EFFECT OF ULTRASOUND CAVITATION VERSUS ELCTROACUPUNCTURE ON SEX HORMONES IN OBESE INFERTILE PATIENTS WITH POLY CYSTIC OVARIAN SYNDROME

By

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CHAPTER I

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder that occurs in 6 – 10% of women at the reproductive age **(March et al., 2010).** It is associated with an-ovulation, infertility, hyperandrogenism, obesity and insulin resistance **(Williams et al., 2016).**

Endocrine characteristics of PCOS are elevated serum concentrations of androgens and Luteinizing hormone (LH) and decreased concentrations of sex hormone binding globulin (SHBG). The an-ovulation is associated with disturbance in the feedback from ovarian steroid hormones to the hypothalamus and pituitary, resulting in disturbances of the pulsatility of gonadotropin releasing hormone (GnRH) **(Williams et al., 2016).**

Ultrasound cavitation (UC) (also known as fat cavitation or lipo-cavitation) is the method in handling Subcutaneous Adipose Tissue (SAT), especially in destroying subcutaneous fat and shaping a particular part of the body. As one of the non-surgical correction method, UC is preferred for lowering the risk of complications due to obesity **(Palumbo et al., 2011).**

The suitable parameter of the UC is 20-70 kHz ultrasound energy that will be emitted at certain depth in a convergent way and focused at a certain point to produce unlimited small vacuum bubbles (fat bubbling). These bubbles are compressed to break the bonds among fat cells, and destroy their membranes to form " cavitation's" (holes in the fat layer) then drain them via lymphatic vessels to be excreted from the body **(Brown et al., 2009).**

UC reported a greater decrease of the WHR, suggesting a valuable modification of fat distribution pattern, especially at the abdominal level. It improves rates of ovulation, provides higher incidence of regular menstrual cycles and lower levels of total testosterone and fasting insulin **(Hanan et al., 2011).**

Acupuncture is a treatment method used in Traditional Chinese Medicine (TCM). It has been used for treatment of neurological and musculoskeletal diseases such as intervertebral disk disease and spinal cord injury **(To and Wong, 2003).**

In electro-acupuncture, the therapist inserts the acupuncture needles in acupuncture points and electric current is connected to the body through the acupuncture needles **(Ahsin et al., 2009)**. The stimulation can be measured more objectively and regulated more precisely through adjustments of the electrical current, amplitude and frequency. Electro-acupuncture can produce a higher and more continuous level of stimulation than manual manipulation; this is especially useful in acupuncture anesthesia. In addition, it is possible to apply the current through an electrode on the skin surface, without the aid of a needle inserted subcutaneously **(Steven and William, 2007).**

Electroacupuncture promotes follicle development and corrects reproductive endocrine dysfunction in ovaries by regulating the functions of the hypothalamus, pituitary and ovaries **(Johansson et al., 2013).**

<u>Statement of the problem</u>:

Is there is any difference between the effect of Ultrasound Cavitation and Elctroacupuncture on sex hormones in obese infertile patients with poly cystic ovarian syndrome?

<u>Purpose of the study:</u>

The aim of this study is to determine the difference between the effect of Ultrasound Cavitation and Elctroacupuncture on sex hormones in obese infertile patients with poly cystic ovarian syndrome.

<u>Significance of the study:</u>

PCOS is the most common endocrine abnormality in reproductive-age women. The prevalence of PCOS is traditionally estimated at 4% to 8% from studies performed in Greece, Spain and the USA **(Arslanian et al., 2000).**

PCOS is the most common cause of an ovulatory infertility. It accounts for 90% to 95% of women attending infertility clinics with anovulation. However 60% of women with PCOS are fertile (defined as the ability to conceive within 12 months), although time to conceive is often increased. In those with PCOS and infertility, 90% are overweight. Obesity independently exacerbates infertility, reduces efficacy of infertility treatment and induces a greater risk of miscarriage **(Brassard et al., 2008).**

There is currently an active debate about the appropriate limit for body mass index for assisted reproduction therapies, given the reduced success rates and the demonstrated risks of pregnancy in overweight women. Ideally, weight should be optimized prior to pregnancy. Age-related infertility also exacerbates infertility and timely planning of families may warrant discussion **(Cedergren, 2007).**

Cavitation ultrasound is supposed to correct the negative impacts of abdominal adipose tissues on the ovarian function and clinical manifestations in women with PCOS and abdominal obesity **(Ascher, 2010).**

Many studies reported the efficacy and safety of cavitation in reducing visceral adipose tissues and abdominal subcutaneous tissue, and they showed that there is a great decrease in fat thickness of subcutaneous tissue within the treated area and there is consistent reduction in abdominal circumference >2 cm after a single treatment **(Jewell et al., 2012 and Saedi et al., 2013).**

Regarding the effect of electroacupuncture on infertile patient with PCO, previous clinical trials suggest that acupuncture may induce ovulation, improve menstrual frequency and improve depression, anxiety, and health-related quality of life in PCOS patients (**Stener-Victorin et al., 2013 and Zheng et al., 2013**). In addition, electroacupuncture is able to decrease abnormally high levels of circulating luteinizing hormone (LH), which affect the LH/follicle-stimulating hormone (FSH) ratio and high levels of testosterone **(Jedel et al., 2011).**

Till now, there are no previous studies that compare between the effect of ultrasound cavitation and electroacupuncture on sex hormones in obese infertile patients with PCO. So, this studies will be the first one in this issue. Therefore, this study will be of valuable benefits for medical services organizations and increase body of knowledge of physical therapists in scientific field.

