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TAURINE SUPPLEMENTATION IMPROVES INSULIN SENSITIVITY AND LIPID PROFILE IN PCOS WOMEN

Gynecology

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ABSTRACT

Background: Polycystic Ovarian Syndrome is responsible for 75% of anovulatory infertility in women. Evidence suggests that insulin resistance (IR) and secondary hyperinsulinemia play an important role in its pathogenesis. Metformin the most extensively used insulin sensitizer in PCOS has been reported to exhibit mixed results. Hence in the present study we compared the- add on effect of taurine with metformin on insulin resistance and metabolic features in pcos women.

Design: Experimental study.

MATERIAL AND METHODS: Sixty PCOS women of 18-30 years who fulfilled the Rotterdam criteria were randomized equally into two groups and treated with metformin (1000mg/day) and combined metformin (1000mg/day) and Taurine (1000 mg/day) therapy for 3 months. Fasting Plasma glucose, insulin, HOMA IR, QUICK-I and Lipid profile, insulin indices were measured at the baseline and after 3 months of treatment in both the groups.

RESULTS: Both groups showed significant reduction in fasting insulin levels, HOMA-IR and cholesterol levels. But greater reduction was observed in the combined treatment group than the metformin group alone. The metformin and taurine group also exhibited a significantly raised HDL and QUICK-I than the metformin group. No significant difference was observed in fasting plasma glucose levels in both the groups.

Conclusion: Supplementation of Taurine exerts beneficial effect over metformin alone on insulin resistance and metabolic features and it can be considered as a treatment option for the management of PCOS.

KEYWORDS

Insulin Resistance, Metformin, Taurine.

Introduction

The polycystic ovary syndrome (PCOS) is one of the most common endocrine disorder that affects about 6–21% of women of reproductive age[1]. It accounts for ~ 75% of anovulatory infertility[2]. PCOS is characterized by hyperandrogenism, ovulatory dysfunction and polycystic ovaries[3]. Though the etiology of PCOS is not known, insulin resistance is considered to play an important role in its pathogenesis,4 which may be exacerbated by coexistence of obesity [5]. The compensatory hyperinsulinemia stimulates the ovarian androgen production and increases the likelihood to develop type [2] diabetes, metabolic syndrome, and cardiovascular disease [6].

The recognition of insulin resistance as a key factor in the pathogenesis of PCOS, led to the use of Insulin sensitizers for its treatment 7. The most widely used insulin-lowering agent in the treatment of PCOS is metformin. It inhibits hepatic glucose production and also increases the sensitivity of peripheral tissues to insulin thereby improving insulin sensitivity[8]. Metformin may also exert direct and indirect effects on the ovary and steroidogenic enzymatic activity through this insulin sensitizing action[9]. However available data regarding improvement of insulin resistance by metformin in PCOS women showed mixed results (10). Especially obese women respond poor to Metformin treatment. Metformin is found to restore ovulatory cycles only in approximately 50% of PCOS cases [11]. The impact of Metformin on weight loss in obese PCOS patients is also found to be inconclusive [12].

Taurine is a conditionally essential amino acid and a pharmaco nutrient [13]. It potentiates the effect of insulin and possibly the insulin receptor [14]. The effectiveness of Taurine on insulin resistance and its associated complications in diabetes has been very well established [15]. It also functions as a more potent antioxidant [13]. Human studies have shown taurine to reduce plasma cholesterol concentrations, especially to decrease VLDL and LDL levels 16. Taurine enhanced protective actions of metformin in experimental and in epidemiological studies [17, 18]. There are no studies comparing the add-on effect of Taurine on Metformin treated PCOS women. Hence the present study was designed to find add on effect of taurine with metformin on insulin resistance and metabolic features PCOS women.

METHODS

The present study was done in department of Biochemistry in collaboration with Department of Obstetrics and Gynecology from September 2016 to November 2017 at Rajah Muthiah Medical College & Hospital, Annamalai University. The study was approved by Institutional Human ethics committee. Informed written consent was obtained from participants of the study.

