Original Research Article

EFFECT OF DIET CONTROL THERAPY ON THE DERMATOLOGICAL SYMPTOMS OF OBESE POLYCYSTIC OVARIAN SYNDROME WOMEN: REPEATED MEASURE DESIGN

Noha F. Mahmoud *.

* Department of Physical Therapy for Surgery, Faculty of Physical Therapy, October 6 University.

* Department of Rehabilitation, College of Health and Rehabilitation Sciences, Princess Nourah Bint Abdulrahman University.

ABSTRACT

Background: Polycystic ovarian syndrome (PCOS) is the most common endocrinal disorder in female causing metabolic, cutaneous, and reproductive disorders.

Purpose: This repeated measure study was designed to investigate the effect of diet control therapy on hyperandrogen symptoms (Acne & Hirsutism) in obese PCOS women.

Subjects and Methods: Thirty PCOS obese women were recruited, their age ranged from 20 to 30 years and their BMI ranged from 30 to 34.9 kg/m². All of them received diet control therapy, and were evaluated before, after 12 weeks and after 24 weeks of therapy through measuring their weight, C-reactive protein, luteinizing hormone (LH) / follicular stimulating hormone (FSH) ratio, androgen excess symptoms (modified Ferryman–Gallwey (mFG) scoring system & global acne grading system (GAGS).

Results: Repeated Measure MANOVA showed a statistically significant difference (P < 0.05) between the pre-treatment compared to after therapy (in both 12 and 24 weeks) in LH/FSH ratio, CRP, mFG and GAGS, however no significance difference was found between 12 weeks and 24 weeks for all the dependent variables. As well as, Pearson's product-moment correlation revealed a weak positive correlation between C-reactive protein and androgen excess symptoms (Acne & Hirsutism).

Conclusion: Three months following the recommended diet control therapy is an effective therapy for improving the cutaneous symptoms and fertility through the hormonal variables of PCOS patients. Diet control therapy for another consequent three months is also recommended to keeping this improvement.

KEY WORDS: Polycystic ovarian syndrome, Diet therapy, Hyperandrogen, hirsutism, Acne.

Address for correspondence: Noha Fekry Mahmoud, Department of Physical Therapy for Surgery, Faculty of Physical Therapy, October 6 University. Department of Rehabilitation, College of Health and Rehabilitation Sciences, Princess Nourah Bint Abdulrahman University.
E-Mail: nfmahmoud@pnu.edu.sa; nohfek@gmail.com

INTRODUCTION

Affecting between 2-7% [1] or 5-10 % [2] of re-productive-aged women, and with a prevalence rate of 20–30% among Caucasian women [3], Polycystic ovary syndrome (PCOS) is considered as the most common endocrinal disorder [1,2]. PCOS is a heterogeneous disorder, characterized by menstrual irregularities or infertility, metabolic, and cutaneous disorders as clinical signs of excess androgen that include acne and

hirsutism [4]. In those women with PCOS, 92% shows cutaneous manifestations with hyperandrogenism associated signs [1,5]

Hirsutism, a reliable cutaneous marker for hyperandrogenism [6], is a feminine condition of excessive terminal hair growth in an androgen-sensitive skin distribution [1], causing lack of self-confidence and a remarkable amount of emotional stress. As the sense of self-consciousness is originated from the concept "ideal hair pattern" known inside the patients' social and cultural environment [4].

Khomami et al., mentioned that in PCOS diagnosed Iranian women, hirsutism has the strongest impact on the health-related quality of life [7].

Acne is the most common disease of the skin with a prevalence of 15% in all age groups. Almost three quarter of acnetic women had clinical or biochemical hyperandrogenemia [8]. Acne is a pilosebaceous unit disorder, characterized by excess amount of sebum production, abnormal follicular epithelial differentiation, desquamated epithelial cells clogging the pilosebaceous follicles and inflammation [8,9]. and though acne is not a good marker of hyperandrogenism, It was found in 53% of PCOS patients representing the second most common symptom [10].

Although the diagnostic criteria of PCOS does not include obesity, almost half of women with the condition were found to be overweight or obese [11].

Oligomenorrhea and hyperandrogenism are commonly proceeded by weight gain which signify the role of obesity in the consequent symptoms [12].