Delimitations:

This study will be delimited to:

1- Forty obese infertile patients with poly cystic ovarian syndrome.
2- Their ages will be ranged between 20-35 year old.
3- Their body mass index will be ranged from 30-40 kg/m^2.
4- All of them are married women.

Limitations:

This study will be limited to the following criteria:

1- Psychological status.

2- Cooperation of the patients may affect the result of the study.

3- Environmental factors which may have affected the patient's response.

4- The daily effort may affect the result of the study.

Null Hypothesis:

It will be hypothesized that, there is no difference between the effect of ultrasound cavitation and electroacupuncture on sex hormones in obese infertile patients with poly cystic ovarian syndrome.

Basic assumptions:

It will be assumed that:

1- All patients will show adequate cooperation with study procedure.

2- All patients will follow the instructions that will be given to them.

3- Clinical methods of evaluation will be reliable and valid.

4- Results obtained from this study will be of value in physical therapy.

CHAPTER II

LITERATURE REVIEW

PCOS is the major endocrine disorder affecting females in age of reproduction and is considered to be the most common cause of an ovulatory infertility. According to diagnostic criteria, PCOS affects 12-21% of women in child bearing period of life; however, many cases are undiagnosed **(Stabile et al., 2014).** It represents a condition in which an estimate of 10 small cysts of a diameter ranging between 2 and 9 mm develop on one or both ovaries and/or the ovarian volume in at least one ovary exceeds 10 ml **(Balen and Rajkowha, 2003).**

Although it was previously considered as a disorder of adult women, recent evidence suggests that PCOS is a lifelong syndrome, manifesting since prenatal age. In fact, according to the Rotterdam diagnostic criteria, the prevalence of PCOS, in adolescents varies between a minimum of 3% **(Hashemipour et al., 2004)** and a maximum of 26% **(Driscoll, 2003).** However, the prevalence of the disease in children is still considered unknown **(Kamangar et al., 2015).**

The economic burden of PCOS is significantly huge. Around 4 billion dollars are spent annually in the United States to screen for the disease and treat its various morbidities, including hirsutism, infertility, and diabetes mellitus. The Australian Health System spends more than 800 million dollars every year to account for the disease **(Azziz et al., 2005).** Therefore, accurate and early diagnosis of PCOS is necessary not only to prevent future health comorbidities but also to reduce financial cost and burden **(Kamangar et al., 2015).**

Obesity and PCO

The prevalence of obesity reaches 80% in the United States and 50% outside which indicates that this figure depends on local environmental factors, ethnic backgrounds, and lifestyle, and not on the mere presence of PCOS itself. On the other hand, women with PCOS are at a higher risk of developing obesity **(Balen et al., 1995 and Randeva et al., 2012).**

Many studies explain that females with PCOS have increased visceral and subcutaneous body fat distribution due to increased androgen production rates; this central obesity follows a masculinized body fat distribution where the amount of visceral fat correlates with the degree of insulin resistance **(Karabulut et al., 2012 and Borruel et al., 2013).**

Obese women with PCOS have a characteristic distribution of a central pattern of body fat known as android obesity in which fat deposited in the abdominal wall and visceral mesenteric area. This fat is more sensitive to catechol-amines and less sensitive to insulin **(Pasquali and Casimirri, 2003).** In addition, women with higher waist/hip ratios (i.e. more abdominal relative to hip fat) have higher total androgen and lower SHBG levels **(Pasquali et al., 1997).**

Moreover, obesity plays a significant role in expressing the metabolic features of PCOS. Women with PCOS have an atherogenic lipid profile, associated with elevated levels of low-density lipoprotein, triglycerides and cholesterol, along with decreased levels of high-density lipoprotein. They are also at a higher risk of developing atherosclerosis, arterial stiffness, and altered vascular endothelium **(Hart and Norman, 2006).** In addition, women with PCOS show a worsened cardiovascular profile and associated complications **(Randeva et al., 2012).**

However, obesity by itself is not the main reason behind these features. This is evident in lean women with PCOS who demonstrate the same metabolic features as those who are obese **(Balen et al., 1995).** Whether obesity leads to PCOS or whether PCOS leads to obesity is still debatable **(Kamangar et al., 2015).**

Obesity is also seen and associated with insulin resistance and decreased SHBG as well as, in many cases, increased testosterone concentrations **(Velazquez, 2006).** Thus, obesity appears to be strongly related to affect the activity of hypothalamic-pituitary axis which causes excessive LH concentrations resulting in a lower chance of conception **(Regan et al., 2005).**

