Original Study

The Effect of Chromium Supplementation on Polycystic Ovary Syndrome in Adolescents

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A B S T R A C T

Background: Polycystic ovary syndrome (PCOS) is a common condition. Treatment with chromium has been shown to improve insulin sensitivity in adults with PCOS. Treatment of adolescents with PCOS remains a challenge.
Objective: To investigate the effect of chromium supplementation on the various components of polycystic ovary syndrome in adolescent girls.
Patients and Methods: Thirty-five adolescent girls with PCOS were enrolled. History of menstrual irregularities was recorded. All underwent physical examination for presence of acne, scoring of hirsutism, and calculation of body mass index. Pelvic ultrasonography was done and serum free testosterone was measured in all subjects. All subjects received 1000 μg chromium picolinate for 6 months followed by re-evaluation.
Results: Mean (SD) age was 15.5 (1) years (range: 14-17 y). No significant change in BMI standard deviation score (SDS) with chromium supplementation was noted (1.9 (0.7) SDS vs 2 (0.7) SDS, $P = .638$). The number of patients with oligo/amenorrhea decreased with treatment (29/35 (83%) versus 11/35 (31%), $P < .001$). Significant reduction in mean ovarian volume ($P < .001$), total follicular count ($P < .034$), and free testosterone ($P < .002$) was observed. No significant improvement in acne or hirsutim was noted.
Conclusion: Supplementation with chromium to adolescents with PCOS is a promising treatment option.
Key Words: Polycystic ovary syndrome, Adolescents, Chromium

Introduction

Polycystic ovary syndrome (PCOS) is a condition characterized by hyperandrogenism, menstrual irregularities, and polycystic ovaries. It affects 6%-8% of women in the reproductive age.[1,2] Its prevalence among adolescents varies between populations and according to criteria used for definition.[3] Prevalence rates of 8%, 18%, and 26% are reported from different populations,[3–5] PCOS risk is increased among obese patients. Obesity, particularly with abdominal fat distribution, is observed in 50% of women with PCOS.[6] Since obesity starts in early life, obese adolescents are a high risk population for PCOS.[6]

The etiology of PCOS remains unclear. Studies increasingly show that epigenetic, genetic, and environmental factors interact.[7,8] Insulin resistance is implicated in the pathogenesis of PCOS especially among obese girls,[9] and at the same time PCOS is associated with increased incidence of glucose intolerance,[7] and metabolic syndrome[5,10] Thus which starts first is largely unknown. Insulin sensitizers have a positive effect on obesity, ovarian morphology, insulin sensitivity, and hyperandrogenemia in PCOS, and are used in its treatment.[9]

The role of trace elements in the pathogenesis of many diseases including PCOS has recently been elucidated.[11] Lucidi et al showed that chromium picolinate supplementation in adults with PCOS improves glucose tolerance, and may further improve insulin sensitivity and ovulation rates.[12] Chromium picolinate consists of trivalent chromium, a trace element combined with picolinic acid to improve its gut absorption. No adverse effects are reported with high levels of intake of chromium picolinate.[13] The dose and duration of chromium supplements needed in this regard remain unknown. The aim of this study is to investigate the effect of chromium supplementation on the various components of polycystic ovary syndrome in adolescent girls.

Patients and Methods

Thirty-five girls were recruited from the Obesity Clinic of Ain-Shams University Hospital, Paediatric Department and from the Gynaecology Clinic of Bab El-Shareya University Hospital in Cairo during the period from 1st July, 2012 until 25th September, 2013. Inclusion criteria included age less than eighteen years, menarche for at least 2 years, and established diagnosis of polycystic ovary syndrome according to the revised 2004 Rotterdam Consensus Workshop Criteria.[14] Patients were diagnosed with PCOS if they had 2 out of 3 of the following criteria:

1. Oligo/amenorrhea: oligomenorrhea was defined as menstrual cycles ≥ 45 days, and amenorrhea was defined as absence of menstruation for ≥ 90 days.[15]
2. Enlarged polycystic ovary on ultrasonography: defined as one or more ovary with a volume > 10 cm^3 or 12 or more follicles between 2 and 9 mm diameter.[16]
3. Clinical and/or biochemical hyperandrogenism: Clinical hyperandrogenism (HA) included acne or hirsutism.[14]

The authors indicate no conflicts of interest.

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Hirsutism was defined by a Ferriman-Gallwey (FG) score of ≥8.[17] Acne was assessed according to severity.[18] Biochemical HA was defined by elevated levels of free testosterone (FT).[14]

Menstrual irregularities were ascertained by recalling menstrual pattern in the preceding year. All subjects underwent physical examination including assessment for the presence of acne and hirsutism, measurement of weight, height, and calculation of body mass index (BMI). Overweight was defined as BMI ≥85th percentile for age and sex, and obesity was defined as BMI ≥95th percentile for age and sex. BMI Standard deviation scores (SDS) were calculated.[19]

Conditions including congenital adrenal hyperplasia, adrenal tumors, Cushing syndrome, thyroid gland dysfunction, hyperprolactinemia were excluded. Patients on multivitamins, food supplements, and insulin sensitizers were excluded. All patients and their families signed an informed consent prior to participation in the study. The study protocol was approved by the local ethics committee of Ain-Shams and Al-Azhar University Hospitals.

