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## Management of obesity in polycystic ovary syndrome induced albino rats with *Pergularia daemia*

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### Abstract

Obesity plays a major role on both pathophysiology and manifestation of Polycystic syndrome (PCOS). PCOS is a common disorder with various signs and symptoms related to reproductive changes in female. In the present study PCOS was induced in the female rats *Rattus norvegicus* by injecting Testosterone Propionate. The results indicated an increase in the level of Low density lipoprotein in the serum sample which will lead to obesity. Such a situation was attempted using leaf extract of *Pergularia daemia* to clear obesity by reducing the cholesterol level in the serum. Thus obesity which has a clinical effect on PCOS can be treated using the extract of the plant chosen for the present study.

**Keywords:** Obesity, PCOS, lipoprotein, Testosterone, hyperandrogenism

### 1. Introduction

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder with multiple potential and uncertain aetiologies. The heterogeneity of the morphological structure of the ovary and the clinical findings in women with PCOS syndrome was first recognized by Stein and Leventhal in 1935. Their report only helps to establish the term Polycystic ovary syndrome. Hence this syndrome is otherwise called as Stein – Leventhal syndrome.

The experts stated that PCOS could be diagnosed when any two features out of the following are present: ovulatory dysfunction, clinical or biochemical hyperandrogenism, and PCO (Zawadzki & Dunaif, 1992) [28]. The signs and symptoms of PCOS can be classified into three major categories namely clinical symptoms which include irregular menstrual cycles, hirsutism, acne, alopecia, anovulatory infertility and recurrent miscarriages too, elevated amount of androgens, Luteinizing hormone (LH), prolactin and lower level of Follicular stimulating hormone (FSH) and thyroid hormones. Insulin resistance, obesity, lipid abnormalities and increased risk factors for glucose tolerance and type 2 diabetes (Tsilchorozidou *et al.*, 2004) [24] are the other symptoms.

Obesity appears to be closely associated with PCOS. Azziz *et al.* (2004) [2] stated that more than 50% of the patients with PCOS are overweight or obese in United States. They also stated that obesity also have the major influences in the expression of PCOS. Many factors have been attributed to an epidemic of obesity including sedentary life style, high fat diet and consumption of modern fast foods (Grundty, 1998) [9]. Fat not only increases the taste of food but it gets converted to body fat more effectively than carbohydrates (Rebuffe – Scriver *et al.*, 1993) [20]. The mechanism of diet induced obesity is unclear, but on long exposure to fat diet can increase body fat and adiposity also it induces a low sympathetic activity which in turn reduces the energy expenditure. The term obesity also plays a key role in the pathophysiology of hyperandrogenism and chronic anovulation. The etiopathogenesis of obesity in PCOS has not yet been exactly clarified. There clearly is a vicious circle of abdominal obesity, insulin resistance, and hyperandrogenemia (Vrbikova and Hainer, 2009) [25]. The study of PCOS has been hampered by the lack of clear diagnostic criteria. It is necessary to emphasize that PCOS is still a ‘syndrome’, and no single test is diagnostic. The first attempt to define PCOS was undertaken in 1990 by the consensual conference sponsored by the National Institutes of Health (NIH) (Zawadzki and Dunaif, 1992) [28].

Ovulatory dysfunction together with clinical or biochemical hyperandrogenism was defined as necessary for the diagnosis of PCOS. The pathogenic importance of obesity in the development of PCOS is stressed by the results of a prospective study determining the relationship between body size and self-reported PCOS symptoms. Both abdominal obesity and weight gain after adolescence were predictive for the development of PCOS. An increased risk of self-reported PCOS symptoms was observed among 30-year-old overweight or abdominally obese women who had either normal weight in adolescence or who were overweight or obese at both adolescence and adult age (Laitinen *et al.*, 2003) [12]. Increased adiposity is associated with several abnormalities of sex steroid metabolism and results in increased androgen production and suppression of Sex Hormone Binding Globulin (SHBG) (Pasquali, 2006) [18]. (Cattrall and Healy, 2004) [4] described that the patients with obesity and PCOS have the highest cardio-metabolic risk factor than that of the lean patients with PCOS. Management of weight loss through diet and exercises has a fortune effect on metabolic, endocrine and reproductive outcome in PCOS (Clark *et al.*, 1995 and 1998) [6, 7]. The prevalence of obesity in the women with PCOS ranges from 1% to 80%. Obese persons report difficulties in achieving and maintaining weight loss. Once the person has achieved weight loss they should be encouraged to maintain this in the long term and to have a normal weight (Tannys *et al.*, 2010) [22].

