Use of Metformin versus Chromium Picolinate in the Management of Polycystic Ovarian Syndrome: A Randomized Controlled Clinical Trial

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Abstract

Objective: To compare the effects of metformin and chromium picolinate on females with polycystic ovarian syndrome.

Background: Polycystic ovarian syndrome is the most common endocrinopathy of reproductive-aged women. It presented with excessive hair growth(hyperandrogenism), menstrual irregularities (anovulation), and polycystic ovaries.They are commonly accompanied by obesity, insulin resistance, and infertility.

Methods: Sixty female patients with polycystic ovarian syndrome were enrolled for our study at Suez Canal University Hospitals, from January 2016 to December 2016. They were randomly assigned into 2 groups. FSH, LH, testosterone, TSH, prolactin, fasting blood sugar, fasting insulin, QUICKI, HOMA-IR were measured for all patients. The first group received metformin 500 mg twice daily while the other group received chromium picolinate 200 µg once daily for 3 months.

Results: Fifty-four patients completed the study, we compared the effect of metformin and chromium in patients with PCOs, it showed significant difference regarding free testosterone, serum prolactin (p=0.01), FSH level, FBS, Fasting insulin and QUIKI between the two groups (p=0.001).

In Group I, there was significant difference regarding the values of BMI, free testosterone, TSH, fasting blood sugar, fasting insulin, HOMA-IR, QUICKI, ovarian volume(p <0.001)prolactin (p=0.01), and hirsutism score (0.02) before and after treatment with metformin. In Group II, there were significant differences regarding the values of testosterone (p=0.01), BMI LH, FSH, TSH, fasting blood sugar, fasting insulin, HOMA-IR, QUICKI, ovarian volume and hirsutism score before and after treatment with chromium picolinate(p =0.001).

After treatment, twenty-two (81.48%) patients had normal menstruation in Group I compared to 24 (88.89%) patients in Group II (p=0.35) meanwhile, 11(40.7%) patients had normal ovulation in Group I compared to 12 (44.4%) patients in Group II (p=0.78). Pregnancy occurred in 6 (22.2%) patients in group I and 5 (18.5%) patients in Group II with no significant difference (p=0.73). After 3 months of treatment, there were no significant differences between the groups regarding the side effects except abdominal discomfort which was more significant with metformin (p= 0.018).

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Conclusion: Chromium picolinate was better tolerated than metformin due to lower side effects; nevertheless, no significant differences were observed between the two groups regarding ovulation and pregnancy rates. Therefore, metformin could be replaced by chromium in some PCOS patients.

Key words: Polycystic Ovarian Syndrome – metformin – Chromium Picolinate

Introduction

Polycystic ovarian syndrome (PCOS) is the most common endocrinopathy of reproductive-aged women, affecting 6–8% of this population (1). The major clinical features are excessive hair growth (hyperandrogenism), menstrual irregularities (anovulation), and polycystic ovaries. This triad of symptoms is commonly accompanied by obesity, insulin resistance, and infertility (2).

The biguanide, metformin (dimethylbiguanide), was introduced in 1957 as an oral glucose-lowering agent to treat non-insulin dependent diabetes mellitus (3). For women who remain anovulatory with such simple measures, metformin therapy was found to be as effective as treatment with gonadotrophins but without the associated risk factors of multiple pregnancy and Ovarian Hyperstimulation Syndrome (4).

Chromium picolinate, consists of trivalent chromium, is an extremely safe and highly tolerable trace mineral which is present in normal diet and is combined with picolinate acid in order to enhance gut absorption (5). It effectively reduces insulin resistance and treats hyperinsulinemiaas well as hyperandrogenemia but it did not significantly affect the hormonal changes (6). In the women with PCOS, chromium picolinate (200 μg daily) improved the glucose tolerance but did not improve ovulation or hormonal profiles (7).