Inclusion criteria: Sixty women of age group 18-30 years who were diagnosed as PCOS by Rotterdam criteria, after exclusion of other etiologies such as congenital adrenal hyperplasia, androgen-secreting tumors, Cushing's syndrome were randomized equally into two groups (n=30) who received either Metformin (500 mg twice daily) as a monotherapy -Metformin treatment group or a combined treatment with Metformin (500 mg twice daily) and Taurine (1000 mg/day) for 3 months – Combined Treatment group.

Exclusion criteria: Subjects with the history of diabetes, hypertension, systemic inflammatory conditions, clinical evidence of acute infections, systemic diseases, renal and hepatic diseases and Oral contraceptive pill usage were all excluded from the study. Complete physical examination was recorded including anthropometric measurements (Height and weight, BMI, Blood pressure, waist circumference, Hip circumference and Waist hip ratio) and fasting plasma glucose, lipid profile and serum insulin were all measured before and after the treatment. Plasma glucose, Serum total cholesterol, triglycerides and HDL were measured using standard kits in auto analyzer. LDL was calculated using Friedewald formula. Insulin was measured by ELISA method. Insulin resistance was calculated using Homeostasis Model Assessment of insulin resistance : HOMA-IR = [fasting plasma glucose (mg/dL) × fasting insulin

(IU/mL)]/405 and the quantitative insulin sensitivity check index (QUICKI). QUICKI = 1/[log fasting insulin (μU/mL)+ log fasting glucose (mg/dL)].

Statistical analysis: All statistical analysis was performed using SPSS statistics version 20.0. The results are expressed as mean ± SD. For comparison of all quantitative variables, clinical, biochemical, and hormonal parameters between the two groups at the baseline and after the third month, Mann Whitney test was used. For the comparison of changes in quantitative variables between the two groups unpaired t test was employed. p value of <0.05 was considered to be statistically significant.

Table.1: Anthropometric characteristics at the baseline and after three months of treatment in both the groups.

Parameters	Metformin Treatment group n=28			Combined Treatment group n=27		
	Before Treatment	After Treatment	p Value	Before Treatment	After Treatment	p Value
Weight (Kg)	63.87± 6.39	59.40±6.34	p< 0.01	64.63±7.64	57.87±6.52	P<0.01
BMI (Kg/m2)	26.29± 3.14	24.46±3.18	P<0.05	26.14±3.07	23.44±2.66	P<0.01
WHR	0.85±0.02	0.83±0.02	P<0.05	0.85± 0.02	0.81± 0.02	P<0.01
SBP (mm Hg)	119.07±4.01	118.93±3.24	NS	117.97± 3.29	118.07± 2.24	NS
DBP (mm Hg)	78.20± 2.20	78.90±1.81	NS	77.73±2.90	77±1.62	NS

Table 2. The Insulin Resistance indices at the baseline and after three months of treatment in both the groups.

Parameters	Metformin Treatment group n=28			Combined Treatment group n=27		
	Before Treatment	After Treatment	p Value	Before Treatment	After Treatment	p Value
Fasting Pl. Glucose (mg/dl)	84.93±4.02	83.83±3.58	NS	85.97±3.85	84.70±1.76	NS
Fasting Insulin (IU/mL)	17.93± 3.11	14.64±2.10	p< 0.01	18.02±3.20	12.13±2.37	p<0.01
HOMA-IR	3.76±0.65	3.02±.49	p<0.01	3.84± 0.78	2.55± 0.51	p<0.01
QUICK-I	0.315±0.01	0.325±0.01	p<0.01	0.314±0.01	0.333±0.01	p<0.01

Table 3. The lipid profile at the baseline and after three months of treatment in both the groups.

Parameters	Metformin Treatment group n=28			Combined Treatment group n=27		
	Before Treatment	After Treatment	p Value	Before Treatment	After Treatment	p Value
TOTAL CHOLESTEROL (mg/dl)	193.33±30.43	172.20±23.31	P<0.01	193.70± 32.66	146.50± 11.12	P<0.01
TGL (mg/dl)	148.20±34.62	132.37±22.27	P<0.05	143.30± 25.56	125.47± 9.94	P<0.01
HDL-C (mg/dl)	40.20±4.75	44.47±3.49	P<0.01	40.42±4.92	50.10±2.94	P<0.01
LDL-C (mg/dl)	114.85±24.33	95.80±18.56	P<0.01	114.96± 27.09	72.30±9.23	P<0.01
VLDL (mg/dl)	29.64± 6.92	26.47±4.45	P<0.05	28.66±5.11	25.09±1.99	P<0.01

