic ovary syndrome (PCOS) is a prevalent hormonal disorder in reproductive-aged women [1, 2]. It causes irregularities such as disturbance in the menstrual cycles and infertility [3, 4]. It was reported that PCOS affects 4-12% of reproductive-aged females 40% of whom experience infertility [5]. Hyperandrogenism and elevated levels of luteinizing hormone (LH) mainly disturb the normal ovarian function [6], leading to multiple cysts [7]. PCOS increases the secretion of gonadotropin-releasing hormone (GnRH), which enhances the production of LH over follicle-stimulating hormone (FSH) [8]. Subsequently, the increased level of LH promotes androgen production in the theca cells, while the relative deficiency of FSH reduces the ability of granulosa cells to convert androgen into estrogen and impairs the maturation and ovulation of follicles [9].

Vitamin E is not produced by the human body, thus it must be consumed from the diet. Vitamin E is an essential lipid-soluble vitamin that acts mainly as an antioxidant in the human body [10, 11]. It was first discovered in 1922 [12] and described as a "substance X" that is important for fertility and reproduction in rats. Further extensive researches were conducted and years later, "substance X" was named 'Vitamin E'. There are two substances present in vitamin E, which are tocopherols (TOCs) and tocotrienols (TCTs). Each has 8 subtypes: δ -TCT, γ -TCT, β -TCT, α -TCT, α -TOC, δ -TOC, γ -TOC, and β -TOC [13]. From these subtypes, α -TOC has been widely reported to be used in disease treatments such as cancers [14-16].

Vitamin E and PCOS - Summary of Clinical Trials Reports

It is a well-known fact that the roles of vitamin E including antioxidant, anticancer, anti-proliferative, anti-angiogenic, anti-inflammatory agent, and many other roles have been extensively proven and reported. Ironically, the reports on the roles of vitamin E against reproductive disorders are still lacking, especially in females even when its history of discovery goes back to its essentiality in reproduction. In this review, the conducted literature search on the specific reports on vitamin E and PCOS

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(clinical trials) resulted in the retrieval of a limited number of papers, which are summarized in **Table 1**.

Table 1. Reported clinical research on the effect of Vit E on polycystic ovary syndrome (PCOS)

Type of Study	Study Results	Year Published	References
Network meta-analysis	Supplementation with inositols showed positive results in improving glycolipid metabolism. Vitamin E could be a potential substance to improve the hormonal regulation of total testosterone and the sex hormone-binding globulin (SHBG).	2021	[17]
Nested case control study	The dietary intake of the micronutrients including vitamin E could probably have a protective effect on metabolic syndrome.	2021	[18]
Pilot randomized, placebo-controlled trial	8 weeks of vitamin E supplementation in women with PCOS showed positive effects on body weight, Ang-1/Ang-2 ratio, Ang-1, and vascular endothelial growth factor (VEGF) level.	2021	[19]
Double-blind, randomized clinical trial	Omega-3 and vitamin E synergistically exerted positive effects on total antioxidant capacity, malondialdehyde concentrations, glutathione levels, and catalase activity.	2020	[20]
Prospective, randomized, controlled, open-label study on females with CC-resistant PCOS	Vitamin E may be not effective in increasing pregnancy and ovulation rates in females with clomiphene citrate-resistant PCOS.	2020	[21]
Retrospective cohort study	A short-term vitamin E supplementation ameliorated oxidative stress, and reduces exogenous HMG dosage, but did not affect the pregnancy rate in the ovulation induction cycle.	2020	[22]
Randomized, double-blind, placebo-controlled trial	Co-supplementation for twelve weeks with magnesium and vitamin E may show positive results in women with PCOS on hirsutism and other studied parameters.	2019	[23]
Monocentral, randomized, controlled, double-blinded trial	A minimum of 3 months of micronutrients supplementation including vitamin E showed benefits in women with PCOS.	2019	[24]
Randomized clinical trial	Supplementation with CoQ10 and/or Vit E showed beneficial effects on cardiometabolic outcomes among women with PCOS.	2019	[25]
Randomized, double-blind, placebo-controlled clinical trial	CoQ10 with or without vitamin E supplementation showed beneficial effects.	2019	[26]
Randomized, double-blind, placebo-controlled trial	A 12-week co-supplementation with magnesium showed the beneficial effects of Vit E on parameters of insulin metabolism.	2019	[27]
Interventional study (Case report)	Results indicated an eminent relief in acne, hirsutism, menstrual cycle, and hormonal levels. Vitamin E may be added to the current PCOS treatment guideline, which will be more cost-effective.	2019	[28]
Clinical trial	Co-supplementation with omega-3 and Vit E improved the parameters of mental health.	2018	[29]
Critical review	Vit E can exert beneficial effects on PCOS-related symptoms.	2018	[30]
Randomized double-blind, placebo-controlled trial	Co-supplementation for twelve weeks with omega-3 and Vit E significantly improved indices of insulin resistance, total and free testosterone.	2017	[31]
Double-blinded RCT	Vitamin E and D3 may not significantly play a role in the success rate of IVF via an antioxidant mechanism.	2017	[32]
Randomized double-blind, placebo-controlled trial	Co-supplementation for twelve weeks with omega-3 and Vit E significantly improved gene expression of lipoproteins and biomarkers of oxidative stress.	2017	[33]
Clinical trial	Serum malondialdehyde (MDA) and protein carbonyl (PC) levels were high, and the enzyme activities of glutathione (GSH), vitamin C, and E were reduced.	2012	[34]

Conclusion

The summary of papers on vitamin E and PCOS presented in **Table 1** clearly indicates that these studies were only actively being carried out recently within the last 5 years. This shows that it is still a long way ahead before the mechanisms of actions and outcomes from vitamin E interventions against PCOS could be understood in detail, and yet to suggest the use of vitamin E as one of the natural-based treatment options in the future clinical use.

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Conflict of interest: None

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Ethics statement: None

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