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## **Effect of Chromium Supplementation on Insulin Resistance and Weight Reduction in Polycystic Ovarian Syndrome Cases**

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### **Abstract**

Polycystic ovary syndrome (PCOS) has some degree of insulin resistance .. Chromium picolinate, improves insulin sensitivity at the insulin receptor level without adverse effects but was not tested in ovulation .A randomized controlled study was conducted in shatby Maternity hospital , Alexandria where hundred PCOS cases with body mass index between 30 and 34.5 were divided into two groups: GroupA; 50 cases received chromium 600 mcg and Group B; 50 cases did not receive chromium.All participants received clomiphene citrate for three cycles to induce ovulation and were followed up for: body mass index, follicular maturation and

Pregnancy. There was a statistically significant difference in body mass index , fasting blood sugar, ovulation and pregnancy in the chromium group .

Chromium picolinate improved insulin resistance, ovulation and pregnancy in polycystic ovarian syndrome

**Keywords;** insulin resistance, body mass index , ovulation, pregnancy

## **Introduction**

Polycystic ovary syndrome is a common endocrinological disorder affecting 4-12% of women. Approximately 50% to 70% of all women with polycystic ovary syndrome (PCOS) have some degree of insulin resistance, and this hormone insensitivity probably contributes to the hyperandrogenism that is responsible for the signs and symptoms of PCOS [1], Early detection and treatment of insulin resistance in this population could reduce the incidence or severity of diabetes mellitus, dyslipidemia, hypertension, and cardiovascular disease.

Obesity worsens insulin resistance and is present in 50% of PCOS subjects [2] . Weight loss through diet and exercise is most effective for long-term prevention of type 2 diabetes mellitus (T2DM) and impaired glucose tolerance [3]. Metformin has gained acceptance for treatment of PCOS-associated insulin resistance improving ovulation [4] reducing spontaneous abortion risk [5], reducing hyperandrogenism [6,7] and slow progression of impaired glucose tolerance to type II Diabetes mellitus [1]. The thiazolidinedione insulin sensitizers, rosiglitazone and pioglitazone, are potential alternatives to metformin [7]. Unfortunately, metformin [8] and thiazolidinediones [9-12] could have adverse effects influencing tolerance and compliance. Therefore, it would be ideal to find an effective insulin sensitizer, with few adverse effects, to be used long-term.

Chromium picolinate , a dietary product, improves insulin sensitivity at the insulin receptor level [13] with no adverse effects in human studies [14]. Chromium picolinate consists

of trivalent chromium ( $\text{Cr}^{3+}$ ), an extremely safe [15] and highly tolerable trace mineral that is present in the normal diet [15], complexed to picolinic acid to enhance gut absorption. Picolinic acid naturally occurs in human breast milk. After cleavage of picolinic acid,  $\text{Cr}^{3+}$  is transported by transferrin and later, by chromodulin, its binding protein. This complex binds the insulin receptor [15]. Active glucose transport is enhanced through tyrosine kinase phosphorylation, without inhibition of phosphotyrosine phosphatase [13].

The use of chromium supplements is widespread for the prevention and treatment of diabetes mellitus but there are conflicting reports on efficacy in assisting ovulation stimulation. In the present study, we test the hypothesis that chromium supplementation improves insulin sensitivity in PCOS patients thereby reducing weight and improving ovarian response to stimulation.

### **Registration**

Registration number ; PACTR201506001153655

### **Methods and patients**

A randomized controlled study was conducted in Alexandria, Egypt. Cases having polycystic ovarian syndrome were counseled to participate.,they had a body mass index between 30 and 34.5, diagnosed as having polycystic ovarian syndrome according to the criteria of diagnosis

### **These criteria include**

1-- Gynecologic ultrasonography: According to the Rotterdam criteria:

- 12 or more small follicles should be seen in an ovary on ultrasound examination (16) The follicles may be oriented in the periphery, giving the appearance of a 'string of pearls'.
- Increased size of the ovaries, that is, 1.5 to 3 times larger than normal.

2-Some blood tests :

- Serum FSH and Serum LH.

- The ratio of LH (Luteinizing hormone) to FSH (Follicle stimulating hormone), measured in international units greater than 1:1 <sup>[25]</sup> tested on Day 3 of the menstrual cycle. (16)
- Total testosterone, Free Testosterone
- 2-hour oral glucose test (GTT) after 100 gm oral glucose
- Fasting insulin , fasting blood glucose .
- QUICKI: Quantitative insulin sensitivity check index

### **Sample size calculation**

Based on the assumption that a 2.0 difference (4.40 versus 2.4 )- (17) in mean HOMA-IR (mg/dl X uU/ml /22.5 )would represent a clinically significant difference. A sample size of 50 patients per group is the minimum required sample to detect an effect size of 2 .0 in the primary outcome (HOMA-IR) , as statistically significant with 85% power and at a significance level of 0.05 (two – tailed significance ). (18) The sample size was calculated using IBM SPSS Sample Power Program version 3.0.1

Women who agreed to participate were randomly allocated into two groups:

Group A: 50 cases received chromium in a dose of

Group A: 50 cases received chromium in a dose of 600 mcg in addition to clomiphene citrate for stimulation of ovulation.

Group B :50 cases received only clomiphene citrate

All cases will be examined clinically, where body mass index will be calculated and induction of ovulation will be achieved using clomiphene citrate in a dose of 100mg \ day for five days starting from day 2 of the cycle to be followed up for:

1-changes in body mass index.