Guzick (1998) [10] stated that the elevated low density cholesterol and insulin resistance clustered together to have PCOS as a genetic component. Wild in 1997 proved that the women with PCOS have higher levels of total cholesterol, LDL, Very - low density lipoprotein (VLDL) and triglycerides when compared to the healthier women. The level of High density lipoprotein (HDL) is higher in normal women than that of PCOS women. Haslam and James (2005) [11] said that there is a worldwide public health emergency due to the increasing epidemic of obesity and its related diseases.

Azziz *et al.* (1995) [1] commented that the character of obesity is not found in all PCOS patients. But to the controversy of this statement Ehrmann (2005) [8] reported that obesity is thickly associated with PCOS. Although the case is unknown, but obesity is present in nearly 30% of cases and in some cases the percentage is even higher like 75%. Women with PCOS condition have the risk factors of dyslipidemic factors with hypertriglycerolemia and reduced HDL and increased LDL when compared to that of the normal BMI women (Berneis *et al.*, 2007) [3]. LDL is associated with the increase risk of Coronary heart disease and ischemic stroke in diabetic and non - diabetic population (Zeljko *et al.*, 2009) [29]. Tanskinen, 2003 gives a clear picture about LDL and describes that small particles of LDL can easily penetrate into the endothelium. High concentration of the LDL shows a correlation with the progression of atherosclerosis and severe cardiovascular diseases (Moon *et al.*, 2007) [16].

*Moringa oleifera* and lovastatin were found to lower the serum cholesterol, phospholipid, triglyceride, VLDL, LDL, cholesterol to phospholipid ratio and atherogenic index, but were found to increase the HDL ratio (HDL/HDL-total cholesterol) as compared to the corresponding control groups. Treatment with *Moringa oleifera* or lovastatin in normal rabbits decreased the HDL levels. However, HDL levels were significantly increased or decreased in *Moringa*

*oleifera* or lovastatin-treated hypercholesterolaemic rabbits, respectively (Mehta *et al.*, 2003) [15].

Treatment with the cyproterone acetate with the combination of the oral contraceptives have a tendency to reduce the level of triglycerides and it helps to decrease the level of androgen and effective with hirsutism (Mastorakos *et al.*, 2002) [14]. Apart from cyproterone many other allopathic medicines are there to treat obesity, but they lead to some side effects. In order to avoid the side effects natural therapy is the best way to cure. The main objective of the current study is to observe the physiological and the biochemical changes in the PCOS induced rats and to identify a special natural drug for the human with the help of animal model.

## 2. Materials and Methods

### 2.1. Experimental Animal

Female Albino Wistar strain rats (*Rattus norvegicus*) were used as an experimental animal with the body weight 150 – 200 grams purchased from King's Institute Chennai. The animals were acclimatized to the laboratory conditions for 15 days fed with pellet and water *ad libitum*, pellets were purchased from Sai Durga Enterprise. These animals were exposed to natural light and dark conditions for 12 hrs each (Day & Night). After the acclimatization period the rats were used for the experimental work with the approval of Institutional Animal Ethical Committee (437/01/c/CPCSEA) (Ref. 01/2011).

### 2.2. PCOS induction in rats

#### 2.2.1. Preparation of Testosterone Propionate

5 grams of Testosterone Propionate (TP) were purchased from Himedia Company (Mumbai) and were dissolved in sesame oil.

#### 2.2.2 Experimental Design

In the current experiment four different groups of twenty four animals were taken one as Normal which receives nothing, control receiving only olive oil, injected with testosterone propionate (400mg concentration) dissolved in olive oil over a period of seven days and the treated group with fresh crude extract of *Pergularia daemia* over a period of three days. After the experimental period the animal were sacrificed and the blood was collected for the analysis of serum Lipid profile.

### 2.3. Preparation of aqueous extract

*Pergularia daemia*, commonly called as Trellis – vine belongs to Apocynaceae family. This plant is found in the tropical regions of Asia commonly called “Veli – paruthi. It is a perennial vine was collected from Golden rock, Tiruchirappalli. This plant is found on the fences of the garden or in the waste land, which is a climber with thick and leathery leaves containing milky latex content in it with horny fruit that consists of the cotton like material inside it. Fresh leaves were washed, chopped and were crushed well in the Mortar and Pestle. The fresh juice (crude extract) from the leaves were collected and used for this study (Figure 1).



Fig 1: Pergularia daemia

2.4. Biochemical Analysis

The serum collected from the different groups was analyzed biochemically for lipid profile and were analyzed through ADVIA CENTAUR immunoassay system (auto analyzer).

2.5. Statistical Analysis

All the results were statistically analyzed and interpreted using Statistical Package for Social Sciences (SPSS V.17).

3. Results

The study includes four groups as Normal, Control, PCOS induced and the Pergularia daemia leaf extract treated. Table 1 depicts about the descriptive mean of four different groups.