Suggested by many studies; Weight loss, even as little as 5% from baseline, can have positive effects on hyperinsulinemia and hyperandrogenemia in patients with PCOS [13].

This repeated measure study aims to investigate how far can weight reduction through diet control therapy affects the clinical symptoms of hyperandrogenism (namely acne and hirsutism) and their association with LH/FSH as well as C-reactive protein CRP in Egyptian obese women diagnosed with PCOS according to the diagnostic features of Rotterdam Consensus Workshop.

METHODOLOGY

Subjects: Thirty obese PCOS women diagnosed as having PCOS through ultrasonographic examination, their age ranged from 20 to 30 years old and their BMI ranged from 30 to 34.9 kg/m^2 participated in this study. They were assigned in one group, in which all of them were submitted to diet control therapy for 24 weeks. This study was approved by the faculty council of physical therapy committee and was conducted from June 2016 till November 2017 with the guidelines of the Declaration of Helsinki.

Individuals with hyperprolactinemia, androgen screening neoplasia, thyroid dysfunction, Cushing's syndrome, ovarian tumor, malignancy, using medication (that affects hypothalamic pituitary ovarian drugs, anti-inflammatory drugs, and weight reduction drugs) were excluded from this study.

Instruments

Evaluative instruments

Diagnostic ultrasonography: Medison ultrasound machine, made in Korea, model number Sa8000 EX, serial number A82505300004653, used to confirm the diagnosis of PCOS for all women in both groups A and B before starting the study.

Weight/height scale: used to measure the weight and height of each patient in the study before starting the study to calculate their BMI. Weight was measured also after 12 weeks and after the end of the study.

Enzyme Linked Immunosorbent Assay (ELISA): micro plate reader (MRX) made in USA with DYNEX technologies, with serial number ICXD3442 and barcode number 052100119, used to measure hormones as; luteinizing hormone (LH) and follicular stimulating hormone (FSH).

Vitros 350 (Ortho Clinical Diagnostic, Inc): made in Rochester, NY14626-5101, and model number ET1529L-7SWA-1-RNBCG, used to measure blood CRP concentration.

Modified Ferriman-Gallwey scoring system (mFG): used to assess hirsutism.

The Global Acne Grading System (GAGS): used to assess acne.

Treatment instruments

Diet control therapy: All women in this study

underwent the same diet guidelines therapy during the whole study period for 24 weeks. Before the beginning of diet an orientation session was given to the participant about the definition, symptoms, complications of PCOS, and the importance of weight reduction. Another session of orientation has been given to them by the end of 12th weeks; teaching the patient how to calculate their new weekly caloric diet as a preparation of a self-monitored home program for another 12 weeks, to be followed by an evaluative measures. This study recommended the hypocaloric diets; followed the literature dietary advice which considered in women with PCOS include high-carbohydrate (55% calories) and low fat (30% of calories) with average protein (15%) [14]. In order to determine the daily caloric requirement of each woman; firstly, the total daily energy requirement for each woman was calculated according to Harris-Benedict formula [15]; [for women: BMR= 655 + (9.6*weight in kg) + (1.8*height in cm) - (4.7* age in years)], then multiply the result by the activity multiplier (BMR * 1.2 , 1.375, 1.55, 1.725 and 1.9 for sedentary, lightly active, moderately active, very active and extremely active); respectively. Then reduce a 500–1000 kcal/day of the calculated total daily energy requirement. Additionally, low glycemic index carbohydrates, fresh vegetables, and at least 2 liters of water were encouraged. On the other hand, caffeine and saturated fats was discouraged. This procedure was repeated in the beginning of each week according to each woman new weight to determine her allowed caloric intake.

Procedure

Evaluative procedure: Diagnostic criteria for selecting PCOS cases in this study were done through Rotterdam Consensus Workshop, in which he stated that PCOS can be diagnosed when 2 of the following 3 features are present: (1) oligo- or anovulation, (2) clinical and/or biochemical signs of hyperandrogenism (ie, hirsutism, acne, male pattern balding, elevated serum androgens), and (3) polycystic ovaries. It is important to exclude other disorders with a similar clinical presentation before a diagnosis of PCOS is made [16].

Prior to entering the study, all women apply

Ultrasonographic examination to confirm the diagnosis of PCOS through studying the ovarian morphology.

