ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 9, Suppl. 1, 2016

Online - 2455-3891
Print - 0974-2441

Research Article

A PROSPECTIVE STUDY ON THE EFFICACY OF METFORMIN IN OBESE AND NON-OBESE PATIENTS WITH POLYCYSTIC OVARY SYNDROME

SAVEETHA V*, SOMA SUNDARAM I, SHANMUGASUNDARAM P

Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels University (VISTAS), Chennai - 600 117, Tamil Nadu, India.
Email: savee2509@gmail.com

Received: 06 May 2016, Revised and Accepted: 14 May 2016

ABSTRACT

Objective: The aim of the study was to assess the efficacy of metformin on fasting blood glucose (FBG), postprandial blood glucose (PPBG), total cholesterol (T. chol), blood pressure (BP), weight and hence body mass index (BMI) in women with polycystic ovary syndrome (PCOS).

Methods: In a prospective study, 90 women aged 18-45 were treated with metformin 500 mg twice daily for 1 year. women were grouped as obese and non-obese based on their BMI. The changes in measured parameters were analyzed statistically.

Results: There was a reduction in weight, systolic BP (SBP), FBG, PPBG and T. chol (p=0.04, p=0.03, p=0.032, p=0.037, p=0.042 and p=0.047, respectively) in the obese group. There was no significant difference in diastolic BP in both the groups.

Conclusion: Metformin treatment lowered weight and SBP and T. chol in women with PCOS. FBG and PPBG were also reduced in obese patients while Non-obese women did not benefit from metformin.

Keywords: Polycystic ovary syndrome, Metformin, Obese, Non-obese.

INTRODUCTION

The polycystic ovary syndrome (PCOS) - which is an endocrine disorder diagnosed on the basis of hyperandrogenism, oligo-ovulation with associated oligomenorrhea, and polycystic ovaries on ultrasonography (USG) - affects up to 5-10% of reproductive age women and is the most common cause of anovulatory infertility [1]. Women with PCOS had an elevated prevalence of impaired glucose tolerance, Type 2 diabetes mellitus (DM2), and metabolic syndrome in both body mass index (BMI) and non-BMI-matched studies [2]. A family history of DM2 and gestational diabetes [3], elevated age, testosterone [4], and abdominal adiposity [5] are considered to be the risk factors for abnormal glucose tolerance in women with PCOS. With a prevalence of 30-70%, elevated BMI is a common feature in women with PCOS [6,7]. In randomized studies, metformin had positive effects on body weight [8], ovulation [9], insulin sensitivity, hirsutism, and androgen levels [8,10] though its effect is less convincing.

Metformin reduces the incidence of diabetes in prediabetic subjects and lowers body weight in patients with and without Type 2 diabetes [11]. In a recent meta-analysis, it was reported that metformin treatment was associated with a significant decrease in BMI compared with placebo which also reported an effect related to both the duration and dose of the treatment [12]. The aims of this prospective study were, (1) To assess the efficacy of metformin in obese and non-obese patients with PCOS, (2) to compare the effect between both obese and non-obese women.

METHODS

The study was performed at the Department of Obstetrics and Gynaecology, ESI Hospital, Ayanavaram, Chennai. Women visiting the hospital were recruited in the study if they fulfilled the following criteria: (1) Aged within 18-45, (2) irregular cycles and anovulation, (3) PCOS diagnosed by USG. Exclusion criteria include patients with renal or hepatic impairment, taking hormonal treatment, pregnancy, lactation or if they wish for fertility treatment. The study was approved by Institutional Ethics Committee (IEC/DOPV/2015/25), and written informed consent was obtained from all the patients participating in the study.

Eligible patients were divided into two groups based on their BMI as obese (>29.9) and non-obese (18-24.5). Both the groups were treated with metformin 500 mg twice daily (Vivekpharmachem Ltd., India). Baseline characteristics were measured for the following: Weight, BMI, systolic blood pressure (SBP), diastolic BP (DBP), fasting blood glucose (FBG), postprandial blood glucose (PPBG), and total cholesterol (T. chol). This was repeated every 3 months to find changes in the parameters. The student t-test was performed using Microsoft Excel 2010 programme to assess the efficacy of the drug in both the groups. Mean and standard deviation (SD) were also obtained from the same. There was statistical significance in the following among the obese group: Weight *p<0.05, BMI *p<0.05, SBP *p<0.05, FBG p*<0.05, PPBG p*<0.05, and T. chol p*<0.05.

RESULTS

The following results were obtained from the study:

The mean age of study population was 25.02±6.6 among the obese patients and 27.7±8.0 among the non-obese patients. Among both the groups, most of the women (68% in obese and 51% in non-obese) affected with PCOS were in the range 18-25 (Table 1).

It was found that 37 (70%) obese patients were in the BMI range 30-34.9 and 16 (30%) were in the range 35-40, whereas 18 (49%) non-obese patients were in the BMI range 18.5-21.9 and 19 (51%) were in the range 22-24.9 (Table 2).

The study shows that 49 (54%) patients had a family history of PCOS and 41 (45.5%) patients did not have a family history (Table 3).