The average mean value for the normal group of the HDL is 34.00 mg/dl and the control group is 44.00 mg/dl (Figure 2). In TP injected group the mean value is 10.05 and the Pergularia daemia treated group the mean value is 39.83 mg/dl. The LDL mean level in the normal group is 94.33 mg/dl, in control group the mean value is 70.33 mg/dl, in the injected group the mean value is drastically increased (141.33 mg/dl) indicates that PCOS condition in animals stores excess amount of the low density lipoprotein which is a major source that causes obesity, where as in the Pergularia daemia treated group the mean value is 60.50 mg/dl (Figure 3). This shows that the Pergularia daemia reduces the serum LDL level and helps to control obesity. The VLDL mean values of the Normal, control, injected and Pergularia daemia treated group are 28.95, 26.16, 44.02 and 16.08 mg/dl respectively (Figure 4). This proves that the Pergularia daemia reduces the very low density lipoprotein content too. One way analysis of variance analysed for the lipid profile indicates that treatment of Pergularia daemia shows a significant (P<0.05) reduction in the treated groups and it proves that Pergularia daemia is an effective medicine to cure PCOS in rat models.

Table 1: The Lipid Profile of Normal, Tp Injected and Plant Extract Treated Groups

Groups	HDL (mg/dl)	LDL ( mg/dl)	VLDL (mg/dl)
Control	44.00 ± 2.366	70.33 ± 1.966	26.16 ± 2.316
Normal	34.00 ± 1.414	94.33 ± 2.160	28.95 ± 0.187
TP injected	10.05 ± 0.187	141.33 ± 2.581	44.02 ± 0.109
Plant I treated	39.83 ± 1.471	60.50 ± 1.870	16.08 ± 0.248

Table 2: One way analysis of variance between the experimental groups and lipid profile of the groups

Lipid profile		Sum of Squares	Degrees	Mean Square	F-Value	Significance
Level of HDL	Between Groups	4146.961	3	1382.320	564.116	0.000
	Within Groups	49.008	20	2.450		
	Total	4195.970	23			
Level of LDL	Between Groups	23402.125	3	7800.708	1668.601	0.000
	Within Groups	93.500	20	4.675		
	Total	23495.625	23			
Level of VLDL	Between Groups	2402.217	3	800.739	584.978	0.000
	Within Groups	27.377	20	1.369		
	Total	2429.594	23			

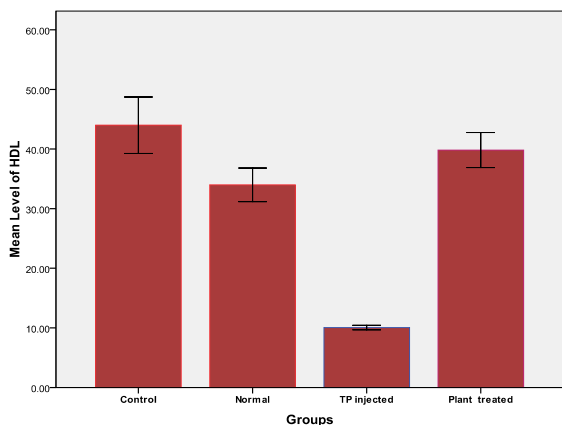


Fig 2: The level of HDL-cholesterol (mg/dl) normal, TP injected and Plant extract treated groups

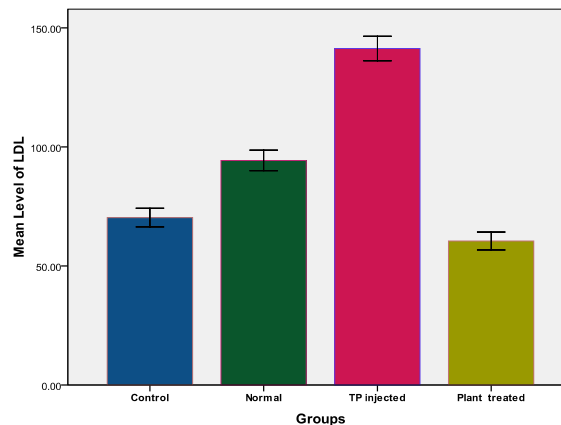
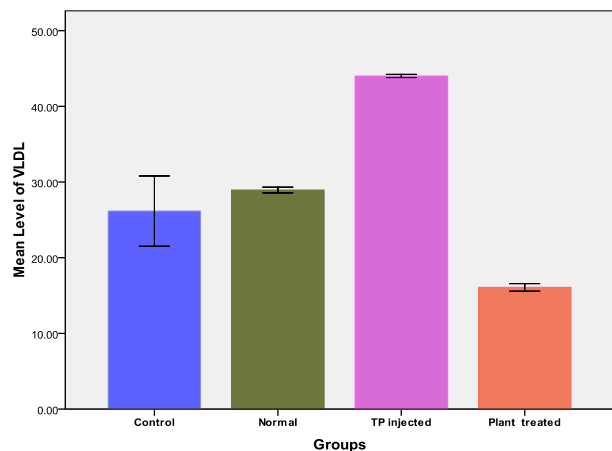