<u>Infertility and PCO:</u>

Women with PCOS may have reduced fertility due to the associated endocrine and gynecologic abnormalities that impact ovarian quality and function **(Hart and Norman, 2006).** Accounting for up to 90% of ovulatory disorders, PCOS associated persistent periods of anovulation are positively correlated with infertility **(Imani et al., 1998).**

In 1995, a study reported up to 50 and 25% of women in a PCOS population suffering from primary and secondary infertility respectively **(Balen et al., 1995).** On the other hand, some studies suggested that females with PCOS who conceive might suffer from pregnancy-related complications such as gestational diabetes, pregnancy induced hypertension and preeclampsia to a higher extent in comparison to matched controls **(Sir-Petermann et al., 2012; Bruyneel et al., 2014 and Katulski et al., 2015)**.

Various research data also suggest an increased risk of miscarriage in women with PCOS **(Winter et al., 2002).** Concerning the effects on

the embryo, women with PCOS are 2.5 times at a higher risk of giving birth to small for gestational age children in comparison to healthy females **(Katulski et al., 2015)** and offspring show an increased morbidity and mortality compared to control **(Fauser et al., 2012).**

Various methods used in the treatment of PCO:

Therapeutic strategies in PCOS include diet-induced weight loss, exercise and medical therapy fail to optimally treat PCOS and all of these can reduce but not reverse IR **(Sabbour et al., 2009).**

1- Hypocaloric diet :

Standard dietary management of obesity and related comorbidities is a nutritionally adequate, low fat (approximately 30% of energy, saturated fat approximately 10%), moderate protein (approximately 15%) and high carbohydrate intake (approximately 55%), with increased fiber-rich wholegrain breads, cereals, fruits and vegetables and moderate regular exercise. A moderate energy reduction diet (500 to 1,000 kcal/day reduction) reduces body weight by 7% to 10% over a period of 6 to 12 months **(Dansinger et al., 2005).**

2- Life style modification:

Lifestyle change is first line treatment in an evidence-based approach in the management of the majority of PCOS women who are overweight **(Moran et al., 2009).**

Furthermore, prevention of excess weight gain should be emphasized in all women with PCOS of both normal or increased body weight. As little as 5% to 10% weight loss has significant clinical benefits improving psychological outcomes, reproductive features (menstrual cyclist, ovulation and fertility) and metabolic features (insulin resistance and risk factors for CVD and DM2) **(Galletly et al., 1996)**. Evidence

shows that lifestyle change with small achievable goals results in clinical benefits even when women remain in the overweight or obese range (**Wahrenberg et al., 1999).**

3- Exercise:

Incorporating simple moderate physical activity including structured exercise (at least 30 min/day) and incidental exercise increases weight loss and improves clinical outcomes in PCOS compared to diet alone. Exercise alone also improves clinical outcomes **(Poehlman et al., 2000).**

Aerobic exercise for 12 weeks is an effective method to decrease visceral fat, waist circumference, in obese subjects with T2DM even without weight loss. Frequent aerobic exercise has been shown to increase HDL-C levels by approximately 5% as early as 2 months from start of regular exercise in sedentary but otherwise healthy individuals **(Dekker et al., 2007).**

4- Medical treatment:
A- Oral contraceptive pills (OCP):

OCP are the most commonly used medications for the long-term treatment of women with PCO and have been recommended by the Task Force and the Endocrine Society **(Legro et al., 2013)**, the Australian Alliance **(Misso et al., 2014)** and the PCOS Consensus Group as first-line treatment for hyperandrogenism and menstrual cycle irregularities in women with PCOS **(Fauser et al., 2012)**.

By suppressing the hypothalamic-pituitary-ovarian axis, OCP decrease LH secretions, increase sex hormone binding globulins, and decrease free testosterone levels. This addresses hyperandrogenism-mediated symptoms improving acne and hirsutism, corrects menstrual

cycle abnormalities and provides a mean for effective contraception **(Costello et al., 2007)**.

Even though guidelines do not specify the use of one OCP over another and the best choice for symptomatic treatment is considered to be low-dose oral contraceptives that contain anti-androgenic or neutral progestin **(Fauser et al., 2012 and Legro et al., 2013).**

A number of clinical trials encouraged the use of OCP in patients with PCOS with increased risk of insulin resistance **(Baillargeon et al., 2003 and Legro et al., 2013).** Concerns have been also raised about the negative effects of OCP on the cardiovascular profile of females with PCOS **(Baillargeon et al., 2005).**

B- Metformin:

Metformin (Glucophage), an oral anti-diabetic biguanide drug, acts by impeding hepatic glucose production and increasing the peripheral insulin sensitivity **(Bailey and Turner, 1996).** Some data revealed that metformin does not improve insulin resistance itself, rather it improves glucose effectiveness, i.e., the ability of glucose per se to repress endogenous glucose synthesis and stimulate glucose uptake **(Pau et al., 2014).**

