IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 10 Ser.1 (October. 2023), PP 19-23
www.iosrjournals.org

Taurine Supplementation Improves Insulin Resistance And Oxidative Stress In PCOS Women.

*Dr.G.Hariprasath[1], Dr.S.Sethupathy[2], Mr.G.Kanagasabai[3].
1. Assistant Professor, Department of Biochemistry, Madha Medical College & Research Institute, Chennai, India.
2. Professor & Head, Department of Biochemistry, Sri Venkateshwaraa Medical College and Research center, Puducherry, India.
3. Biochemist, Department of Biochemistry, Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalainagar, Tamilnadu, India.

Abstract
Background: *PCOS is frequently associated with metabolic disturbances such as insulin resistance and oxidative stress. Metformin the widely used insulin sensitizer in PCOS has been reported to exhibit mixed results. Taurine is a conditionally essential amino acid known for its antioxidant role. In the present study we studied the combined effect of taurine with metformin on insulin resistance and oxidative stress in pcos women.*
Design: *Experimental study.*
Material & Methods: *Sixty PCOS women of 18-30 years who fulfilled the Rotterdam criteria were randomized equally into two groups and were treated with metformin (1000mg/day) and combined metformin (1000 mg/day) and Taurine (1000 mg/day) for three months. Fasting Plasma glucose, serum insulin, HOMA-IR, Biomarkers of oxidative stress – Malondialdehyde and Total antioxidant capacity (FRAP) were measured at the baseline and after three months of treatment in both the groups.*
Results: *While both the treatment groups showed significant reduction in fasting insulin and HOMA-IR levels, a greater reduction was observed in the combined treatment group. Metformin and taurine treated group also exhibited a significantly greater increase of Total antioxidant capacity (FRAP) and reduced Malondialdehyde (MDA) levels than metformin treated group.*
Conclusion: *Taurine supplementation exerts additional beneficial effect in alleviating insulin resistance and oxidative stress and it can be considered as a treatment option for the better management of PCOS.*
Key words: *FRAP, MDA, Insulin Resistance, Metformin & Taurine.*

Date of Submission: 24-09-2023 Date of acceptance: 04-10-2023

I. INTRODUCTION

Polycystic Ovarian Syndrome is the most common endocrine disorder affecting female fertility [(1)]. PCOS is characterized by hyperandrogenism, ovulatory dysfunction and polycystic ovaries [(2)]. Though the etiology of PCOS is not known, insulin resistance is considered to play an important role in its pathogenesis, the compensatory hyperinsulinemia increases ovarian androgen production, thereby contributing to the hyperandrogenism and chronic anovulation [(3)].

PCOS is most frequently linked with increased oxidative stress [(4)]. Oxidative stress is the disturbance in the balance between production of free radicals (ROS) and antioxidant defences [(5)]. The excess ROS triggers membrane lipids resulting in the formation of Malondialdehyde (MDA), which serves as a good marker for oxidative stress [(6)]. The degree of antioxidant defense present in our body is known as Total Antioxidant Capacity (TAC) [(7)]. The ferric reducing antioxidant power (FRAP) assay is widely used to assay the Total Antioxidant Capacity [(8)]. Oxidative stress serves as an important factor in the pathogenesis of PCOS by generating a proinflammmatory state, which enhances insulin resistance and hyperandrogenism [(9)].

Metformin is the most widely used insulin sensitizer in the treatment of PCOS. While Metformin therapy seems to reduce oxidative stress and improve insulin resistance, the benefit of Metformin in PCOS remains limited which might be due to patient's phenotype as well as their variations in metabolic parameters [(10)]. Taurine is a conditionally essential amino acid and a pharmaconutrient [(11)]. It potentiates the effect of insulin and possibly the insulin receptor [(12)]. It also functions as a more potent antioxidant [(13)]. Hence the present study was designed to explore the beneficial effect of taurine supplementation on oxidative stress and insulin resistance in PCOS women on metformin treatment.

II. MATERIALS AND METHODS

The present study was done in Department of Biochemistry Rajah Muthiah Medical College & Hospital, Annamalai University. The study was approved by Institutional Human ethics committee. Informed written consent was obtained from all the participants of the study.

Inclusion criteria: Sixty women of age group 18-30 years with PCOS were randomized equally into two groups (n=30) who received either Metformin (500 mg twice daily) - Metformin treatment group or a combined treatment with Metformin (500 mg twice daily) and Taurine (1000 mg/day) for three months – Combined Treatment group.

Exclusion criteria: Subjects with the history of diabetes, hypertension, systemic inflammatory conditions and 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, Weight, BMI and Blood pressure), fasting plasma glucose, serum insulin, Oxidative stress marker - serum Malondialdehyde (MDA) and antioxidant status marker – FRAP (ferric reducing antioxidant power) were all measured before and after the treatment. Insulin resistance was calculated using Homeostasis Model Assessment of insulin resistance: HOMA-IR = [fasting plasma glucose (mg/dL) × fasting insulin (IU/mL)]/405.