Fig 3: The level of LDL-cholesterol (mg/dl) normal, TP injected and Plant extract treated groups



**Fig 4:** The level of VLDL-cholesterol (mg/dl) normal, TP injected and Plant extract treated groups

#### 4. Discussion

Cholesterol is a component of cell membranes and a precursor for steroid hormones and bile acids synthesized by body cells and absorbed with food. Cholesterol is transported in plasma via lipoproteins, namely complexes between lipids and apolipoproteins. There are four classes of lipoproteins: high density lipoproteins (HDL), low density lipoproteins (LDL), very low density lipoproteins (VLDL) and chylomicrons. While LDL is involved in the cholesterol transport to the peripheral cells, HDL is responsible for the cholesterol uptake from the cells. The four different lipoprotein classes show distinct relationship to coronary atherosclerosis. LDL - cholesterol contributes to atherosclerotic plaque formation within the arterial intima and is strongly associated with coronary heart disease and related mortality. Even with total cholesterol within the normal range an increased concentration of LDL - cholesterol indicates high risk. HDL -cholesterol has a protective effect impeding plaque formation and shows an inverse relationship to coronary heart disease prevalence. In fact, low HDL - cholesterol values constitute an independent risk factor. The determination of the individual total cholesterol level is used for screening purposes while for a better risk assessment it is necessary to measure additionally HDL - cholesterol assessment and LDL - cholesterol. In the last few years several controlled clinical trials using diet, life style changes and different drugs (particularly HMG CoA reductase inhibitors) have demonstrated that lowering total cholesterol and LDL - cholesterol levels reduce drastically coronary heart disease risk.

The DHT – induced PCOS in rats recapitulates the metabolic and the ovarian features in the human PCOS (Manneras *et al.*, 2007) [13]. The signs and the symptoms of the PCOS are irregular cycle, increased body fat, enlarged adipocytes, elevated leptin levels and insulin resistance. Similarly Letrozole induced PCOS rats also have some changes in the morphology which is similar to that of the human beings. The similarities is based on the weight of the ovaries due to the case of anovulation and thickening of the thecal layer. He also explained that the Letrozole induced rat shows an increase in body weight, which is a major symptom for obesity.

Ota *et al.* (1983) [17] successfully induce PCOS condition by giving Testosterone propionate (TP) to the younger rats. They proved that in the 40<sup>th</sup> day the formation of PCOS and

hyperthecosis occurred. They were due to the thickening of tunica albuginea nor corpora lutea.

Androgen Excess Society (AES) which is an internationally recognized organization promotes research in all androgen excess disorders. These organization identified a criteria related to obesity and PCOS. They determined that there is a metabolic risk for PCOS infected patients particularly insulin resistance. Both the insulin resistance and PCOS can lead to obesity which is a major risk for some other diseases too. So the presence of biochemical parameter is necessary to confirm PCOS and its metabolic disorders (Vrbikova and Hainer, 2009) [25]. The present study also proves the same statement and the biochemical study helps to prove the same. Yildiz *et al.* (2008) [27] described about the prevalence of PCOS with increased degree of obesity. They collected some data which shows the prevalence of PCOS is higher in the reproductive age women with that of the general population. They also scrutinized that PCOS is caused by intrinsic or inherited factors.

Christian *et al.* (2003) [5] explained that the obese women have the chance of getting coronary heart diseases. He also explained that increased LDL level in the PCOS patients have a higher risk of visceral adiposity. They suggested that the early treatment for obesity and coronary heart disease in PCOS condition can prevent atherosclerosis. Phelan *et al.*, 2010 commented that the lipid metabolism and insulin resistance are independent in nature to cause PCOS but hyperandrogen state with the increased central adiposity are the causative agents for PCOS.

#### 5. Conclusion

The current research work is performed to know about the obesity pattern in the PCOS induced rat models through the lipid profile. There are several allopathic medicines to treat the obesity and many people are rushing to the many fitness centers and consuming the huge amount of the steroids and multivitamins which cause side effects. There are several plants in our traditional medicine remains unknown to the world that brings cure for many diseases one such plant is *Pergularia daemia*. The leaf extract of the *Pergularia daemia* cures not only the PCOS but it's also a cure for the obesity which is a threatening problem for the cause of infertility. The statistical evidence also proves a significant result between the control, normal and the *Pergularia daemia* treated groups. Thus the current work proves that *Pergularia daemia* is an effective and active medicine to cure obesity which is a common problem in all the Indian people.

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