Amooee et al. (2013) compared the effect of combination of clomiphene + metformin and clomiphene + chromium picolinate on ovulation induction and pregnancy rate in clomiphene citrate-resistant patients with PCOS. They concluded that chromium picolinate was better tolerated compared to metformin (8). So, we aimed to compare the effects of metformin and chromium on patients with polycystic ovarian syndrome.

PATIENTS AND METHODS

Amooee et al. (2013) compared the effect of combination of clomiphene + metformin and clomiphene + chromium picolinate on ovulation induction and pregnancy rate in clomiphene citrate-resistant patients with PCOS. They concluded that chromium picolinate was better tolerated compared to metformin (8). So, we aimed to compare the effects of metformin and chromium on patients with polycystic ovarian syndrome.

This prospective randomized controlled clinical trial was conducted at Gynecology outpatient clinic, Suez Canal University Hospitals. The study was approved by faculty of medicine, Suez Canal University and an informed written consent was obtained from all participants. The study included 60 female patients with polycystic ovarian syndrome in the period from January 2016 to December 2016.Six patients were lost during follow-up, so they were excluded from the study (Fig.1).

The inclusion criteria included patients with age ranging from 18 to 30 years and fulfilling two out of three of the criteria in diagnosis of PCOS according to the revised Rotterdam Consensus Workshop Criteria (9); Chronic anovulation, Clinical and/or biochemical evidence of androgen excess and Polycystic-appearing ovaries on transvaginal ultrasound. Patients were excluded if they had kidney disorders (metformin and chromium picolinate excreted via the kidney), diabetes, adrenal tumors, Cushing's syndrome, Thyroid gland dysfunction, Hyperprolactinemia, Lung diseases, Liver diseases or Heart failure. Patients received oral contraceptives in the past 2 months were excluded from the study.Semen analysis for the husband was done to exclude medical problem for the husband.

Thorough examination was done to all patients, hirsutism was assessed according to the modified Ferriman-Gallwey score (9 body locations) (10) and Body mass index (BMI) was calculated.

On the third day of a spontaneous or induced/ cycle and after 8 hours of overnight fasting (at 9 am in the morning), Serum FSH, LH, total testosterone, free testosterone, prolactin, fasting blood sugar (FBS) and fasting Insulin were done. Oral Glucose Tolerance test was performed. Insulin sensitivity was assessed through quantitative insulin sensitivity check index (QUICKI) defined as 1/ [log (fasting insulin) + log (fasting glucose)] while insulin resistance was assessed by Homeostasis model assessment (HO-

MA-IR) defined as [fasting glucose - fasting insulin] / 22.5 (11). All the hormonal assays were performed twice at baseline and after 3 months of treatment.

Baseline transvaginal ultrasound was done,ultrasonographic criteria used for the diagnosis of PCOS were the presence of 12 or more 2–9-mm ovarian follicles, a peripheral distribution of ovarian follicles (necklace appearance), the increased echogenity or surface of ovarian stroma on a cross-sectional cut, anovulation and endometrial thickness and an ovarian volume of more than 10 cm3.Sixty patientswere randomly (using a computer-based random digit generator) assigned to one of the two groups.Fifty-four completed the study, Group I included 27 patients received metformin 500 mg twice daily for 3 months in the form of Cidophage Tablets (Manufactured by CID Company) and group II included 27 patients received chromium picolinate 200 µg once daily for 3 months in the form of Chromium Capsules (Manufactured by MepacoMedifood Company). Women were evaluated for possible side effects of therapy including abdominal discomfort, vomiting, diarrhea, indigestion, headache, nausea, and loss of appetite. β-HCG was checked for detection of pregnancy 1 week after the missed period. If β-HCG level was >25 (by the vidas method), the patient was considered pregnant and medications were discontinued.