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 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.

III. 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 participants in both study groups were of same age group (23.65±4.18 and 24.25±4.01) and no significant difference was observed between the groups.

The Anthropometric characteristics at the baseline and after three months of treatment in both the groups were depicted in Table I. Significant Reductions in Weight and BMI was observed in both the groups after three months of treatment ($p<0.05$). However, a greater reduction of BMI was observed in the combined treatment group ($p<0.01$). No significant change in Blood pressure was observed in both the treatment groups.

Table II shows the changes in Insulin Resistance indices, serum MDA and plasma FRAP levels at the baseline and after three months of treatment in both the groups. Both the treatment groups showed significant reduction in fasting insulin levels and HOMA-IR levels ($p<0.01$). However no significant difference was observed in the fasting plasma glucose in both the groups. The serum MDA level was significantly declined ($p<0.01$) and the plasma FRAP was significantly raised ($p<0.01$) in both the treatment groups.

Table III shows the comparison of changes in Anthropometric measurements, Insulin Resistance indices, Oxidative stress and Antioxidant status markers in PCOS subjects after three months of treatment among the two groups. The taurine supplemented group exhibited a significantly greater reduction ($p<0.01$) in BMI, fasting insulin, HOMA-IR value and serum MDA level ($p<0.05$) and a significantly greater increase in plasma FRAP level ($p<0.01$).

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/m^2)	26.29±3.14	24.46±3.18	P<0.05	26.14±3.07	23.44±2.66	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, Oxidative stress marker - serum MDA and Antioxidant status marker – plasma FRAP 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 Plasma Glucose (mg/dl)	84.93±4.02	83.83±3.58	NS	85.97±3.85	84.70±1.76	NS
Fasting Insulin (µU/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
MDA (µmol/L)	4.82±0.84	3.91±0.68	p<0.01	5.07±.87	3.99±0.72	P<0.01
FRAP (mmol/L)	1.46±0.16	1.7±0.16	p<0.01	1.53±0.17	1.87±0.22	P<0.01

Table 3. Comparison of changes in Anthropometric measurements, Insulin Resistance indices, and Oxidative stress and Antioxidant status markers in PCOS subjects after three months of treatment among the two 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/m^2)	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)	0.7±2.42	0.73±2.45	NS
Fasting Plasma Glucose (mg/dl)	1.10±3.58	1.27±3.75	NS
Fasting Plasma Insulin (µU/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
TBARS (µmol/L)	-0.91±0.25	-1.08±0.28	P<0.05
FRAP (mmol/L)	0.25±0.08	0.34±0.11	P<0.01

IV. Discussion:

The present study was carried out to explore the beneficial effect of taurine supplementation for the effective management of oxidative stress and insulin resistance in PCOS women. All the PCOS subjects were normotensive and no significant change was observed in blood pressure in both the treatments. The mean fasting blood glucose remained normal in both the groups. All of our study subjects were less than 30 years of age with majority of them in the range of 20 to 25 years. Since hyperinsulinemia precedes impaired glucose tolerance, an elevation in fasting insulin levels was observed in these study subjects [(14)].

In the present study significant weight reduction was observed in both the treatment groups (p<0.01). However, compared with metformin the combined treatment exhibited a greater reduction of body weight and was statistically significant (p<0.01). In our study metformin appears to have a modest weight lowering potential [(15)]. This finding is consistent with the studies by Tan et al (2007) [(16)] and Sahin et al (2007) [*(17)*]. However Lord et al (2003) reported no significant effect on body weight upon metformin treatment in PCOS women [(18)]. This conflicting result might be due to ethnicity, diversity of patient's characteristics, dietary habits and life style habits. The mechanisms by which metformin may cause weight loss can be through reducing appetite via attenuation of hypothalamic AMPK activity, increasing leptin and insulin sensitivity, increasing fat oxidation and reducing lipid synthesis [(19)]. Taurine serves as an anti-obesity agent. The pronounced weight reduction by combined treatment could be due to the additional influence of taurine through stimulation of energy expenditure, modulation of lipid metabolism, anorexic effect and anti-oxidative effect [(20)].