Then, all selected women underwent the following assessments before starting, after 12 weeks from the treatment intervention and another measure for assessing the long term effect of the diet control therapy was done after 24 weeks.

Weight and height measurements: weight and height of each woman was measured and recorded in the data collecting sheet, and then the BMI was calculated.

Biochemical assays: blood samples were collected to measure the levels of the woman circulating LH, FSH and CRP.

Assessment of androgen excess symptoms: it was assessed by the same skilled dermatologist.

Modified Ferryman–Gallwey (mFG) scoring system: used to assess hirsutism and considered the standard scoring system that defines hirsutism quantitatively [17, 18], in which 9 androgen-sensitive areas of the body were examined. Each area is scored from 0 to 4 depending on the amount of terminal hair growth. A score of 8 or greater indicates the presence of hirsutism. The examined 9 body areas are the lip, chin, chest, upper abdomen, lower abdomen, upper arm, thigh, upper back, and lower back. All women have been asked not to do any treatment for the excessive hair at least one month before assessment, not to interfere with the results.

The global acne grading system (GAGS): used to assess acne, this system divides the face, chest and back into seven areas (forehead, each cheek, nose, chin and chest and back) and assigns a factor to each area on the basis of size. The factor of forehead and each cheek was 2, the factor of nose and chin was 1, and the factor of chest and back was 3. Each type of lesion is given a value depending on severity: no lesions = 0, comedones = 1, papules = 2, pustules = 3 and nodules = 4. The score for each area (Local score) is calculated using the formula: Local score = Factor × Grade (0-4). The global score is the sum of local scores, and acne severity was graded using the global score. A score of 1-18 is considered mild; 19-30, moder-

ate; 31-38, severe; and >39, very severe [19].

Data analysis: All statistical measures were performed using the Statistical Package for Social science (SPSS) program version 20 for windows. The current test involved one independent variable the measuring periods; within subject factor which had three levels (pre, post one, and post two). In addition, this test involved five tested dependent variables (Weight, CRP, LH/FSH, Hirsutism scale, and Acne scale). Prior to final analysis, data were screened for normality assumption, and presence of extreme scores. This exploration was done as a pre- requisite for parametric calculation of the analysis of difference and analysis of relationship measures. Preliminary analyses showed the relationship to be linear with all variables normally distributed, as assessed by Shapiro-Wilk's test ($p > .05$), and there were no outliers So, repeated measure MANOVA was used to compare the all dependent variables at different measuring periods. A Pearson's product-moment correlation was run to assess the relationship between C-reactive protein and androgen excess symptoms (Acne & Hirsutism). The alpha level was set at 0.05.

RESULTS

As indicated by the repeated measures MANOVA, there was a statistically significant difference in Weight, CRP, LH/FSH, Hirsutism scale, and Acne scale among the three measuring periods (pre and post one of treatment, and post two of treatment) ($p<0.05$). Multiple pairwise comparison tests (Post hoc tests) revealed that there was a statistically significant reduction in the Weight, CRP, LH/FSH, Hirsutism scale, and Acne scale in the post one of treatment and post two of treatment compared with the pre-treatment ($p<0.05$). While, there was no statistically significant difference in the post one of treatment compared with the post two of treatment ($p>0.05$) (table 1).

Pearson coefficient correlation (r) revealed a positive weak correlation between mean value of CRP with mean value of Hirsutism scale, and Acne scale was ($r=0.502$ $p= 00001*$) and ($r=0.373$, $p= 0004*$) respectively. This means that increase in CRP is consistent with increase in

mean value of Hirsutism scale, and Acne scale.

Table 1: Descriptive statistics (mean ± SD) and repeated measures ANOVA for the all dependent variables among the three different measuring periods.