Statistical analysis

All data were collected, tabulated and statistically analyzed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Continuous Quantitative variables were expressed as mean ± SD and range while Categorical Qualitative variables were expressed as number and percentage.Two sample t-test(paired and unpaired) were used to test the significance of difference for quantitative variables while the Chi-square test was used to test the significance for qualitative variables. A probability value (p-value) < 0.05 was considered statistically significant.

RESULTS

Our study included fifty-four patients with PCOS, the first group received metformin and the second group received Chromium picolinate for 3 months.

Demographically, the mean age was 27.1 ± 3.3 and 27.9 ± 3.0years ingroup I and Group II respectively, with no statistically significant difference (p=0.33). The mean BMI was 30.8 ± 2.5 kg/m3 in Group I and 30.7 ± 2.3 kg/m3 in Group II. There were no significant differences between both groups regarding body mass index (p=0.87). Nulliparous women were 62.96% in group I and 55.56% in Group II, there was no significant difference in parity between the two groups (p=0.6) or duration of infertility (p=1.0).Regarding menstrual pattern among the studied groups, only 11.1 % had normal menstrual cyclein group I and 7.5%in group II. The difference was not statistically significant (p=0.94). (Table 1).

There were no significant differences between groups inthe hirsutism score (p=0.17), free testosterone (p= 0.43), luteinizing hormone (p= 0.36), thyroid stimulating hormone (p= 0.14), serum prolactin (p= 0.39), fasting blood sugar (p= 0.49), fasting insulin (p= 0.59), QUICKI (p= 0.36), HOMA-IR (p= 0.64) and ovarian volume (p= 0.32) before treatment (Table 2).

Table (3) compared the effect of metformin and chromium in patients with PCOs, it showed significant difference regarding free testosterone, serum prolactin (p=0.01), FSH level, FBS, Fasting insulin and QUIKI between the two groups (p=0.001).

In Group I, there was significant difference regarding the values of BMI, free testosterone, TSH, fasting blood sugar, fasting insulin, HOMA-IR, QUICKI, ovarian volume(p <0.001)prolactin (p=0.01), and hirsutism score (0.02) before and after treatment with metformin (table 4), while no difference was found in the values of LH and FSH. In Group II, there were significant differences regarding the values of testosterone (p=0.01), BMI LH, FSH, TSH, fasting blood sugar, fasting insulin, HOMA-IR, QUICKI, ovarian volume and hirsutism score before and after treatment with chromium picolinate(p =0.001). There was no difference regarding the values of prolactin (Table 5).

After treatment, twenty-two (81.48%) patients had normal menstruation in Group I compared to 24 (88.89%) patients in Group II with no significant difference (p=0.35). 11(40.7%) patients had normal ovulation after treatment in Group I compared to 12 (44.4%) patients in Group II with no significant difference (p=0.78). Pregnancy occurred in 6 (22.2%) patients in group I and 5 (18.5%) patients in Group II with no significant difference (p=0.73) (Table 6). After 3 months of treatment, there were no significant differences between the groups regarding side effects as nausea, indigestion, vomiting, diarrhea, loss of appetite or headacheonly, abdominal discomfort was more significant with metformin (p= 0.018).

Fig. 1 the flowchart of the studied population.

