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LONG-TERM SPIRONOLACTONE THERAPY AND ITS EFFECT WITH AND WITHOUT DIETARY-INDUCED WEIGHT-LOSS, ON INSULIN LEVELS, LIPID PROFILE, AND CLINICAL FEATURES IN FEMALES WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Aim: The goal of the current prospective clinical study was to evaluate the effects of long-term spironolactone medication on insulin levels, lipid profiles, and clinical characteristics in female PCOS patients, both with and without dietaryly induced weight reduction.

Methods: In this study, 22 women between the ages of 17 and 32 who had indications of PCOS, such as hyperandrogenism with clinical or biochemical evidence of amenorrhoea and/or oligomenorrhea, were included; 12 of them were normal weight and 10 were obese. Prior to and following a 12-month oral spironolactone dosage of 100 mg per day, the individuals underwent assessments. Obese ladies were urged to modify their lifestyle. Metabolic, endocrine, and clinical parameters were evaluated prior to and throughout antiandrogen treatment. When taken orally, spirolactone significantly decreased triglycerides in overweight females and increased HDL in lean, normal-weight individuals.

Results: The area under the insulin curve, insulin resistance using the hemostasis model, and insulin levels during the 60-minute OGTT was all considerably lower in obese females following a year of oral spironolactone medication. Pharmacologic treatment did not cause unfavourable changes in insulin sensitivity and secretion, nor did it cause weight reduction in female PCOS patients.

Conclusion: The current investigation suggests that spironolactone medication is beneficial for the androgenic clinical features of PCOS patients. Additionally, it was observed that the lipid profile and glucose metabolism are not adversely affected by long-term spironolactone medication. These advantageous effects on glucose and lipid metabolism were accompanied by weight reduction in overweight PCOS participants.

Keywords: Adult acne, Efficacy, polycystic ovary syndrome, spironolactone, overweight females

INTRODUCTION

In women in the reproductive age range, PCOS affects around 7% of the female population; the majority of these women also have hyperinsulinism and insulin resistance. Insulin resistance linked to obesity is present in over half of female PCOS patients, and it raises the possibility that these women may develop diabetes mellitus as a result of their insulin resistance. Numerous female PCOS sufferers may have irregular ovulation and elevated testosterone levels as a result of insulin's diverse effects on the female ovary.1

Alternatively, alterations in muscle fibre structure may result from androgen-induced insulin resistance. In females, there are different degrees of PCOS caused by hyperinsulinemia and an increase in androgens. Numerous treatment initiatives have been undertaken in an attempt to find substances that may alter or alleviate the diseases' clinical symptoms.2

According to data from earlier studies, when the lipid profiles of people with PCOS are examined, triglycerides, very low-density lipoproteins, low-density lipoproteins, and total cholesterol levels rise while high-density lipoproteins decrease. Concerning atherogenic outcomes may result from these aberrant levels in lipid profile variables.3

According to prior research, high-density lipoproteins and low-density lipoproteins are trustworthy indicators for predicting the development of coronary heart illnesses in the afflicted individuals.4. Overweight and menstruation abnormalities are definitely connected in women with PCOS, according to prior research. Additionally, female infertility and menstruation issues linked to excess weight can be treated with weight loss. Furthermore, the primary line of treatment for obese female PCOS patients is lifestyle adjustment, which includes increased physical activity and dietary limitations.5

This prospective clinical study was carried out to evaluate the effects of long-term oral spironolactone therapy (100 mg/day) on insulin levels, lipid profiles, and clinical features in females with PCOS (polycystic ovary syndrome) who are normal weight or obese, both with and without dietaryly induced weight loss. In addition, a low-calorie diet was advised for each of the overweight girls in addition to pharmaceutical treatment.

MATERIAL AND METHODS

The current prospective clinical investigation was carried out to evaluate the effects of long-term spironolactone medication on insulin levels, both with and without dietaryly-induced weight reduction, lipid profile, and clinical features in females with PCOS (polycystic ovary syndrome). The study population was comprised of the females visiting the Outpatient department of Obstetrics and gynecology of the Institute.