Around 45 (85%) obese patients and 7 (19%) non-obese patients were diabetic, 30 (57%) obese patients and 8 (22%) non-obese patients were having HTN, 42 (72%) of obese patients were dyslipidemic, 10 (19%) obese patients and 2 (5%) non-obese patients were suffering from coronary heart disease, 5 (9%) and 2 (4%) obese patients had peripheral vascular disease and sleep apnea, respectively (Table 4).

Table 1: Classification based on age

Age	n (%)	
	Obese	Non-obese
18-25	36 (68)	19 (51)
26-34	11 (21)	10 (27)
35-45	6 (11)	8 (22)
Mean	25.02±6.6	27.7±8.0

Table 2: Classification based on BMI

BMI (kg/m^2)	n (%)	
	Obese	Non-obese
18.5-21.9	-	18 (49)
22-24.9	-	19 (51)
25-29.9	-	-
30-34.9	37 (70)	-
35-40	16 (30)	-

BMI: Body mass index

Table 3: Family history of PCOS

FH	n(%)
With FH	49 (54.4)
Without FH	41 (45.5)

PCOS: Polycystic ovary syndrome, FH: Family history

Table 4: Based on comorbidities

Disease	n (%)	
	Obese	Non-obese
Diabetes mellitus	45 (85)	7 (19)
Hypertension	30 (57)	8 (22)
Dyslipidemia	42 (72)	-
CHD	10 (19)	2 (5)
Peripheral vascular disease	5 (9)	-
Sleep apnea	2 (4)	-

CHD: Coronary heart disease

Table 5 gives the baseline variables of age, height, weight, BMI, SBP, DBP, FBG, PPBG, and T. chol. Mean of these parameters in both obese and non-obese patients at the start of the study were noted (Table 5).

Table 6 provides with the mean and SD of the baseline characteristics of both obese and non-obese patients (Table 6).

Table 7 shows that there is a significant difference in the following variables: Weight (p=0.04), BMI (p=0.005), SBP (0.032), FBG (p=0.037), PPBG (p=0.042), and T. chol (p=0.047) among the obese group. However, there was no significant difference in the DBP value and none of the parameters had significant difference among the non-obese group (Table 7).

DISCUSSION

Among 90 patients, 53 (59%) of them were obese and 37 (41%) were non-obese which is similar to that reported by Jeyaprakash and Saul [13], and Melissa Kahsar-Miller and Azziz [14] mentioned that PCOS can be hereditary and have a family history which is the same as this study where 49 (54.4%) patients were having a family history of PCOS. Among the study population, 52 (58%) patients (45 obese and 7 non-obese) were having DM2 as comorbidity which is similar to that reported by Moini and Eslami [15].

In this study, there was a significant difference (p<0.05) in the BMI of obese patients which is identical with that of Ernest

Table 5: Base line characteristics of study subjects

Parameters	Obese (mean)	Non-obese (mean)
Age	25.02 (18-45)	27.7 (18-45)
Weight (kg)	80.4 (61-103)	53.9 (42-168)
Height (cm)	154.3 (145-163)	156.8 (150-167)
BMI (kg/m^2)	33.7 (30.6-39.95)	21.5 (18.6-24.9)
SBP (mmHg)	142.07 (110-170)	118.8 (100-140)
DBP (mmHg)	88.3 (60-1110)	73.3 (60-90)
FBG (mg/dl)	118.64 (98-145)	86.3 (71-110)
PPBG (mm/dl)	154.6 (138-200)	125.25 (105-140)
T. chol (mm/dl)	166.3 (140-200)	85.3 (66-106)

BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, PPBG: Postprandial blood glucose, SD: Standard deviation, T. chol: Total cholesterol

Table 6: Classification based on standard deviation

Parameters	Obese (mean)	Non-obese (mean)
Age	25.02±6.6	27.7±8.0
Weight (kg)	80.4±8.4	53.9±5.9
Height (cm)	154.3±5.02	156.8±4.9
BMI (kg/m^2)	33.7±2.5	21.5±1.5
SBP (mmHg)	142.07±16	118.8±14.1
DBP (mmHg)	88.3±14.2	73.3±9.4
FBG (mg/dl)	118.64±12.7	86.3±10.1
PPBG (mm/dl)	154.6±13.2	125.25±10.4
T. chol (mm/dl)	166.3±16.7	85.3±10.6

BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, PPBG: Postprandial blood glucose, SD: Standard deviation, T. chol: Total cholesterol

Table 7: Changes from baseline to 1 year

Parameters	Obese	p value	Non-obese	p value
Weight (kg)	77.03	0.04	53.08	0.54
BMI (kg/m^2)	32.29	0.005	21.59	0.45
SBP (mmHg)	135.47	0.032	117.7	0.736
DBP (mmHg)	90.18	0.49	74.1	0.714
FBG (mg/dl)	113.22	0.037	85.6	0.793
PPBG (mm/dl)	149.16	0.042	124.7	0.847
T. chol (mm/dl)	159.92	0.047	82.2	0.228

BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, PPBG: Postprandial blood glucose, SD: Standard deviation, T. chol: Total cholesterol

Hung Yu Ng *et al.*, [16]. The FBG and PPBG value in obese patients also had a significant difference (p<0.05) which is almost identical to that of Pasquali *et al.* [17]. There seemed to be a significant change in the T. chol and SBP (p<0.05) which is on par with the findings of Moghetti *et al.* [9]. As Trolle *et al.* [18] have mentioned, metformin did not have any significant changes (p<0.05) among the non-obese patients.