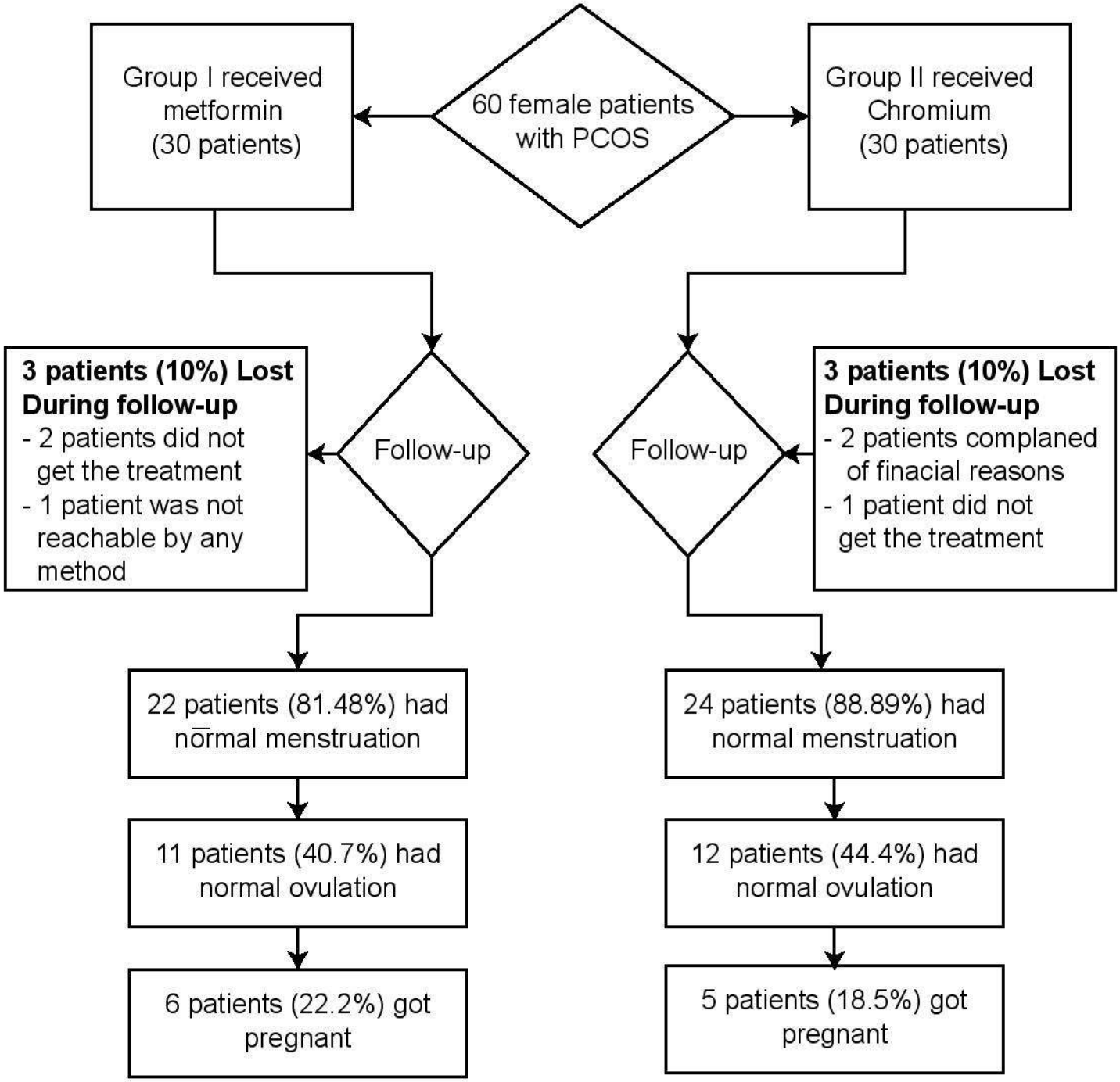

Table (1): Comparison between metformin and chromium picolinate groups regarding demographic characters.

Title		Metformin (n=27)		Chromium (n=27)		P value
		No.	%	No.	%	
Parity	Nulipara	**17**	**62.96**	**15**	**5.56**	**0.6NS**
	Para 1	**6**	**22.22**	**5**	**18.52**	
	Para ≥2	**4**	**14.81**	**7**	**25.93**	
Age (years)	22-26 Y	**13**	**48.15**	**10**	**37.04**	**0.69NS**
	27-31 Y	**11**	**40.74**	**14**	**51.85**	
	32-35 Y	**3**	**11.11**	**3**	**11.11**	
	Mean±SD	**27.56±3.36**		**27.93±3.16**		**0.33 NS**
BMI (kg/m2)	Mean ±SD	**30.83±2.52**		**30.73±2.30**		**0.87 NS**
Infertility duration	Mean±SD	**2.7±1.1**		**2.76±1.3**		**1.0 NS**
Menstrual pattern	Normal N (%) Oligomenorrhea Amenorrhea Irregular	**2 (7.41)** **8 (29.63)** **6 (22.22)** **11 (40.74)**		**3 (11.11)** **7 (25.93)** **5 (18.52)** **12 (44.44)**		**0.94 NS**