In this study, 22 women between the ages of 17 and 32 who had indications of PCOS, such as hyperandrogenism with clinical or biochemical evidence of amenorrhoea and/or oligomenorrhea, were included; 12 of them were normal weight and 10 were obese. Referrals for hirsutism, acne, and/or alopecia were made. All of the female participants did not take any medications that may alter their hormone levels, and they all had non-systemic diseases. Endocrinological abnormalities, such as elevated levels of testosterone, DHEA-S, and rostenedione in the early follicular phase, chronic anovulation accompanied by amenorrhoea and/or oligomenorrhea, hypergonadism signs, such as hirsutism, seborrhea, alopecia, and/or acne, and FG (modified Ferriman-Gallwey scores) of >8 were used to diagnose PCOS. All participants' thyroid and prolactin levels were within normal ranges. Before each individual was finally included, informed permission was obtained after outlining the specifics of the research design.

All research participants had baseline measurements of their blood pressure, BMI, OGTT, alopecia (Ludwig's score), acne (Luck's score), and FG scores. Luteinizing hormone (LH), rostenedione, prolactin, DHEA-S, testosterone, and FSH (follicle-stimulating hormone) are examples of endocrine variables. Metabolic measures include triglycerides, total cholesterol, and high-density lipoproteins.

following obtaining an intravenous blood sample following a 10-hour fast, all blood parameters were evaluated. The following parameters were reviewed in obese female PCOS patients after 12 months of oral spironolactone 100 mg/day with dietary limitations and lifestyle modification: HOMAIR, AUXinsulin, OGTT, HDL, triglycerides, total cholesterol, FG scores, BP, BMI<, and menstrual history. The immunoradiometric assay was used to detect androgens, and the immunometric assay was utilised to assess plasma insulin.

The collected data were subjected to the statistical evaluation using SPSS software version 21 (Chicago, IL, USA) and one-way ANOVA and t-test for results formulation. The data were expressed in percentage and number, and mean and standard deviation. The level of significance was kept at $p<0.05$.

RESULTS

The goal of the current prospective clinical study was to evaluate the effects of long-term spironolactone medication on insulin levels, lipid profiles, and clinical characteristics in female PCOS patients, both with and without dietaryly induced weight reduction. In this study, 22 women between the ages of 17 and 32 who had indications of PCOS, such as hyperandrogenism with clinical or biochemical evidence of amenorrhoea and/or oligomenorrhea, were included; 12 of them were normal weight and 10 were obese. Referrals for hirsutism, acne,

and/or alopecia were made for the subjects. Group I consisted of 5 females whose weight did not change even after medication, diet restriction, and lifestyle improvement; Group II consisted five females whose weight dramatically decreased following 1 year of spironolactone therapy.

The study results have shown that at baseline three women who were normal weight and two who were overweight had acne, and six women—two of whom had normal weight and four of whom had overweight—had alopecia, which in two of them improved after starting spironolactone medication. At baseline, the menstrual cycle was irregular in all research participants, with three females experiencing amenorrhoea and 19 females experiencing oligomenorrhea. Four overweight ladies, one from group I, and three from group II, saw improvements in their menstrual cycles after therapy. Three surgically overweight female patients had polymenorrhea.

When the research subjects' normal weight and overweight female participants' baseline and post-treatment clinical and metabolic characteristics were evaluated, almost all of the parameters were found to be statistically equivalent, with a small exception (Table 1).

The mean age in normal weight and overweight females was 23.6±4.7 years and 22.1±5.4 years respectively in the two groups. After receiving spironolactone medication, it was shown that the OGTT (Oral Glucose Tolerance Test) considerably decreased in overweight females, going from 67.1±13.7 to 51.6±24.5. High-density lipoprotein levels rose significantly in lean females after 13 months of spironolactone treatment, rising from 1.13±0.5 to 1.49±0.3. This rise was statistically significant. In statistically significant reduction, the total triglyceride levels in obese females dropped from 1.56±0.3 to 1.22±0.8. Additionally, overweight females who received pharmaceutical treatment had an improvement in BMI from 29.2±3.8 to 27.2±4.5. There was statistical significance in this difference as well. After using spironolactone for a year, neither thin nor overweight females' HOMAIR, AUCinsulin, fasting glucose, total cholesterol, blood pressure, or FG scores changed substantially (table 1).