Metformin treatment of obese adolescents with PCOS and impaired glucose tolerance proved beneficial in improving glucose tolerance and insulin sensitivity, in lowering insulinemia and in reducing elevated androgen levels **(Arslanian et al., 2002).**

Even though studies show contradictory results regarding metformin effect, it is suggested as first-line treatment for cutaneous manifestations and pregnancy complications in women with PCOS. It is also used as a combination with clomiphene citrate to improve fertility

outcomes in clomiphene citrate resistant patients **(Legro et al., 2013 and Misso et al., 2014).**

5- Ultrasound cavitation:

Ultrasound Fat Cavitation (USFC) is the method in handling obesity, especially in destroying fat and shaping a particular part of the body. As one of the non-surgical correction methods, USFC is preferred at decreasing the risk of complications due to obesity **(Palumbo et al., 2011).**

The cavitation used in the field of aesthetic medicine is an innovative technique for a nonsurgical reduction of the localized fat and cellulite, Ultrasonic vibrations spread in the form of a wave in medium such as a liquid or a solid. When the particles of an elastic medium are under ultrasonic vibration, they act continuously in only one direction **(Sabbour et al., 2009).**

This phenomenon called cavitation is a very smart way to reduce fat because it is converting the fat into liquid and then is naturally eliminated with the urine when cavitation therapy is followed by lymphatic drainage. The process is faster and the drainage is very effective **(Ter-Haar and Coussios, 2007)**.

Studies have proven that ultrasound is characterized as a safe, noninvasive, reliable and predictable ways for body sculpting **(Palumbo et al., 2011).** Despite that, a lot studies claim to produce statistically significant results, the clinical benefits of ultrasound have yet to be approved **(Ascher, 2010).** This reduction in regional fat distribution could contribute to the effect of cavitation in improving the hormonal profiles (higher rates of ovulation, higher rate of regular menstrual cycles, lower

levels of LH/FSH Ratio and total testosterone) in obese women with PCOS **(Hanan et al., 2011).**

6- Electroacupuncture:

Acupuncture has been the subject of active scientific research since the late 20th century but it remains controversial among medical researchers and clinicians. It is able to decrease abnormally high levels of circulating luteinizing hormone (LH), which affect the LH/follicle-stimulating hormone (FSH) ratio and high levels of testosterone **(Ernst et al., 2007).**

<u>**Point selection, location and application:**</u>

There are tender areas at certain points of the body surface with all diseases, regardless of whether they are physical or mental, which disappear when the illness is cured. There are called acupuncture points. **Jayasuria (1993),** stated that the use of acupuncture points to treat diseases of local and adjacent areas is one of the key principles in the practice of acupuncture therapy. It is the first consideration that should govern the selection of the acupuncture points for any regional disease. The local points are the most effective points in treating a majority of disorders. Every acupuncture point has a local effect on the surrounding tissues **(Stux and Pomeranz, 1998).**

<u>**Location methods for body acupuncture :**</u>

There are various methods for locating acupuncture points (Focks, 2008) :

Anatomical approach: many acupuncture points are situated at clearly defined anatomical locations, for example in depressions, at muscle and tendon insertions, in grooves, at joint clefts, at bony prominences, etc.

Proportional measurements: when trying to locate points not situated at any prominent structures, Chinese medicine applies the proportional cun measurement.

Electric tools: these measure the electric resistance of the skin in order to find the correct location of the points. Generally, electric resistance is lower in the immediate area around the point.

Sex hormones changes:

a- Testosterone:

- A total testosterone is likely to be more reliable than a free testosterone given the difficulties seen with many of the assays used for the latter **(Rosner, 2001).**

- Testosterone values may be normal in PCOS. - Oral contraceptives will lower total testosterone, and interpretation in this setting is difficult (3 months off oral contraceptives is best to get a "true" testosterone value).

- Most testosterone values in PCOS will be 200 ng/dL (> 6.9 nmol/L) warrant consideration of an ovarian or adrenal tumor **(Derksen et al., 1994).**

b- Luteinizing Hormone/Follicular Stimulating Hormone:

- Luteinizing hormone/follicle stimulating hormone (LH/FSH) ratio - A ratio >2.0 is suggestive of PCOS but is not highly sensitive or specific **(Fritz MA and Speroff L, 2011).**

c- serum progesterone level:

- If mid-luteal serum progesterone level will be elevated above 6 ng/ml, it will lead to confirm ovulation **(Ellaithy, 2012).**

CHAPTER III

SUBJECTS, MATERIALS AND METHODS

Study Design:

This study will be designed as prospective, randomized, single blind, experimental, pre-post test , controlled- trial study.

I-   Subjects:

Forty obese infertile patients with poly cystic ovarian syndrome will participate in this study to determine the difference between the effect of Ultrasound Cavitation and Elctroacupuncture on sex hormones. They will be selected randomly from Out Patient Clinic of Aga Hospital Central, in Aga on the following criteria:

Inclusion criteria:

1- Their ages will be ranged between 20-35 year old.
2- Their body mass index will be ranged from 30-40 kg/m^2.
3- All of them are married women.