NS: Not statistically significant difference

Table (2): Comparison between metformin and chromium picolinate groups regarding baseline hormonal profile, hirsutism, FBS, fasting insulin, and ovarian volume.

Title	Metformin (n=27)		Chromium (n=27)		P value
	Mean	SD	Mean	SD	
Hirsutism Score (0-36)	22.74	7.52	19.63	8.91	0.17NS
F.Testosterone (ng/dl)	2.67	0.51	2.57	0.41	0.43 NS
LH (mIU/ml)	9.10	1.43	8.70	1.73	0.36 NS
FSH (mIU/ml)	6.60	0.82	7.07	1.43	0.14 NS
TSH (µg/dl)	3.55	0.61	3.24	0.71	0.09 NS
Prolactin (ng/dl)	8.15	2.87	8.81	2.74	0.39 NS
FBS (mg/dl)	115.89	10.02	114.00	9.77	0.49 NS
Fasting insulin (µU/ml)	16.30	3.16	15.80	3.57	0.59 NS
Homa-IR	4.43	0.52	4.37	0.44	0.64 NS
QUICKI	0.31	0.01	0.31	0.01	0.36 NS
Ovarian Volume (cm3)	11.70	1.83	12.10	0.92	0.32 NS

NS: Not statistically significant difference

Table (3): Comparison between metformin and chromium picolinate groups after treatment regarding hormonal profile, hirsutism, FBS, fasting insulinand ovarian volume.

Title	Metformin (n=27)		Chromium (n=27)		P value#
	Mean	SD	Mean	SD	
BMI (kg/m2)	28.51	2.44	28.60	2.35	0.89 NS
Hirsutism Score (0-36)	7.07	4.90	5.52	3.26	0.18 NS
F. Testosterone (ng/dl)	2.10	0.31	2.50	0.38	0.01*
LH(mIU/ml)	9.08	1.22	8.60	1.53	0.21NS
FSH(mIU/ml)	6.50	0.51	4.64	1.17	0.001*
TSH(µg/dl)	3.20	0.31	3.05	0.41	0.13 NS
Prolactin(ng/dl)	7.37	1.87	8.63	1.61	0.01*
FBS(mg/dl)	95.22	7.36	79.81	5.98	0.001*
Fasting insulin (µU/ml)	12.70	2.01	9.10	2.24	0.001*
Homa-IR	3.67	0.32	3.14	0.28	0.001*
QUICKI	0.32	0.01	0.35	0.01	0.001*
Ovarian volume (cm3)	8.37	2.96	8.09	2.28	0.71 NS

* Statistically significant difference
NS: Not statistically significant difference

Table (4): Comparison of metformin group before and after treatment regarding hormonal profile, infertility, hirsutism, FBS, fasting insulin, and ovarian volume.