Ultrasonographic Evaluation

All subjects underwent transabdominal pelvic ultrasonography as part of their PCOS diagnostic workup in the early follicular phase (Days 2-4 of their menstrual cycle). The images were obtained using a General Electric LOGIQ Pro P5 ultrasonography machine with a curved 5 mHz transducer. Ultrasonographic examination was performed by a senior gynecologist. Ovarian volume was calculated using the prolate ellipsoid formula: volume = length × width × thickness × π/6.

Biochemical Evaluation

Venous samples were withdrawn for determination of free testosterone, thyroid function, prolactin level, and 17 hydroxy progesterone. Serum free testosterone level was measured by a commercially available kit (EIA-2924, DRG International, Springfield, NJ) using the principle of competitive immunoenzymatic colorimetric assay; normal values were at a range of 0.2-4.2 pg/ml.

Chromium Supplementation

All subjects received a supply of 200 μg chromium picolinate capsules. Each patient was instructed to ingest 1 capsule 5 times daily for 6 months, and all were instructed to complete a diary for the intake. Patients were asked to report adverse effects such as watery diarrhea, vertigo, headache, and urticaria.

Re-evaluation

All subjects were invited for re-evaluation after 6 months or sooner if they had any unusual symptoms that could be considered as side effects. The intake diary was reviewed to check compliance. Menstrual pattern was re-assessed using a calendar that all participants were asked to fill during the 6 months of treatment with chromium. Physical examination for assessment of acne and scoring of hirsutism was performed. Body mass index was recalculated according to weight and height measurements. Ultrasonographic examination for polycystic ovarian morphology was repeated, and serum free testosterone level was re-measured.

Statistical Analysis

The data were analyzed by SPSS statistical software (version 17.0, SPSS Inc, Chicago, IL). Descriptive statistics are expressed as mean, standard deviation (SD). Paired Student t tests were performed for comparison between the mean values for parametric data. McNemar test was used for comparison of paired proportions. For all tests a probability P less than .05 was considered significant while $P = .01$ and .001 were highly significant.

Results

Mean (SD) age of patients at time of presentation was 15.5 (1) years (min-max: 14-17 y). Twenty-two patients (63%) were obese, 8 (23%) were overweight, and 5 (14%) were of normal weight. Mean (SD) BMI at presentation was 1.9 (0.7) SDS. No significant change in BMI SDS was noted after 6 months of treatment with chromium (mean (SD) BMI: 2 (0.7) SDS, $P = .638$). See Table 1. All patients were compliant on treatment and none of them reported adverse effects.

Six patients (17%) had regular periods at presentation. Twenty-three patients (66%) had oligomenorrhea before treatment of whom 7 patients (7/23, 30%) remained with oligomenorrhea after treatment, and 16 had regular periods (16/23, 70%). Amenorrhea was reported by 6 patients (17%) before treatment, 2 of which had regular periods after 6 months of treatment (2/6, 33%), and 4 patients became oligomenorheic (4/6, 67%). Total number of patients with regular periods significantly increased with treatment ($P < .001$). See Table 1.

No improvement in acne or hirsutism was noted with treatment (Table 1). F-G score of ≥8 was observed in 18 patients (51%) before treatment and in 17 patients (49%) after chromium intake.

Mean ovarian volume was >10 cm^3 in 19 patients (54%) before treatment and in 12 patients (34%) after treatment. Ovarian volume decreased to 10 cm^3 or less in 10 patients (10/19, 53%) who originally had ovaries > 10 cm^3. The change in mean ovarian volume with treatment was highly

Table 1
Clinical, Ultrasonographic, and Biochemical Parameters before and after Treatment with Chromium

	Before Chromium	After Chromium	*P* Value
BMI SDS, mean ± SD	1.9 ± 0.7	2 ± 0.7	.638
Acne, n (%)	25/35 (71.4)	20/35 (57.1)	.063
Ferriman-Galwey score, mean ± SD	8.1 ± 2.4	7.9 ± 2.3	.107
Oligo/amenorrhea, n (%)	29/35 (82.9)	11/35 (31.4)	<.001
Mean ovarian volume, cm^3, mean ± SD	10.6 ± 1.3	9.8 ± 1.2	<.001
Total follicle number 2-9 mm, mean ± SD	20.7 ± 3.4	19.5 ± 3.9	.034
Free testosterone, pg/mL, mean ± SD	6.9 ± 1.4	6.3 ± 1.3	.002

BMI, body mass index; SD, standard deviation; SDS, standard deviation score.