Descriptive statistics for Weight, CRP, LH/FSH, ratio, Hirsutism scale, and Acne scale at the different measuring periods.			
Measuring periods	Pre treatment	Post 12 weeks	Post 24 weeks
Weight	90.8 ± 8.23	79.2 ± 8.12	79.1 ± 6.72
CRP	7.16 ± 1.91	3.23 ± 1.29	3.49 ± 1.34
LH/FSH ratio	2.23 ± 0.31	1.5 ± 0.24	1.59 ± 0.21
Hirsutism scale	12.3 ± 1.15	9.1 ± 0.87	9.4 ± 0.84
Acne scale	20 ± 4.26	14.4 ± 2.01	14.8 ± 2.48

Repeated measures MANOVA		
	F-value	P-value
Weight	70.734	0.0001*
CRP	60.075	*0.0001
LH/FSH ratio	126.926	*0.0001
Hirsutism scale	159.113	*0.0001
Acne scale	32.058	*0.0001

Multiple comparison tests (Post hoc tests)			
	Pre-treatment vs. post one	Pre-treatment vs. post-two	.Post one vs post two
Weight	0.0001*	0.0001*	0.999
CRP	0.0001*	0.0001*	0.42
LH/FSH ratio	*0.0001	*0.0001	0.082
Hirsutism scale	*0.0001	*0.0001	0.243
Acne scale	*0.001	*0.001	0.504

DISCUSSION

The current experimental repeated measure study investigated the effect of short (12 weeks) versus long (24 weeks) low caloric diet control therapy on the clinical symptoms of hyperandrogenism in Egyptian females with poly cystic ovarian syndrome. The study has revealed significant differences of all the measured variable (Weight, CRP, LH/FSH, Hirsutism scale, and Acne scale) among the three measuring periods; A significant improvement in the Weight, CRP, LH/FSH, Hirsutism scale, and Acne scale after 12 weeks of treatment and after 24 weeks of treatment compared with the pre-treatment measures has been proved. However, no significant differences in the outcomes measured after 12 compared to 24 weeks of treatment have been found.

In the current study, women followed the recommended macronutrient composition of weight-loss diets for obese PCOS women

adopted by Moran et al [14], showed a significant weight reduction, acclaiming the benefits of that type of diet therapy. Weight reduction through diet control therapy, was adopted in the current study as obesity play a significant role in the pathology of PCOS [6], and though conservative treatment is recommended for PCOS through lifestyle modification [17], the term lifestyle modification is somehow vague. Lim et al. [20], reported their disagreement with such hypothesis concerning the association between the lack of exercise and the clinical or biochemical characteristics typical of PCOS, supporting the concept of weight reduction in favor of exercise in the field of lifestyle modification.

Many studies support our results concerning the positive effects of weight reduction on obese PCOS women [18-19, 21-22], which is further supported by studying the eating habits of PCOS women compared to controls; Adult PCOS women tend to eat between meals and adolescents PCOS tend to have non healthy snacks which may intensify the phenotype of PCOS. Adolescents also tend to eat out of pleasure rather than out of necessity, which may lead to a progressively increasing caloric intake and a tendency to bulimic eating pattern, which is a common behavior shown among women with PCOS (12, 23).

Following a restricted diet in obese people for a long period of time is difficult and tedious, and in spite of the copious research in this area, an optimal diet parameters are not clear regarding the diet composition, duration, and specific effect on PCOS symptoms. For instance, duration in researches ranged from 16 days [24], one month [25], 16 weeks [26], 6 months [27], 12 months [28], however, an exact explanation of the mechanism of action for this treatment or any other treatment is difficult due to the controversiality of the PCOS definition [29] and the lacking of an exact explanation of the pathophysiological changes accompanied with it. So, it's better to consider PCOS as a vicious cycle syndrome , triggered at any point, and finally ends with hyperandrogen, anovulation [1, 30], and polycystic ovary morphology [31].

This vicious cycle can lead us to Insulin resistance (IR) and hyperinsulinemia which play a central role in PCOS pathogenesis [23], PCOS women are at a high risk of developing impaired glucose tolerance (IGT), type 2 diabetes mellitus (DM2), and cardiovascular disease (CVD) [29]. IR occurs in approximately 50–70 % of women with PCOS and in 95 % of obese women with PCOS [32]. Insulin decreases the hepatic synthesis of sex hormone-binding globulin (SHBG) and stimulate ovarian androgen synthesis [29]. Meanwhile, Kristen and Michael, reported that overproduction of androgens in the ovaries contributes to hyperinsulism (an important features in PCOS) [33].