Title	Before treatment (n=27)		After treatment (n=27)		P value#
	Mean	SD	Mean	SD	
BMI (kg/m2)	30.83	2.52	28.51	2.44	0.001*
Hirsutism Score (0-36)	22.74	7.52	7.07	4.90	0.02*
F. Testosterone (ng/dl)	2.67	0.51	2.10	0.31	0.001*
LH(mIU/ml)	9.10	1.43	9.08	1.22	0.92 NS
FSH(mIU/ml)	6.60	0.82	6.50	0.51	0.33 NS
TSH(µg/dl)	3.55	0.61	3.20	0.31	0.001*
Prolactin(ng/dl)	8.15	2.87	7.37	1.87	0.01*
FBS(mg/dl)	115.89	10.02	95.22	7.36	0.001*
Fasting insulin (µU/ml)	16.30	3.16	12.70	2.01	0.001*
Homa-IR	4.43	0.52	3.67	0.32	0.001*
QUICKI	0.31	0.01	0.32	0.01	0.001*
Ovarian volume (cm3)	11.70	1.83	8.37	2.96	0.001*

*Statistically significant difference
NS: Not statistically significant difference

Table (5): Comparison of chromium picolinate before and after treatment regarding hormonal profile, infertility, hirsutism, FBS, fasting insulinand ovarian volume.

Title	Before treatment (n=27)		After treatment (n=27)		P value#
	Mean	SD	Mean	SD	
BMI (kg/m2)	30.73	2.30	28.60	2.35	0.001*
Hirsutism Score (0-36)	19.63	8.91	5.52	3.26	0.001*
F. Testosterone (ng/dl)	2.57	0.41	2.50	0.38	0.01*
LH(mIU/ml)	8.70	1.73	8.60	1.53	0.60 NS
FSH(mIU/ml)	7.07	1.43	4.64	1.17	0.001*
TSH(µg/dl)	3.24	0.71	3.05	0.41	0.10 NS
Prolactin(ng/dl)	8.81	2.74	8.63	1.61	0.61NS
FBS(mg/dl)	114.00	9.77	79.81	5.98	0.001*
Fasting insulin (µU/ml)	15.80	3.57	9.10	2.24	0.001*
Homa-IR	4.37	0.44	3.14	0.28	0.001*
QUICKI	0.31	0.01	0.35	0.01	0.001*
Ovarian volume (cm3)	12.10	0.92	8.09	2.28	0.001*

*Statistically significant difference
NS: Not statistically significant difference

Table (6): Comparison between metformin and chromium picolinate groups regarding ovulation and pregnancy rates.

Title		Group I	Group II	p value
Menstrual pattern	Regular Irregular	22(81.49%) 5 (18.5%)	24 (88.89%) 3 (11.1%)	0.35NS
Ovulation Rate	Yes	11 (40.7%)	12 (44.4%)	0.78NS
	No	16 (59.3%)	15 (55.6%)	
Pregnancy Rate	Yes	6 (22.2%)	5 (18.5%)	0.74NS
	No	21 (77.8%)	22 (81.5%)	

NS: Not statistically significant difference

DISCUSSION

Polycystic ovary syndrome (PCOS) is the usual cause of anovulatory infertility. Induction of ovulation with clomiphene citrate (CC) was reported in the 1960s with ovulation rate of 75-80% and a cumulative pregnancy rate of 70-75% after 6-9 cycles of treatment (12).

The use of metformin in the treatment of PCOS was started in 1998 by Nestler and colleagues with some skepticism (13) but it is now accepted to be a valuable and inexpensive therapeutic modality (14). Lord and colleagues have indicated that metformin is highly effective in inducing ovulation and increasing pregnancy rates (15).

As data regarding the use of chromium picolinate are not well established so this current research was done in order to compare the effect of metformin and chromium picolinate on ovulation induction and pregnancy rate in patients with PCOS.

In the study, age ranged from 22 to 35 years (27.1 ± 3.3 years in Group I and 27.9 ± 3 years in Group II). There was no considerable variation ($p > 0.05$).

These results are comparable to those reported by Roy et al. (2009) who reported that, the mean age in first group was 28.2±0.7 compared to 28.8±0.9 years in second group with statistically non-significant difference between both groups (16). Amooee et al., (2013) found that the mean age of the patients was 26.9±5.1 (range 18-38) years (8).