Exclusion criteria:

Women will be excluded if they have one of the following criteria:

1- Diabetes mellitus.
2- Thyroid dysfunction.
3- Concomitant cardiovascular disorders.
4- Respiratory, renal and liver dysfunction.
5- Tubal adhesions as well as uterine abnormalities.

All patients will be divided randomly into two equal groups (A&B).

Group A:

It will consist of twenty obese infertile patients with PCO who will be treated by ultrasound cavitation on the abdomen, 2 times per week for 3 months with medical treatment in addition to hypocaloric diet (1200 kcal/day) for 3 months.

Group B:

It will consist of twenty obese infertile patients with PCO who will be treated by electroacupuncture, 3 times per week for 3 months with medical treatment in addition to hypocaloric diet (1200 kcal/day) for 3 months.

All patients will be given a full explanation of the study protocol and consent form will be signed by each woman before participating in the study, the purpose and nature of the study will be explained to all patients **(Appendix I).**

II- Instrumentations:

1- **Recording data sheet** (Appendix II).

2- **Standard weight height scale:**

It will be used to measure weight and height to calculate the body mass index (BMI) for each woman.

3- **Tape measurement:**

It will be used to calculate the waist/hip ratio.

4- **Test tubes:**

Sterilized test tubes will be used to collect the blood samples from obese infertile patients with PCO.

5- **Kites:**

They will be used for assessment of serum progesterone level, testosterone, LH and FSH hormones.

6- Abdominal ultrasongraphy:

It will be used for measuring ovulation rate.

7- Focused ultrasound cavitation:

Fat cavitation, biCAVI (Ultimate). It will be used to apply the treatment procedure for all patients in group A.

8- Electro acupuncture:

It will be used to apply the treatment procedure for all patients in group B.

III- <u>Procedures:</u>
A-<u>Evaluative procedures:</u>

1. Weight and height measurements:

Weight and height measurements will be measured while the patient is wearing a thin layer of clothes to calculate the BMI according to the following equation before and after treatment for both groups (A&B):

BMI = weight/height^2 (kg/m^2).

2. Waist and Hip Ratio:

- It must be taken in order to accurately measure obesity rather than just visually inspecting of naked body (reference of female measurements : minimal waist circumference >88 cm and waist-hip ratio >0.85).

- It is measured by tape, waist Circumference will be measured at the narrowest portion of the torso approximately midway between the lower costal margin and the iliac crest and the hip circumference will be measured over the widest portion of the gluteal and greater trochanteric region then the ratio between them will be calculated.

3. Blood analysis:

Blood samples will be drown from antecubital vein of each patient before and after treatment. It will be centrifuged within 2 hours after withdrawal. Serum is stared at -20 °C and assayed for LH/ FSH Ratio, Testosterone and Luteal Serum Progesterone. They will be measured from 3th day from menstrual cycle **(Richard et al., 2010 and Ellaithy, 2012).**

4. Ovulation rate:

- It will be done before and after treatment for patients in both groups through luteal serum progesterone assay.
- The number of patients who had evidence of successful ovulation during the 3 months.
- Ovulation will be confirmed by the elevation of serum progesterone level.

B- <u>Treatment procedures:</u>

1- Medical treatment:

Both group (A&B) will follow the same medical treatment as prescribed by gynecologist.

2- Hpocaloric diet:

Both group (A&B) will follow the same hypocaloric diet as prescribed by nutrition specialist (1200kcal per day).

3- Ultrasound cavitation:

- Each patient in group A will be treated by ultrasound cavitation, two sessions per week for 3 months.

- Before starting treatment session, each patient will be instructed to evacuate her bladder to make sure that she is comfortable and relaxed throughout the treatment session.

- From standing position, the abdominal area of each patient will be divided transversally into 3 parts; Part I: from the xiphoid process to 3 cm above the umbilicus, Part II: from 3cm above the umbilicus to 2 cm below the umbilicus and Part III: from 2 cm below the umbilicus to the pubic bone, and vertically each part was divided into right and left segments in relation to the linea alba, forming a total of 6 abdominal segments.

- Skin of the anterior abdominal wall will be cleaned with alcohol then, a conducting medium (gel) will be applied to the cavitational head of the ultrasound device, the device will be turned on, the program of cavitation; frequency (40 kHz) will be chosen, the time will be adjusted at 30 minutes and the intensity will be adjusted at 50% in the first 6 sessions while it will be adjusted at 75% at the last 6 sessions.

- Then the cavitational head will be moved very slowly on each abdominal segment in a small circular movement for 5 minutes.

- After finishing the focused ultrasound of the 6 segments of the abdomen, the skin will be cleaned with cotton. The total duration of the ultrasound treatment session on the 6 segments of the abdominal area will be 30 minutes.

4- Electroacupuncture:

- Each patient in group B will be treated by electroacupuncture, three sessions per week for 3 months.

- The electrodes must be applied on the effective acupuncture points in somatic segments that innervates the ovary and uterus (Th12-L2 and S2-4).

- Electric stimulation with low frequency 2Hz, pulse width 0.5ms for 30minutes will be chosen.