In this study the combined treatment of Taurine and Metformin was more effective in alleviating insulin resistance, though the metformin treatment also reduced insulin resistance significantly. The increased reduction might be due to the additional effect exerted by taurine on insulin resistance. Metformin increases the sensitivity to insulin and decreases the chance of diabetes [(21)]. Our finding is consistent with the previous study by Nestler et al (2008) [(21)], but in contrast Zahra et al (2017) [(22)] found no significant reduction in HOMA-IR value in PCOS women after metformin treatment. This discrepancy might be due to small sample size and shorter duration in that study. The improvement in insulin sensitivity by metformin could be attributed to its positive effects on insulin receptor expression and tyrosine kinase activity [(23)]. Studies have shown taurine to be important for functioning of beta-cell and insulin action. Taurine might reduce insulin resistance through modifying the post-receptor events of insulin action [(24)]

Oxidative Stress is considered as a potential inducing factor in the pathogenesis of PCOS [(4)]. Our study showed a significant reduction of MDA and improvement of Total Antioxidant Status (TAS) in both the treatment. But the changes were more pronounced in combined treatment group. This pronounced increase of TAS in combined treatment group could be due to taurine supplementation. Metformin is known for its antioxidant role [(25)]. Studies investigating the effects of metformin on oxidative stress have yielded different results. Pavlovic et al (2000) demonstrated an increase of oxidative stress [(26)] whereas Bonnefont et al (2003) reported a decrease of oxidative stress upon treatment with metformin [(27)]. This discrepancy might be due to small sample size and shorter duration of the study. Metformin seems to reduce oxidative stress by many ways. Through scavenging hydroxyl free radical, by decreasing the production of ROS through reduction of NAD (P) H oxidase activity and also through reducing insulin resistance [(28)]. The antioxidant effect of taurine in this study is consistent with the findings of Rosa et al (2014) [(29)]. Although the mechanisms underlying the antioxidant effects of taurine are not well understood, scavenging ROS, interfering with ROS activity, and regeneration of thiol groups may be the most likely mechanisms [(30)]. In this study we found that even though metformin treatment effectively influenced the metabolic changes, taurine supplementation enhanced the actions of metformin with respect to insulin sensitivity, antioxidant status and weight reduction. Therefore it can be considered as a treatment option for better management of PCOS.