Due to the random distribution of the patients into the 2 groups in this work, there were no significant differences between both groups regarding baseline characteristics, menstrual pattern, hirsutism score and laboratory investigations

In the current study, 22 (81.48%) patients had normal menstruation in Group I and 24 (88.89%) patients in Group II after 3 months of treatment, with no significant difference. Haas et al., (2003) concluded that some (but not all) women with PCOS had improvements in their menstrual cycles while on metformin (17). The effect of metformin on regulation of the menstrual period has also been reported by Kazerooni and Dehghan-Kooshkghazi, (2003) (18). Lucidi et al., (2005) revealed regulation in menstruation after administration of 200 microgram chromium (7).

In our study, ovulation occurred in 11(40.7%) patients in Group I and 12(44.4%) patients in Group II. Metformin has nearly the same effect as chromium on the pregnancy rate. In the study done by Amooee et al., (2013), among those who received chromium picolinate, 22(47.8%) patients ovulated during the study period and 9(19.6%) patients conceived. Also, 20 (43.5%) patients of the metformin group ovulated and 10 (21.7%) conceived during the study period. They concluded that metformin had the same effect as chromium on the pregnancy rate (8). Aruna et al., (2004) stated that using metformin improved ovulation and the pregnancy rate (19) while Lucidi et al., (2005) suggested that regulation in menstruation could be a sign of ovulation (7).

In our study, a significant decrease was observed in BMI in Group I ($p < 0.001$). In the study by Kazerooni and Dehghan-Kooshkghazi, (2003), 500 mg metformin was used three times a day. The decrease in BMI was completely overt (18). Also, Aruna et al., (2004) also conducted a study using 500 mg metformin two times a day in 50 patients and reported a decrease in BMI (19) In contrast, no decrease in BMI was observed in PCOS patients in the study by Genazzani et al., (2004) which used 500 mg metformin two times a day for 6 months (20). In Group II, the difference was also significant between pre and post treatment with chromium for 3 months ($p < 0.001$). In contrast to the present study,Lydic et al., (2006), 1000 μg chromium was used daily in PCOS patients for 2 months, but no significant change was found in BMI (5). In Anderson (1998), no changes in body composition after receiving chromium were encountered (21).

In the current study, there were significant differences in the values of free testosterone, TSH, prolactin, fasting blood sugar and fasting insulin in Group I before and after treatment with metformin. In Group II, the difference was significant in free testosterone, LH, FSH, TSH, fasting blood sugar and fasting insulin.

In Amooee et al., (2013) study, the serum levels of free testosterone decreased by 0.2 and 1.1 in chromium and metformin groups, respectively and the difference was statistically significant (8). The decreasing effect of metformin on testosterone was reported by Kolodziejczyk et al., (2000) (22). No changes were observed in testosterone level in the study by Aruna et al., (2004) (19). Similar results were also obtained by Genazzani et al., (2004) who had conducted their study on non-obese patients (20). In the chromium group, no change was found in free levels of testosterone by Lucidi et al., (2005) and Lydic et al., (2006) (5,7).

Metformin is known to decrease FBS, fasting insulin and QUICKI index and similar results were also achieved in our study. On the contrary, these findings were not reported by Genazzani et al., (2004) which could be due to the low body weight of their study patients (20). Also,Aruna et al., (2004), found no decrease in FBS, fasting insulin and QUICKI index (19), while Kazerooni and Dehghan-Kooshkghazi, (2003) showed using metformin to be effective in decreasing FBS (18). Cabezas et al., (2012) observed an improvement in HOMA-IP in metformin group as in our study (23).

Hummel et al., (2007) have confirmed the effectiveness of chromium in decreasing FBS, HbA1C, fasting and 2 hours insulin in the patients and insulin sensitivity. They stated that Chromium picolinate improved insulin sensitivity as measured by

QUICKI index at the insulin receptor level and, at the elevated level of intake, was devoid of adverse effects in human studies (24). In our study, insulin resistance as measured by HOMA-IR index was improved after chromium administration. Also, Lydic et al. (2006) have shown some improvement in insulin resistance following the use of chromium (5) while Ali et al., (2011) did not observe any change in HOMA-IR after 6 months of chromium when they compared it with placebo (25).

