

The Effect Of Vitamin D Replacement Therapy On Serum Leptin And Follicular Growth Pattern In Women With Resistant Polycystic Ovary

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Abstract

Objective: to detect the effect of vitamin D on serum leptin and follicular growth pattern in women with clomiphene citrate resistant polycystic ovary

Methods: 40 female candidates with polycystic ovary syndrome (PCOS) who attended Fayoum university hospital gynecology outpatient clinic. they are divided into two groups Study group Twenty patients received VIT D ,clomiphene and HMG. Control group twenty patients received only clomiphene and HMG. All women are subjected to measurement of leptin and follicular growth before and after treatment. 25 hydroxyvitamin D3 (OHVD3)was done in the study group before and after treatment and in control group only before treatment.

Results: 26 of the patients have deficiency of 25OHVD3 that represent 65% with the mean in the study group(12.74 ± 13.29) and the control group (13.77 ± 24.12) with no statistical difference ($p = 0.868$). There was no significant improvement in the follicular growth in the group treated with VIT D in comparison to the other group (65% vs 55 %) respectively with p value =0.519. There is also no statistically significant difference in leptin level after

treatment in both groups ($P =0.823$).

Conclusion: Vitamin D deficiency is present in about 65% of the PCOS patient. The vitamin D level is not related to BMI, leptin level or FSH level. There is negative correlation between vitamin D level and LH level and FSH\LH ratio. If vitamin D is given with clomiphene citrate and HMG, there was no statistically significant improvement in the follicular growth pattern or leptinlevel. For that reason, it is recommended to do another study on large number of PCOS patients.

Keywords: polycystic ovary syndrome,follicular growth ,leptin and 25 hydroxyvitamin D3 (OHVD3).

INTRODUCTION

Polycystic ovary syndrome (PCOS) is of clinical and public health importance as it is very common, affecting up to one in five women of reproductive age. [1]

In 2003 a consensus workshop sponsored by ESHRE

/ASRM in Rotterdam indicated PCOS to be present if any 2 out of 3 criteria are met: oligoovulation and /or anovulation, and excess androgen activity and polycystic ovaries (by gynecologic ultrasound). [2]

Medical treatment of PCOS is tailored to the patient's goals. Which include Lowering of insulin resistance levels, Restoration of fertility, Treatment of hirsutism or acne and Restoration of regular menstruation.[3]

Vitamin D insufficiency and deficiency are considered serious public health problems. Recent studies demonstrate that vitamin D deficiency may predispose an individual to metabolic bone diseases and to cancer, insulin resistance, metabolic syndrome, type 2 diabetes, cardiovascular diseases and problems in reproductive health [4]

Selimoglu et al discovered that Women with PCOS have mostly insufficient vitamin D levels, and vitamin D replacement therapy may have a beneficial effect on insulin resistance (IR) in obese women with PCOS in a study done in Division of Endocrinology, Malatya State Hospital, Malatya, Turkey.[5]

Leptin plays a key role in regulating energy intake and expenditure, including appetite and hunger, metabolism, and behavior. It is one of the most important adipose – derived hormones[6]

Serum leptin was positively correlated with body mass index (BMI), body weight, serum insulin, serum triglyceride, and serum free testosterone concentrations. Serum leptin was inversely correlated with serum sex hormone binding globulin (SHBG) concentrations. There were no significant correlations between serum leptin and testosterone,

androstenedione, or gonadotropin concentrations.[7]

Patient and Method

40 female candidates with polycystic ovary syndrome who attended Fayoum university hospital gynecology outpatient clinic during 2014. All candidate women were subjected to informed consent after explaining the aim of the search for every patient, then they are divided into two groups Study group Twenty patients received VIT D, clomiphene and HMG. Control group Twenty patients received only clomiphene and HMG.

The inclusion criteria included are BMI more than 25.0 kg/m², the patients diagnosed as PCO by presence of 2 out of 3 criteria which are submitted by ESHRE/ASRM in Rotterdam in 2003 and finally the patients are resistant to induction with clomiphene citrate alone.

The exclusion criteria included are BMI more than 35.0 kg/m² and infertile women due to any factor other than PCO.