Statistical analysis:

Data will be collected and statistically analyzed using:

- Descriptive statistics including mean and stander deviation.
- Unpaired t-test will be conducted for comparison of mean values of pre and post-treatment between groups.
- Paired t-test will be conducted for comparison between pre and post-treatment mean values in each group.
- Level of significance, the degree of significance will be selected at 5%, P value <0.05 will indicate non-significant results, P value > 0.05 will indicate a highly significant result.

REFERENCES

Ahsin S, Saleem S, Bhatti A, Iles R and Aslam M. 2009: Clinical and endocrinological changes after electroacupuncture treatment in patients with osteoarthritis of the knee. Pain; 147: 60-6.

Arslanian S A, Lewy V, Danadian K and Saad R. 2002: Metformin therapy in obese adolescents with polycystic ovary syndrome and impaired glucose tolerance: amelioration of exaggerated adrenal response to adrenocorticotropin with reduction of insulinemia/insulin resistance.J. Clin. Endocrinol. Metab. 87, 1555–1559.

Ascher B. 2010: Safety and efficacy of ultra-shape contour I treatments to improve the appearance of body contours. : Multiple treatments in shorter intervals. A.S.J., 30 (2): 217-24.

Asuncion M, Calvo RM, San Millan JL, Sancho J, Avila S and Escobar-Morreale HF. 2000: A prospective study of the prevalence of the polycystic ovary syndrome in unselected Caucasian women from Spain. J Clin Endocrinol Metab.;85:2434–2438.

Azziz R, Marin C, Hoq L, Badamgarav E and Song P. 2005: Health care-related economic burden of the polycystic ovary syndrome during the reproductive life span. J. Clin. Endocrinol. Metab. 90, 4650–4658.

Bailey C J and Turner R C. 1996: Metformin. N. Engl. J. Med. 334, 574–579.

Baillargeon J P, Iuorno M J, Nestler J E. 2003: Insulin sensitizers for polycystic ovary syndrome. Clin. Obstet. Gynecol. 46, 325–340.

Baillargeon J P, McClish D K, Essah P A and Nestler J E. 2005: Association between the current use of low-dose oral contraceptives and cardiovascular arterial disease: a meta-analysis. J. Clin. Endocrinol. Metab. 90, 3863–3870.

Balen A H, Conway G S, Kaltsas G, Techatrasak K, Manning P J, West C et al., 1995: Polycystic ovary syndrome: the spectrum of the disorder in 1741 patients. Hum. Reprod. 10, 2107–2111 .

Balen A and Rajkowha M. 2003: Polycystic ovary syndrome–a systemic disorder? Best Pract. Res. Clin. Obstet. Gynaecol. 17, 263–274.

Borruel S, Fernández-Durán E, Alpañés M, Martí ., Álvarez-Blasco F, Luque-Ramírez M, et al., 2013: Global adiposity and thickness of intraperitoneal and mesenteric adipose tissue depots are increased in women with polycystic ovary syndrome (pcos). J. Clin. Endocrinol. Metab. 98, 1254–1263.

Brassard M, AinMelk Y, Baillargeon JP. 2008: Basic infertility including polycystic ovary syndrome. Med Clin North Am. 92:1163–1192.

Bruyneel A, Catteau-Jonard S, Decanter C, Clouqueur E, Tomaszewski C, Subtil D, et al., 2014: Polycystic ovary syndrome: what are the obstetrical risks?. Gynecol. Obstet. Fertil. 42, 104–111. **Cedergren MI. 2007**: Optimal gestational weight gain for body mass index categories. Obstet Gynecol. 110:759–764.

Costello M, Shrestha B, Eden J, Sjoblom P and Johnson N. 2007: Insulin-sensitising drugs versus the combined oral contraceptive pill for hirsutism, acne and risk of diabetes, cardiovascular disease, and endometrial cancer in polycystic ovary syndrome. Cochrane Database Syst. Rev. CD005552.

Dansinger ML, Gleason JA, Griffith JL, Selker HP and Schaefer EJ. 2005: Comparison of the Atkins, Ornish, Weight Watchers, and Zone

diets for weight loss and heart disease risk reduction: a randomized trial. JAMA. 293:43–53.

Dekker MJ, Lee S, Hudson R, Kilpatrick K, Grahamte, Ross R and Robinson LE. 2007: An exercise intervention without weight loss decreases circulating interleukin-6 in lean and obese men with and without type 2 diabetes mellitus. Metabolism Clinical and Experimental, 56: 332-8.

Derksen J, Nagesser S K, Meinders A E, Haak H R and van de Velde C J. 1994: Identification of virilizing adrenal tumors in hirsute women. N Engl J Med; 331:968-973.

Driscoll D A. 2003: Polycystic ovary syndrome in adolescence. Semin. Reprod. Med. 21, 301–307.

Ellaithy. 2012: Secondary outcome measures in PCO. 321:868-873.

Ernst E, Pittler M and Wider B. **2007**: Acupuncture: its evidence-base is changing. Am J Chin Med. 35 (1): 21-5.