Additionally, two groups of study females with PCOS had their clinical and metabolic baseline and post-treatment characteristics evaluated by this investigation (Table 2). Based on the study findings, there were five females in the overweight group and four females in the lean group, with mean ages of 23.8±5.5 and 19.6±4.8 years, respectively. The AUCinsulin levels significantly decreased in overweight females, going from 6092±3789 to 4502±2118, but the decline in normal weight females was not statistically significant. The HOMAIR levels of overweight females decreased significantly from 3.4±0.2 to 1.8±0.6, whereas the levels of normal e=weight females increased non-significantly. After a year of spironolactone medication, there was no significant difference in the fasting glucose levels of lean and obese females.

In obese females, OGTT 60 minutes demonstrated a substantial drop from 62.8±14.2 to 41.1±24.5 mmol/l after pharmacologic treatment. The study found that there was a substantial decrease in total triglycerides from 1.3±0.3 to 1.0±0.5 in lean ladies, but there was no significant reduction in overweight females. Additionally, BMI in overweight females decreased significantly from 30.1±3.7 to 26.1±3.6 following spironolactone. Both lean and overweight females saw non-significant changes in HDL, total cholesterol, and FG scores after taking spironolactone for a full year (Table 2).

DISCUSSION

The current prospective clinical study aimed to evaluate the effects of long-term spironolactone medication on insulin levels, lipid profiles, and clinical characteristics in females with PCOS (polycystic ovarian syndrome), both with and without dietary-induced weight reduction.

In this study, 22 women between the ages of 17 and 32 who had indications of PCOS, such as hyperandrogenism with clinical or biochemical evidence of amenorrhoea and/or oligomenorrhea, were included; 12 of them were normal weight and 10 were obese. Referrals for hirsutism, acne, and/or alopecia were made for the subjects. Group I consisted of 5 females whose weight did not change even after medication, diet restriction, and lifestyle improvement; Group II consisted five females whose weight dramatically decreased following 1 year of spironolactone therapy. The study's findings indicate that three women who were normal weight and two who were overweight had acne at baseline, and six women—two of whom was normal weight and four of whom were overweight—had alopecia, which in two of them improved after starting spironolactone medication.

All research participants had irregular menstrual cycles at baseline, with three females experiencing amenorrhoea and 19 females experiencing oligomenorrhea. After receiving therapy, four overweight females—one from group I and three from group II—saw improvements in their menstrual cycles. Following surgery, three overweight

female patients developed polymenorrhea. The findings of Legro Rs et al. (2006) and Vrbikova J et al. (2005), whose authors presented data comparable to the current investigation, were congruent with these results.

Assessing baseline and post-treatment clinical and metabolic characteristics in female research participants who were overweight or normal weight revealed that almost all measures were statistically equivalent in all but a few cases.

For females who were normal weight and those who were overweight, the mean age was 23.6±4.7 years and 22.1±5.4 years, respectively. After receiving spironolactone medication, it was shown that the OGTT (Oral Glucose Tolerance Test) considerably decreased in overweight females, going from 67.1±13.7 to 51.6±24.5. High-density lipoprotein levels rose significantly in lean females after 13 months of spironolactone treatment, rising from 1.13±0.5 to 1.49±0.3. This rise was statistically significant. In statistically significant reduction, the total triglyceride levels in obese females dropped from 1.56±0.3 to 1.22±0.8. Additionally, overweight females who received pharmaceutical treatment had an improvement in BMI from 29.2±3.8 to 27.2±4.5.

There was statistical significance in this difference as well. After using spironolactone for a year, neither lean nor overweight females' HOMAIR, AUCinsulin, fasting glucose, total cholesterol, blood pressure, or FG scores changed substantially. These findings corroborated those of studies by Spritzer Tm et al. (2000) and Haas DA et al. (2003), which found that spironolactone was effective in treating female PCOS patients. On assessing the pre- and post-treatment clinical and metabolic parameters in two groups of PCOS-afflicted study females. According to the study's findings, the mean ages of the four girls in the lean group and the five females in the overweight group were 19.6±4.8 and 23.8±5.5 years, respectively.

The AUCinsulin levels in females who were overweight decreased significantly from 6092±3789 to 4502±2118, but the drop in females who were normal weight was not statistically significant. Additionally, HOMAIR levels demonstrated a non-significant rise in normal e=weight females and a substantial decrease in overweight females, from 3.4±0.2 to 1.8±0.6. After a year of spironolactone medication, fasting glucose levels in both lean and obese females did not significantly alter. After receiving pharmaceutical medication, obese ladies' OGTT levels significantly decreased, going from 62.8±14.2 to 41.1±24.5 mmol/l in 60 minutes. The total triglycerides of thin ladies decreased significantly, from 1.3±0.3 to 1.0±0.5, while the reduction in overweight females was not statistically significant.