2-Follicular growth maturation evaluated by ultra-sonographic scanning starting at day 11 of the cycle.

This will be repeated for three cycles

The results of the present study are presented as comparison between the two main groups

### **Statistical analysis**

The Data was collected and entered into the personal computer. Statistical analysis was done using Statistical Package for Social Sciences (SPSS/version 20) software. Arithmetic mean, standard deviation, for two groups t-test was used. categorized parameters, chi square test was used,  $P < 0.05$  was considered as statistically significant.

**Table 1:** Comparison between the two studied groups regarding the demographic and anthropometric measurements.

The mean age of the patients was  $26.98 \pm 3.84$  in group A and  $27.01 \pm 4.01$  in group B., There was no statistically significant difference in age between the two groups This assures that the age was matched among the studied groups and homogeneously distributed. There was a statistically significant difference in the body mass index between the two groups

**Table 2:** Comparison between the two studied groups regarding follicular scanning.

There was a statistically significant difference in follicular maturation between the two groups .

**Table 3:** Pregnancy rate in the two studied groups

There was a statistically significant difference in the pregnancy rate between the two groups .

**Table 4:** Relation between pregnancy rate and decreasing in BMI.

There was a statistically significant difference between the change in Body mass index and occurrence of pregnancy between the two groups.

### **Discussion**

Serum chromium levels normally range from less than 0.05 up to 0.5 micrograms/milliliter (mcg/mL) [11,12]. Although there is no direct evidence of chromium deficiencies in humans, dietary supplements exist to provide supraphysiological doses of

absorbable chromium<sup>3+</sup>. Chromium<sup>3+</sup> may act clinically by interfering with iron absorption, decreasing the high iron stores that are linked to diabetes and heart disease. [13] Chromium functions as a part of an auto amplification system for insulin signaling and promotes enhancement of insulin sensitivity [14].

Studies suggest that chromium deficiency may increase the risk of cardiovascular diseases, elevate the blood glucose, lipid, and insulin level, and decrease the BMI [14].

While WebMD states that more evidence is needed for chromium's effectiveness in treating PCOS and PCOS symptoms [15] early studies are promising.

A 2006 study published in *Fertility and Sterility* found that chromium picolinate supplements improved blood sugar levels by 38 percent in women with PCOS [16].

Another study, published in the December 2005 issue of *Fertility and Sterility*, found that lower doses of chromium picolinate, 200 µg/d, given to women with Polycystic ovarian syndrome, improved insulin resistance but did not have much effect on hormonal imbalances or ovulation [19].

In the same line, in the study by Lydic *et al* 1000 µg chromium was used daily in PCOS patients for 2 months, but no significant change was found in BMI [20]. Another study (Anderson) also reported no changes in body composition after receiving chromium [21]. Furthermore, in another study by Albarracin *et al* using 600 µg chromium in diabetes mellitus type 2 patients had no significant effect on BMI [22]

In our study, chromium supplementation improved the body mass index. In the chromium group, on the other hand, no change was found in total and free levels of testosterone. Similar results were also obtained by Lydic *et al* and Lucidi *et al*. [19, 20]. However, we cannot provide any explanation for the effect of chromium on testosterone.

Lucidi *et al* used 200 microgram chromium in 6 patients in order to investigate the effect of chromium on ovulation. The study results revealed regulation in menstruation which could be a sign of ovulation [19].

In our study using chromium improved follicular response to stimulation proved by follicular scanning and the higher pregnancy rate in the group receiving chromium.

**Table 1: Comparison between the two studied groups regarding the demographic and anthropometric measurements.**

	Group A	Group B	P
Age	26.98±3.84	27.01±4.01	0.521
BMI before treatment	32.74±1.52	32.96±1.00	0.108
BMI after treatment	31.86±2.04	32.45±1.2	0.076
Percent change of BMI	-2.74±2.73	-1.54±1.66	0.033*

**Table 2: Comparison between the two studied groups regarding follicular scanning.**

	Group A		Group B		P
	No.	%	No.	%	
<b>Cycle 1</b>					
Good	14	56.0	15	60.0	0.213
Poor	11	44.0	10	40.0	
<b>Cycle 2</b>					
Good	11	44.0	7	28.0	0.238
Poor	14	56.0	18	72.0	
<b>Cycle 3</b>					
Good	4	16.0	1	4.0	0.15
Poor	21	84.0	24	96.0	

**Table 3: Pregnancy rate in the two studied groups**

	Group A		Group B	
	No.	%	No.	%
Yes	5	20.0	2	8.0
No	20	80.0	23	92.0
p	0.22			

**Table 4: Relation between pregnancy rate and decreasing in BMI.**

	Pregnant	Non pregnant	P
<b>BMI before chromium</b>			
Mean	31.9	33.01	0.013
S.D.	1.0	1.25	
<b>BMI After chromium</b>			
Mean	30.1	32.50	0.001*
S.D.	1.4	1.48	
<b>Percent of change in BMI</b>			
Mean	-5.7	-1.56	0.0015*
S.D.	2.8	1.63	

### **Conclusion**

Chromium supplementation in polycystic ovarian syndrome could have a role in increasing the insulin resistance and thereby decreasing blood glucose level and bodymass index which could improve response to stimulation of ovulation and increase the pregnancy rate.

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