Fauser B C, Tarlatzis B C, Rebar R W, Legro R S, Balen A H, Lobo R, et al., 2012: Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam Eshre/Asrm-Sponsored 3rd PCOS Consensus Workshop Group. *Fertil. Steril.* 97, 28–38.e25.

Fritz MA and Speroff L. 2011: Clinical gynecologic endocrinology and infertility. TEXT. 8th ed. Philadelphia: Lippincott Williams & Wilkins; pp. 501–518.

Focks C. 2008: Atlas of Acupuncture. Textbook. 1st ed. Churchill and Livingstone Inc, NewYork. 8-63.

Galletly C, Clark A, Tomlinson L and Blaney F. 1996: A group program for obese, infertile women: weight loss and improved psychological health. J Psychosom Obstet Gynaecol. 17:125–128.

Hart R and Norman R. 2006: Polycystic ovarian syndrome–prognosis and outcomes. *Best Pract. Res. Clin. Obstet. Gynaecol.* 20, 751–778.

Hashemipour M, Amini M, Iranpour R, Sadri G H, Javaheri N, Haghighi S et al., 2004: Prevalence of congenital hypothyroidism in Isfahan, Iran: results of a survey on 20,000 neonates. *Horm. Res.* 62, 79–83.

Hanan S, Hassan O and Bull. 2011: This reduction in regional fat distribution. Fac. Ph. Th. Cairo Univ. 22-16(1).

Imani B, Eijkemans M J C, te Velde E R, Habbema J D F and Fauser B C J M. 1998:Predictors of patients remaining anovulatory during clomiphene citrate induction of ovulation in normogonadotropic oligoamenorrheic infertility. *J. Clin. Endocrinol. Metab.* 83, 2361–2365.

Jayasuria A. 1993: Clinical acupuncture .Textbook.16th edition. Chadinkanthi press international; Sri Lanka.

JedelE, LabrieF, OdenA, HolmG, NilssonL, JansonPO, etal. 2011: Impact of electro-acupuncture and physical exercise on hyperandrogenism and oligo/amenorrhea in women with polycystic ovary syndrome: a randomized controlled trial. Am J Physiol Endocrinol Metab. 300(1):E37–45.

Jewell , Weiss RA and Baxter J. 2012: Efficacy and safety of cavitation in reducing visceral adipose tissues and abdominal subcutaneous like these several previous studies. Aesthet. Surg., 1868-1876.

Johansson J, Redman L, Veldhuis PP, Sazonova A, Labrie F and Holm G. 2013: Acupuncture for ovulation induction in polycystic ovary syndrome: arandomized controlled trial. Am J Physiol Endocrinol Metab. 304(9):E934–43

Kamangar F, Okhovat J P, Schmidt T, Beshay A, Pasch L, Cedars M I, et al., 2015: Polycystic ovary syndrome: special diagnostic and therapeutic considerations for children. *Pediatr. Dermatol.* 32, 571–578.

Karabulut A, Yaylali G F, Demirlenk S, Sevket O and Acun A. 2012: Evaluation of body fat distribution in PCOS and its association with carotid atherosclerosis and insulin resistance. *Gynecol. Endocrinol.* 28, 111–114.

Katulski K, Czyzk A, Podfigurna-Stopa A, Genazzani A R and Meczekalski B. 2015: Pregnancy complications in polycystic ovary syndrome patients. *Gynecol. Endocrinol.* 31, 87–91.

Legro R S, Arslanian S A, Ehrmann D A, Hoeger K M, Murad M H, Pasquali R et al., 2013: Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. *J. Clin. Endocrinol. Metab.* 98, 4565–4592.

March WA, Moore VM, Wilson KJ, Philips DI,Norman RJ and Davies MJ. 2001: The prevalence of polycystic ovarian syndrome in a community sample assessed under contrasting diagnostic criteria. Hum.Reprod. 25, 544-551.

Misso M, Boyle J, Norman R and Teede H. 2014: Development of evidenced-based guidelines for PCOS and implications for community health. *Semin. Reprod. Med.* 32, 230–240.

Moran LJ, Pasquali R, Teede HJ, Hoeger KM and Norman RJ. 2009: Treatment of obesity in polycystic ovary syndrome: a position statement of the Androgen Excess and Polycystic Ovary Syndrome Society. Fertil Steril. 92:1966–1982.

Palumbo P, B Cinque, G miconi, C LA Torre, G Zoccali and M Giuliani. 2011: Biological effects of low frequency high intensity ultrasound application on ex vivo human adipose tissue. IPP, 24 (2): 411-22.

Pasquali R and Casimirri F. 2003: The impact of obesity on hyperandrogenism and polycystic ovary syndrome in premenopausal women. Clin Endocrinol, 39: 1-16.

Pasquali R, Casimirri F and Vicennati V. 1997: Weight control and its beneficial effect on fertility women with obesity and polycystic ovary syndrome. Hum Reprod, 12(1): 82-87.