Table 4. Comparison of change in clinical parameters of PCOS patients among the two treatment groups

Parameters	Metformin Treatment Group n=28	Combined Treatment Group n=27	p value
Weight (kg)	4.47±1.53	6.77±1.41	p<0.01
BMI (kg/m2)	1.83±0.6	2.73±0.54	p<0.01
WHR	0.02±0.02	0.04±0.02	p<0.01
SBP (mm Hg)	0.13±3.92	0.13±3.47	NS
DBP(mm Hg)	0.70±2.42	0.73±2.45	NS
Fasting Plasma Glucose (mg/dl)	1.10±3.58	1.27±3.75	NS
Fasting Plasma Insulin (IU/ml)	3.35±1.33	5.85±1.30	P<0.01
HOMA IR	0.73±0.27	1.29±0.37	P<0.01
QUICKI	0.01±0.00	0.02±0.00	P<0.01
TOTAL CHOLESTEROL (mg/dl)	21.13±10.34	47.20±22.94	P<0.01
TGL (mg/dl)	15.83±14.03	17.83±16.74	NS
HDL-C (mg/dl)	4.27±2.50	9.68±4.58	P<0.01
LDL-C (mg/dl)	23.01±9.72	53.32±23.51	P<0.01
VLDL (mg/dl)	2.39±2.44	3.57±3.35	NS

Results

The present study included 30 subjects in both the groups. 28 subjects in the Metformin Treatment group and [27] subjects in the Combined Treatment group completed the study. The Anthropometric characteristics at the baseline and after three months of treatment in both the groups were depicted in Table 1. Significant Reductions in Weight, Waist hip ratio and BMI was observed in both the groups after 3 months of treatment (p<0.05). However greater reductions of these measures were observed in the combined group. No significant change in Blood pressure was observed in both the treatment groups. Table 2 shows the insulin resistance indices changes in the baseline and after 3 months of treatment. Both the treatment groups showed significant improvement in fasting insulin, HOMA-IR and QUICK-I levels. However no significant difference was observed in the fasting plasma glucose in both the groups. Overall the combined treatment group showed greater improvement in insulin sensitivity. Table 3 represents the changes in lipid profile before and after the treatment. There was a significant drop in Total cholesterol, TGL, LDL and a raise of HDL in both the groups. The combined Treatment group had a significantly greater decrease in Total Cholesterol and LDL levels and a significantly greater increase of HDL compared to metformin group. Table 4 shows the comparison of changes in clinical parameters of PCOS patients among the two treatment groups. Taurine supplemented group showed greater reduction of BMI, WHR, LDL, serum total cholesterol and insulin resistance.

Discussion

The present study was done to explore the beneficial effect of taurine supplementation in PCOS women for the management of insulin resistance which plays a major role in its pathogenesis. In this study we have observed that combined therapy with taurine and metformin had a positive impact on insulin resistance and lipid profile in pcos women. PCOS subjects in both the groups were of same age group 23.65±4.18 Vs 24.25±4.01. The markers of the central adiposity such as WHR, BMI which are associated with atherosclerotic cardio vascular disease [20] were significantly decreased in both groups but taurine treated group showed greater reduction. In addition, greater reduction in LDL and significant increase of HDL indicates the effect of taurine on cardiovascular risk reduction. Our findings about metformin effect are in contrast to G Karoon Shahebrahimi et al (2016) who didn't observe any change in lipid levels during the course of metformin treatment in PCOS women 19. Taurine stimulates bile acid synthesis which might decrease the cholesterol level by increasing the catabolism of cholesterol in the body [21]. So the combination of Metformin and Taurine may have greater impact on cardiovascular disease risk s reduction than metformin alone in women with PCOS. The combined treatment of Taurine and Metformin was more effective on insulin resistance than metformin alone in PCOS women. Several reports have shown taurine to be important for beta-cell function and

insulin action [22]. Taurine might exhibit this beneficial effect through modifying the post-receptor events of insulin action [23]. Hence it is suggested that taurine supplementation would be more beneficial in the management PCOS with respect to improvement of insulin sensitivity and cardiovascular risk reduction.

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