Badawy and Elnashar, (2011) observed that chromium picolinate effectively reduced insulin resistance and HOMA-IR index and treated hyperinsulinemia as well as hyperandrogenemia. They concluded that chromium picolinate (200 µg daily) improved the glucose tolerance in women with PCOS but did not improve ovulation or hormonal profiles (6).

There were significant reductions in ovarian volumes in both groups. In Group I, it was 11.7 ± 1.8 ml before treatment and 8.37 ± 2.91 ml after treatment ($p < 0.001$). In Group II, the ovarian volume was 10.9±1.5 ml before treatment and 9.7 ± 1.24 ml after treatment ($p < 0.001$). Sanoee et al., (2011) investigated the possible effects of metformin administration in women with PCOS on the ovarian volume. The mean ovarian volume was 11.2 ± 4.31 ml before treatment. After three months of treatment the mean ovarian volume declined to 8.17 ± 3.71 ml (p 0.001). They concluded that metformin therapy, even in a relatively short time such as three months, in patients with PCOS may cause a decrease in the ovarian volume by decreasing intraovarian stromal androgens (26). In Amr and Abdel-Rahim, (2015) study, the mean ovarian volume was >10 cm3 in 19 (54%) patients before treatment and in 12 (34%) patients after treatment with chromium. Ovarian volume decreased to 10 cm3 or less in (10/19, 53%) patients who originally had ovaries >10 cm3. The change in mean ovarian volume with treatment was highly significant ($p < 0.001$). They concluded that the observed effects of chromium on ovarian morphology might be due to the effect of chromium on insulin sensitivity, or due to an otherwise unknown mechanism, or it may also be due to rectified pre-existing chromium deficiency (27).

There were significant reductions in hirsutism score in both groups. In Group I, it was 22.7 ± 7.5 before treatment and 7.07 ± 4.9 after treatment ($p < 0.001$). In Group II, it was 19.61 ± 8.9 before treatment and 5.52 ± 3.26 after treatment ($p < 0.001$). The aim of Harborne et al., (2003) study was to elucidate whether metformin does have an effect on hirsutism in women with PCOS. The beneficial effects do not appear to be mediated by suppression of circulating androgens, which makes it possible that hyperinsulinemia or related metabolic pathways may be important determinants of end-organ responses at the level of the hair follicle. They found that the FG score was significantly reduced after treatment with metformin and the results of this prospective, randomized, controlled study showed that metformin is an effective treatment for moderate to severe hirsutism in women with PCOS (28). In Amr and Abdel-Rahim, (2015) study, no significant improvement in hirsutim was noted with chromium. This was most likely explained by the fact that the life cycle of the hair follicles is relatively long so it could improve with longer period of follow-up. The reduction of free testosterone levels is expected to slow the growth of terminal hair and reduce new hair growth (27).

In our study, there were no significant differences between chromium picolinate group and metformin group regarding side effects, except for abdominal discomfort which exhibited statistically a significant difference between the two groups. In Albarracin et al., (2008), chromium had very low side effects (29). In the study done by Amooee et al., (2013), the patients who received metformin experienced more side effects compared to those receiving chromium picolinate. Moreover, metformin administration was accompanied by higher incidence of abdominal discomfort, nausea, vomiting, diarrhea, and indigestion, while chromium picolinate was accompanied by loss of appetite and headache (8).

CONCLUSION

Chromium picolinate was better tolerated than metformin due to lower side effects; nevertheless, no significant differences were observed between the two groups regarding ovulation and pregnancy rates. Therefore, metformin could be replaced by chromium in some PCOS patients.

Conflict of interest

The authors declare that they have no conflict of interest.

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