Pau C T, Keefe C, Duran J and Welt C K. 2014: Metformin improves glucose effectiveness, not insulin sensitivity: predicting treatment response in women with polycystic ovary syndrome in an open-label, interventional study. *J. Clin. Endocrinol. Metab.* 99, 1870–1878.

Poehlman ET, Dvorak RV, DeNino WF, Brochu M and Ades PA. 2000: Effects of resistance training and endurance training on insulin sensitivity in nonobese, young women: a controlled randomized trial. J Clin Endocrinol Metab. 85:2463–2468.

Randeva H S, Tan B K, Weickert M O, Lois K, Nestler J E, Sattar N et al., 2012: Cardiometabolic aspects of the polycystic ovary syndrome. *Endocr. Rev.* 33, 812–841.

Regan L, Qwen E and Jacobas H. 2005: Hypersecretion of LH infertility and miscarriage. Lancet, 336: 1141.

Richard S Legro. 2010: Total testosterone assays in women with polycystic ovary syndrome. J Clin Endocrinol Metab;95(12):5305-13.

Rosner W. 2001: An extraordinarily inaccurate assay for free testosterone is still with us. J Clin Endocrinol Metab; 86:2903.

Sabbour A, Omar H, M El-banna A. and M D. 2009: The Efficiency of Cavitation Ultrasound Therapy on Visceral Adiposity in Perimenpausal Women. Bull Fac. Ph. Th. Cairo Univ., 14 (1): 93-102.

S A Brown, Greenbaum L, Shtukmaster S, Zadok Y, Ben-Ezra S, Kushkuley L and Plast Reconst Surg J. 2009: Mechanism of ultrasound cavitation.

Saedi , Kaminer M, Seminars in Cutaneous Medicine and Surgery. 2013: All patients showed a great decrease in fat thickness of subcutaneous tissue within the treated area. 32(1), 26-30.

Sir-Petermann T, Ladrón de Guevara A, Villarroel A C, Preisler J, Echiburu B and Recabarren S. 2012: Polycystic ovary syndrome and pregnancy. *Rev. Med. Chil.* 140, 919–925.

Stabile G, Borrielli I, Artenisio A C, Bruno L M, Benvenga S, Giunta L et al., 2014: Effects of the insulin sensitizer pioglitazone on menstrual irregularity, insulin resistance and hyperandrogenism in young women with polycystic ovary syndrome. *J. Pediatr. Adolesc. Gynecol.* 27, 177–182.

Stener-Victorin E, Holm G, Janson PO, Gustafson D and Waern M. 2013: Acupuncture and physical exercise for affective symptoms and health-related quality of life in polycystic ovary syndrome: secondary analysis from a randomized controlled trial. BMC Complement . Alter Med. 13:131

Steven K and William P. 2007: Clinical introduction to medical acupuncture. journal of chinese med; 199-200.

Stux G and Pomeranz B. 1998: Scientific bases of acupuncture. Textbook. 5th ed. New York: Springer-Verlag; pp.315-325.

Ter-haar G and Coussios C. 2007: High intensity focused ultrasound: Physical principle and devices. Hyperthermia, 23: 89-104.

To W and Wong M. 2003: Factors associated with back pain symptoms in pregnancy and the persistence of pain 2 years after pregnancy. Acta Obstet Gynecol Scand; 82(12), 1086-1091.

Velazquez E, Bellabarba G, Mendoza S and Sanchez L. 2006: Postprandal triglyceride response in patient's polycystic ovary syndrome: relationship with waist to hip ratio and insulin. Fertil and Steril, 74(6): 1159- 1163.

Wahrenberg H, Ek I, Reynisdottir S, Carlstrom K, Bergqvist A and Arner P. 1999: Divergent effects of weight reduction and oral anticonception treatment on adrenergic lipolysis regulation in obese women with the polycystic ovary syndrome. J Clin Endocrinol Metab.;84:2182–2187.

William T, Mortada R and Porter S. 2016: Diagnosis and treatment of polycystic ovary syndrome. American Family Physician. 94(2): 107-112.

Winter E, Wang J, Davies M J and Norman R. 2002: Early pregnancy loss following assisted reproductive technology treatment. *Hum. Reprod.* 17, 3220–3223.

Zheng YH, Wang XH, Lai MH, Yao H, Liu H and Ma HX. 2013: Effectiveness of abdominal acupuncture for patients with obesity-type polycystic ovary syndrome: a randomized controlled trial. J Altern Complement Med. 19(9):740–5.

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Appendix I

Informed consent form

I am Misses /   freely and voluntarily consent to participate in research study under the direction of the researcher /Mohamed Abdel Hamid Elgaedy . A through description of the procedures has been explained and I understand that I may withdraw my consent and discontinue participation in this research at any time without prejudice to me.

Participant: **Date:**

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Appendix II

Recording data sheet

Number:

Name:

Group:

Age:

Address:

Occupation:

	Group	
	Before treatment	After treatment
Weight		
Height		
BMI		
Waist/Hip Ratio		
Testosterone		
LH/FSH Ratio		
Progesterone		