The following investigations are done Serum Leptin and Folluciclotometry by Trans- vaginal U/S before and after treatment in both groups. FSH and LH only before treatment in both groups. Serum 25 hydroxy VIT D3 before and after treatment in the study

group and only before treatment in control group.

The Study group received 300.000 I.U single dose of VIT D IM injection and in the next menstrual cycle induction done by clomiphene citrate 100mg daily for 5 days starting from third day of menstruation and HMG single dose on 8th day ,and The Control group received only clomiphene citrate and HMG.

The collected data was organized, tabulated and statistically analyzed using SPSS software statistical computer package version 18 (SPSS Inc, USA).

Results

26 of the patients have deficiency of 25OHVD3 that represent 65% with the mean in the study group(12.74 ± 13.29) and the control group (13.77 ± 24.12) with no statistical

difference (p = 0.868).there is no significant difference between the two groups as regard the basal level of leptin , vitamin D ,FSH, LH and LH/ FSH ratio as present in(**table 1**).

There is negative correlation between basal OHVD3 and LH/FSH ratio and LH level only as shown in (**figure 1 and 2**),and there was no relation between basal OHVD3 and BMI , FSH or leptin.(**table2**)

There is no statistically significant increase in the percentage of the patients who improved in follicular growth in the study group (65%) than the control group (55%) as present in (**table 2**).

There in no significant difference in leptin level before and after TTT between both groups as present in (**table3**)

Table 1 Comparison between the groups in as regard serum hormones and 25 OHVD3 levels

Variable	Study group (20)	Control group (20)	P-value
	Mean ± SD		
FSH	4.69 ± 1.21	± 1.30 ٤.٦٢	0.871 (NS)
LH	8.87 ± 3.83	± 2.84 ٨.٠١	0.452 (NS)
LH/FSH ratio	1.97 ± 0.99	± 0.69 ١.٨٢	0.585 (NS)
Vitamin D	12.74 ± 13.29	13.77 ± 24.12	0.868 (NS)
Leptin	16.32 ± 8.26	16.05 ± 6.32	0.908 (NS)

Table 2 correlation between basal OHVD3 and BMI , FSH ,LH , LH/FSH ratio and serum leptinlevel.

Variables	OHVD3 (before)	
BMI	R	-0.277
	P-value	0.084
FSH	R	0.138
	P-value	0.396
LH	R	-0.339
	P-value	0.033(S)
LH\FSH	R	-0.431
	P-value	0.005(S)
Leptin (before)	R	-0.300
	P-value	0.060

Table 3 Comparison between the groups in the effect of Treatment on folliculargrowth.

Follicular growth after intervention	Study group(20)	Control group(20)	P-value
	Number (percentage)		
Improved	13(65.0%)	11 (55.0%)	0.519 (NS)
Not improved	7 (35.0%)	9 (45.0%)	

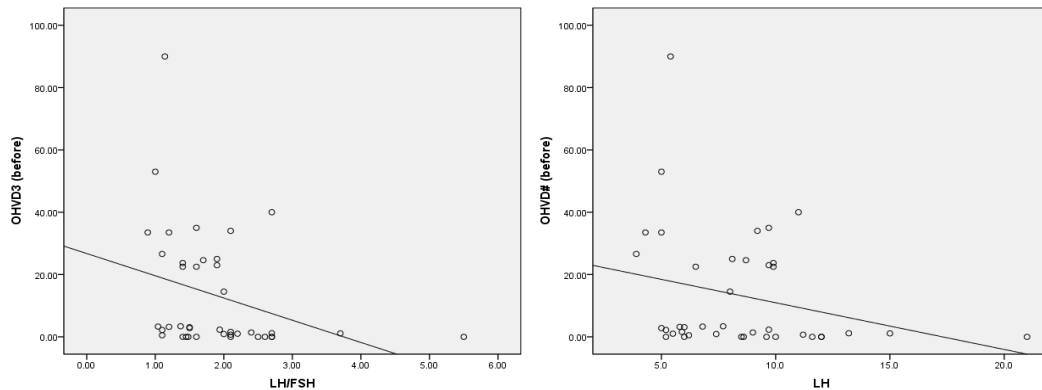
Table 4 Comparison between the groups in the effect of Treatment on serum leptinlevel.