CONCLUSION

This study reveals that the treatment with metformin had significant result among obese group of patients in BMI, FBG, PPBG, SBP and T. chol, but there was no reduction in the DBP. These parameters were not changed among the non-obese group which shows the null effect of metformin among them.

REFERENCES

1. Legro RS, Brzyski RG, Diamond MP, Coutifaris C, Schlaff WD, Casson P, *et al.* Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. N Engl J Med 2014;371(2):119-29.
2. Moran LJ, Misso ML, Wild RA, Norman RJ. Impaired glucose tolerance, Type 2 diabetes and metabolic syndrome in polycystic ovary syndrome: A systematic review and meta-analysis. Hum Reprod Update 2010;16(4):347-63.

3. Koivunen RM, Juutinen J, Vauhkonen I, Morin-Papunen LC, Ruokonen A, Tapanainen JS. Metabolic and steroidogenic alterations related to increased frequency of polycystic ovaries in women with a history of gestational diabetes. J Clin Endocrinol Metab 2001;86(6):2591-9.
4. Espinós-Gómez JJ, Corcoy R, Calaf J. Prevalence and predictors of abnormal glucose metabolism in Mediterranean women with polycystic ovary syndrome. Gynecol Endocrinol 2009;25(3):199-204.
5. Legro RS, Kunselman AR, Dodson WC, Dunaif A. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: A prospective, controlled study in 254 affected women. J Clin Endocrinol Metab 1999;84(1):165-9.
6. Broekmans FJ, Knauff EA, Valkenburg O, Laven JS, Eijkemans MJ, Fauser BC. PCOS according to the Rotterdam consensus criteria: Change in prevalence among WHO-II anovulation and association with metabolic factors. BJOG 2006;113(10):1210-7.
7. Vrbikova J, Hainer V. Obesity and polycystic ovary syndrome. Obes Facts 2009;2(1):26-35.
8. Gambineri A, Pelusi C, Genghini S, Morselli-Labate AM, Cacciari M, Pagotto U, *et al.* Effect of flutamide and metformin administered alone or in combination in dieting obese women with polycystic ovary syndrome. Clin Endocrinol (Oxf) 2004;60(2):241-9.
9. Moghetti P, Castello R, Negri C, Tosi F, Perrone F, Caputo M, *et al.* Metformin effects on clinical features, endocrine and metabolic profiles, and insulin sensitivity in polycystic ovary syndrome: A randomized, double-blind, placebo-controlled 6-month trial, followed by open, long-term clinical evaluation. J Clin Endocrinol Metab 2000;85(1):139-46.
10. Ganie MA, Khurana ML, Eunice M, Gupta N, Gulati M, Dwivedi SN, *et al.* Comparison of efficacy of spironolactone with metformin in the management of polycystic ovary syndrome: An open-labeled study. J Clin Endocrinol Metab 2004;89(6):2756-62.
11. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, *et al.* Reduction in the incidence of Type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346(6):393-403.
12. Nieuwenhuis-Ruifrok AE, Kuchenbecker WK, Hoek A, Middleton P, Norman RJ. Insulin sensitizing drugs for weight loss in women of reproductive age who are overweight or obese: Systematic review and meta-analysis. Hum Reprod Update 2009;15(1):57-68.
13. Jeyaprakash K, Saul S. Influence of obesity on insulin resistance in polycystic ovary syndrome. Asia Pacific Journal of Research 2013;2(9):141-8.
14. Kahsar-Miller M, Azziz R. The Development of the polycystic ovary syndrome: Family History as a risk factor. Trends Endocrinol Metab 1998;9(2):55-8.
15. Moini A, Eslami B. Familial associations between polycystic ovarian syndrome and common diseases. J Assist Reprod Genet 2009;26(2-3):123-7.
16. Ernest Hung Yu Ng, Nelson Ming Sun Wat, Pak Chung Ho. Effect of metformin on ovulation rate, hormonal and metabolic profiles in women with clomiphene resistant polycystic ovaries: A randomized, double blinded placebo controlled trial. Hum Reprod 2001;16(8):1625-31.
17. Pasquali R, Gambineri A, Biscotti D, Vicennati V, Gagliardi L, Colitta D, *et al.* Effect of long-term treatment with metformin added to hypocaloric diet on body composition, fat distribution, and androgen and insulin levels in abdominally obese women with and without the polycystic ovary syndrome. J Clin Endocrinol Metab 2000;85(8):2767-74.
18. Trolle B, Flyvbjerg A, Kesmodel U, Lauszus FF. Efficacy of metformin in obese and non-obese women with polycystic ovary syndrome: A randomized, double-blinded, placebo-controlled cross-over trial. Hum Reprod 2007;22(11):2967-73.