REFERENCES

[1]. Homburg R. (1996). Polycystic Ovary Syndrome—From Gynecological Curiosity To Multisystem Endocrinopathy. Human Reproduction; 11: 29–39.
[2]. Susan M Sirmans And Kristen A Pate. Epidemiology, Diagnosis, And Management Of Polycystic Ovary Syndrome Clin Epidemiol. 2014; 6: 1–13.
[3]. Essah, P.A., Nestler, J.E. (2006). Insulin Resistance And Hyperinsulinism In The Polycystic Ovary Syndrome. In: Azziz, R., Nestler, J.E., Dewailly, D. (Eds) Androgen Excess Disorders In Women. Contemporary Endocrinology.
[4]. Sabuncu T, Vural H., Oxidative Stress In Polycystic Ovary Syndrome And Its Contribution To The Risk Of Cardiovascular Disease. Clin Biochem 2001; 34(5): 407-13.
[5]. Betteridge DJ. What Is Oxidative Stress? Metabolism. 2000 Feb;49(2 Suppl 1):3-8.
[6]. Gaweł S, Wardas M, Niedworok E, Wardas P. Malondialdehyde (MDA) As A Lipid Peroxidation Marker. Wiad Lek. 2004;57(9-10):453-5.
[7]. Agarwal A, Gupta S, Sharma R. (2005). Role Of Oxidative Stress In Female Reproduction. Reprod Biol Endocrinol, 3: 28.
[8]. Benzie IFF, Strain JJ. The Ferric Reducing Ability Of Plasma (FRAP) As A Measure Of "Antioxidant Power": The FRAP Assay. Analytical Biochem. 19960 ; 239 : 70-76.
[9]. González F, Considine RV Et Al., Oxidative Stress In Response To Saturated Fat Ingestion Is Linked To Insulin Resistance And Hyperandrogenism In Polycystic Ovary Syndrome. J Clin Endocrinol Metab. 2019 Nov 1;104(11):5360-5371.
[10]. Hany Lashen. Role Of Metformin In The Management Of Polycystic Ovary Syndrome. Ther Adv Endocrine Metab. 2010 Jun; 1(3): 117–128.
[11]. Gupta RC. Is Taurine A Pharmaconutrient? J Pharmacol Ther Res 2018;2(2):18-20.
[12]. Lampson WG, Kramer JH, Schaffer SW. Potentiation Of The Actions Of Insulin By Taurine. Can J Physiol Pharmacol. 1983 May;61(5):457-63.
[13]. Schaffer S.W., Azuma J., Mozaffari M., Role Of Antioxidant Activity Of Taurine In Diabetes. Can J Physiol Pharmacol. 2009, 87(2):91-99.
[14]. Pelusi B[1], Gambineri A, Pasquali R. Type 2 Diabetes And The Polycystic Ovary Syndrome. Minerva Ginecol. 2004 Feb;56(1):41-51.
[15]. Malin SK[1], Kashyap SR. Effects Of Metformin On Weight Loss: Potential Mechanisms. Current Opinion In Endocrinology, Diabetes And Obesity. 2014 Oct;21(5):323-9.
[16]. Tan S, Hahn S, Benson S, Dietz T. Metformin Improves Polycystic Ovary Syndrome Symptoms Irrespective Of Pre-Treatment Insulin Resistance. Eur J Endocrinol. 2007 Nov;157(5):669-76.
[17]. Sahin Y[1], Unluhizarci K, Yilmazsoy A, Yikilmaz A, Aygen E, Kelestimur F. The Effects Of Metformin On Metabolic And Cardiovascular Risk Factors In Nonobese Women With Polycystic Ovary Syndrome. Clinical Endocrinology (Oxf). 2007 Dec; 67(6):904-8. Epub 2007 Jul 30.
[18]. Lord JM[1], Flight IH, Norman RJ. Metformin In Polycystic Ovary Syndrome: Systematic Review And Meta-Analysis. BMJ. 2003 Oct 25;327(7421):951-3.
[19]. Malin SK, Kashyap SR. Effects Of Metformin On Weight Loss: Potential Mechanisms. Curr Opin Endocrinol Diabetes Obes. 2014 Oct;21(5):323-9.
[20]. Murakami S. Role Of Taurine In The Pathogenesis Of Obesity. Mol Nutr Food Res. 2015 Jul;59(7):1353-63.
[21]. Moghetti P, Castello R, (2000). Metformin Effect On Clinicalfeatures Endocrine And Metabolism Profile, And Insulinsensitivity In Polycystic Ovary Syndrome. Journal Of Clinical Endocrinology And Metabolism. 85; 139-146.
[22]. Nestler JE. (2008). Metformin For The Treatment Of The Polycystic Ovary Syndrome. The New England Journal Of Medicine. 358(1):47-54.
[23]. Zahra M, Shah M, Ali A, Rahim R. (2017). Effects Of Metformin On Endocrine And Metabolic Parameters In Patients With Polycystic Ovary Syndrome. Hormones And Metabolic Research. 49(2):103-108.
[24]. Karoon Shahebrahimi, Nasrin Jalilian, Nasrin Bazgir, Mansour Rezaei. (2016). Comparison Clinical And Metabolic Effects Of Metformin And Pioglitazone In Polycystic Ovary Syndrome. Volume : 20. Issue : 6 Page :805-80.
[25]. Nandhini AT, Thirunavukkarasu V, Anuradha CV. Taurine Modifies Insulin Signaling Enzymes In The Fructose-Fed Insulin Resistant Rats. Diabetes Metab 2005; 31 (4 Pt 1): 337-344.
[26]. Alzoubi KH, Khabour OF, Al -Azzam SI. Metformin Eased Cognitive Impairment Induced By Chronic L - Methionine Administration: Potential Role Of Oxidative Stress. Curr Neuropharmacol. 2014;12(2):186 -92.
[27]. Pavloviç D, Kocic R, Kocic G, Jevtovic T, Radenkovic S, Mikic D, Stojanovic Mand Djordevic PB. (2000). Effect Of Four Week Metformin Treatment Onplasma And Erythrocyte Antioxidative Defense Enzymes In Newly Diagnosed Obese Patients With Type 2 Diabetes. Diabetes Obesity And Metabolism. 2, 251–256.

[28]. Bonnefont-Rousselot D, Raji B, Walrand M, Gardes-Albert M, Jore D,Legrand A, Peynet J And Vasson MP. (2003). An Intracellular Modulation Of Free Radical Production Could Contribute To The Beneficial Effects Of Metformin Towards Oxidative Stress. Metabolism 52,586–589.
[29]. Esteghamati A, Eskandari D, Mirmiranpour H, Noshad S, Mousavizadeh M, Hedayati M, Nakhjavani M. Effects Of Metformin On Markers Of Oxidative Stress And Antioxidant Reserve In Patients With Newly Diagnosed Type 2 Diabetes: A Randomized Clinical Trial. Clin Nutr. 2013 Apr;32(2):179-85.
[30]. Rosa FT, Freitas EC, Deminice R, Jordão AA, Marchini JS. (2014). Oxidative Stress And Inflammation In Obesity After Taurine Supplementation: A Double-Blind, Placebo-Controlled Study. European Journal Of Nutrition. 53(3):823-830.
[31]. Maleki V, Mahdavi R, Hajizadeh-Sharafabad F, Alizadeh M. The Effects Of Taurine Supplementation On Oxidative Stress Indices And Inflammation Biomarkers In Patients With Type 2 Diabetes: A Randomized, Double-Blind, Placebo-Controlled Trial. Diabetol Metab Syndr. 2020 Jan 29;12:9.