Additionally, following spironolactone, the BMI of overweight females decreased significantly from 30.1±3.7 to 26.1±3.6. In both lean and overweight females, spironolactone treatment for a full year resulted in non-significant changes in HDL, total cholesterol, and FG scores. This was similar to research published in 2004 by Ganie MA et al. and in 2013 by Ganie MA et al., who reported better clinical and metabolic characteristics in female PCOS patients after using spironolactone.

CONCLUSION

Within the constraints of the study, spironolactone is found to be useful in treating hyperandrogenism in PCOS patients, and there are no noteworthy negative effects associated with long-term spironolactone treatment in terms of glucose and lipid metabolism. In PCOS people exposed to a high risk of metabolic and cardiovascular illness, spironolactone has beneficial effects on lipid profile and insulin resistance. Nevertheless, the cross-sectional design, limited sample size, and biases related to geographic location were some of the study's shortcomings. Therefore, further long-term research with bigger sample sizes and longer observation periods will aid in coming to a conclusive result.

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TABLES

Parameter	Normal weight females (BMI <25) (n=4)		Overweight females (BMI >25) (n=5)	
	Pre-treatment	**Post-treatment**	**Pre-treatment**	**Post-treatment**
Age (years)	19.6±4.8		23.8±5.5	
$AUC_{insulin}$	5882±1590	5006±2187	6092±3789	4502±2118*
$HOMA_{IR}$	4.3±1.3	4.4±1.6	3.4±0.2	1.8±0.6*
Fasting Glucose (mmol/l)	18.4±6.6	16.6±3.4	17.6±3.2	13.7±7.8
OGTT 60 min (mmol/l)	73.2±15.7	66.4±18.0	62.8±14.2	41.1±24.5*
OGTT 120 min (mmol/l)	40.6±13.5	44.8±21.4	31.8±23.5	15.55±6.6
HDL (mmol/l)	1.14±0.3	1.16±0.4	1.0±0.3	1.0±1.3
Total cholesterol (mmol/l)	4.54±0.3	4.70±0.6	4.47±0.2	4.87±0.2
Total triglycerides (mmol/l)	1.3±0.3	1.0±0.5*	1.4±0.3	1.0±0.4
BMI (kg/m^2)	28.4±4.9	28.8±5.6	30.1±3.7	26.1±3.6*
FG scores	10.4±2.9	5.4±2.9	9.5±3.5	4.8±3.0

Table 2: Clinical and metabolic Baseline and post-treatment parameters in two groups of study females with PCOS

Parameter	Normal weight females (BMI <25) (n=12)		Overweight females (BMI >25) (n=10)	
	Pre-treatment	**Post-treatment**	**Pre-treatment**	**Post-treatment**
Age (years)	23.6±4.7		22.1±5.4	
$AUC_{insulin}$	3862±1302	3633±1248	6004±2964	4712±2072
$HOMA_{IR}$	2.04±0.7	2.3±0.9	3.4±1.1	2.7±1.5
Fasting Glucose (mmol/l)	9.3±3.8	10.4±2.6	17.2±5.7	14.7±6.2
OGTT 60 min (mmol/l)	39.3±15.41	39.5±14.4	67.1±13.7	51.6±24.5*
OGTT 120 min (mmol/l)	40.5±32.3	31.4±14.23	38.4±20.6	27.6±20.3
HDL (mmol/l)	1.13±0.5	1.49±0.3*	1.18±0.1	1.17±0.13
Total cholesterol (mmol/l)	4.37±1.7	4.8±1.5	4.46±0.2	4.76±0.5
Total triglycerides (mmol/l)	0.88±0.4	0.95±0.5	1.56±0.3	1.22±0.8*
BMI (kg/m^2)	22.2±2.1	22.1±2.2	29.2±3.8	27.2±4.5*
Diastolic B.P (mmHg)	80.2±3.7	75.6±5.4	79.4±3.1	77.7±5.2
Systolic B.P (mmHg)	126.7±9.3	115.6±6.8	121.5±10.3	118.1±10.1
FG scores	12.4±2.7	6.6±3.67	10.3±2.9	5.4±2.8

Table 1: Baseline and post-treatment parameters in normal weight and overweight females with PCOS