		Study group (20)	Control group (20)	P-value*
		Mean \pm SD		
leptin	Before	16.32 \pm 8.26	16.05 \pm 6.32	0.908 (NS)
	After	16.81 \pm 7.88	16.29 \pm 6.56	0.823 (NS)
P-value**		0.671 (NS)	0.793 (NS)	

* Between study and control group

** Within the groups

Figure 1 and 2: The negative correlation between basal OHVD3 and LH/FSH ratio and LH level only as shown in



Discussion

The results of our study show that 26 of the patients have deficiency of 25OHVD3 that represent 65% of the patients .

Similarly another observational study done on 52 women (25 with PCOs group and 27 without PCOs)found that 25 (OH) D deficiency was present in 44% and 11.2% of subjects in the PCOs and control groups ,respectively. [8]

This study show that there is no significant improvement in the follicular growth in the group treated with VIT D in comparison with the other group (65% vs 55 %).

A randomized clinical trial study including 60 infertile PCOs patients divided in three equal groups showed that the number of the dominant follicles (equal or more than 14 mm) during the 2-3 months of follow up was more in the patients that receive calcium -

VIT D and metformin than those who receives each drug alone [9]also **Bonakdaran S et al in 2012** found that Calcitriol treatment in PCOS may be prior to metformin in ovulation induction in their study which was done on Fifty one untreated PCOS patients after their division into three groups and treatment with calcitriol, metformin, or placebo.[10]

This research also found that level of 25 hydroxyvitamin D3 has negative correlation with LH/FSH and LH level only and no correlation with leptin level ,BMI or FSH level .

On the same side **Firouzabadi Rd et al** in 2012 found no correlation between BMI and 25-OH-VD ($p \geq 0.01$) after his study on 100 PCOS women.Also **Kozakowski J et al 2014** found thatIn PCOs womenwithabdominal obesity vitamin D correlated with LH/FSH ratio (LH/FSH) .[11,12]

Against our study, **Hahn S et al** found that 25-OH-VD concentrations were negatively correlated with body mass index ($r=-0.2765$), body fat ($r=-0.2490$), HOMA-IR ($r=-0.1947$), hyperinsulinemia ($r=-0.1892$) and leptin levels ($r=-0.2834$) in 120 untreated PCOs study women dependant study. [13] And also **Moini et al** found significantly negative correlations of 25(OH)D levels with BMI [14]

Although **Ghadimi R et al** shared our observation about that No significant correlations were found between 25(OH) D levels and FSH, they were against us and proved that no correlation between 25(OH) D levels and LH on their study on 192 Iranian girls between them there was 104 had PCOS and 88 non PCOS. [15]

Conclusion

Vitamin D deficiency is present in about 65% of the PCOS patient. The vitamin D level is not related to BMI, leptin level or FSH level. There is negative correlation between vitamin D level and LH level and FSH/LH ratio. If vitamin D is given with clomiphene citrate and HMG, there was no statistically significant improvement in the follicular growth pattern or leptin level. For that reason, it is recommended to do another study on large number of PCOS patients.

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المخلص العربي

الهدف من الرساله هو معرفه هل هناك تأثير للعلاج بفيتامين (د) على معدل نمو البويضات وهرمون الليبتين في متلازمه المبيض متعدد التكيسات في النساء اللاتي يعانون من عدم استجابته للعلاج بالكوموفين سترات .

وقد اجريت هذه الرساله في مستشفى الفيوم الجامعي بعد اخذ موافقه لجنه اخلاقيات البحث العلمى فى الفتره مابين فبراير ٢٠١٤ حتى يناير ٢٠١٥ على ٤٠ امراه يعانون من متلازمه المبيض متعدد التكيسات .

وتم تصنيف المشاركين في مجموعتين متساويتين. مجموعة الدراسة التي شملت النساء المصابات بمتلازمة المبيض المتعدد التكيسات وتلقى فيتامين د ، كلوموفين سترات ، وهرمون سن اليأس البشرى. والمجموعة الضابطة وتلقت كلوموفين سترات ، وهرمون سن اليأس البشرى فقط.

وبعد التحليل الإحصائي للنتائج، وجدنا أن فيتامين د ليس له تأثير على معدل نمو البويضات الشهرية في مرضى متلازمة المبيض المتعدد التكيسات وليس له تأثير على مستوى الليبتين .