Polycystic ovarian syndrome (PCOS) is the most common cause of hirsutism, in women [4]. Most women (91.7%) meeting the criteria for PCOS had at least one skin finding, with higher burden of acne, hirsutism, and acanthosis nigricans (AN) than women who did not meet the criteria [6]. In the present study, following the recommended diet for 12 weeks has significantly reduced acne and hirsutism scores and maintained that effect for another 12 weeks, which may be beneficial for improving all the other symptoms related to it, as beside all the previous mentioned symptoms, PCOS women may display several psychological disorders such as depression, anxiety, marital and social problems, which aggravate the psychological impact of hirsutism as, not only is hirsutism itself a major concern for women diagnosed with PCOS, but the time and effort spent eliminating it aggravates the distress [7], hence emerge the importance of measuring hirsutism because hirsutism score is the main predictor of psychological distress [34] and can significantly predict reduction of body hair, emotions, menstrual problems, weight and infertility problems, in their order of severity [7] Hirsutism was also associated with a higher mean HOMA-IR, body mass index, and triglycerides level, as well as a lower HDL-C level [6].

Although acne is not a reliable marker of hyperandrogenism, Androgens are important in the development of acne and its prevalence is high among patients who meet PCOS diagnosis [6]. Testosterone inside the sebaceous gland is converted into dihydrotestosterone, potent androgen, which causes increase in sebum secretion and abnormal desquamation in follicular epithelial cells and that's how comedones

are formed. When comedones are colonized with bacteria, papules and pustules may be seen [9]. Despite the enormous amount of research, acne pathogenesis is not completely understood. According to Uysal et al., the relation of acne to increased serum androgen is not fully elucidated, so, it's the raised amount of blood androgen, the hyper sensitivity of the tissue, or the increased local production of androgen in the sebaceous gland that might be the cause of acne [8].

Inspite of the strong association between hyperandrogenism and inûammation in PCOS women [32], based on the current results, CRP (marker of systemic inflammation) is not a suggestive marker for hirsutism or acne as there is weak positive correlations between them. However, CRP showed significant reduction compared to pre-treatment, which might be attributed to the association between CRP with insulin resistance [35, 36] and adipocyte excess [37] supporting the effect of diet and weight loss on insulin resistance and consequently hyperandrogenism.

The current experiment is limited to the mentioned diet therapy protocol, it's also limited to 12 weeks and 24 weeks measuring intervals, and to the exact measured dermatological, biochemical, and anthropometric parameters that were gathered. The symptoms of PCOS can be quite variable depending on the patients' ethnicity [1], this study was conducted and limited to adult Egyptian PCOS females. To the best of our knowledge, only one study on Egyptian females was performed, it investigating the effect of diet only on PCOS [13] with differences in the design, sample characteristics, and the measured outcomes.

In spite of the significance difference found comparing post 24 weeks with pre-treatment measures, the insignificant difference found between the measured outcomes after 12 weeks compared to 24 weeks suggests the importance of diet therapy on maintain the benefits achieved after 12 weeks. However, It might be attributed to a curve of weight reduction peaks during the first three months and then slop down after that through one year period of time but doesn't reach the original baseline measures, for example, In a study 6.8% weight loss was achieved in one year of treatment [38] and in another study 4.69% in 3 months [39], so, may be there's an improvement that is sloping down by time. Further repeated measures studies are needed to measure the effect of diet therapy on different time intervals through one or more than one year, or till reaching the optimum body mass index, additional work is also needed to investigate the exact effect and mechanism of action of different type of treatment protocols in such patients and their effect on each symptom of the disease.

ACKNOWLEDGEMENTS

Conflicts of interest: None

REFERENCES

[1]. Afifi L, Saeed L, Pasch LA, Huddleston HG, Cedars MI, Zane LT, Shinkai K. Association of ethnicity, Fitzpatrick skin type, and hirsutism: A retrospective cross-sectional study of women with polycystic ovarian syndrome. International journal of women's dermatology. 2017 Mar 1;3(1):37-43.

[2]. Eisenhardt S, Schwarzmann N, Henschel V, Germeyer A, Von Wolff M, Hamann A, Strowitzki T. Early effects of metformin in women with polycystic ovary syndrome: a prospective randomized, double-blind, placebo-controlled trial. The Journal of Clinical Endocrinology & Metabolism. 2006 Mar 1;91(3):946-52.

[3]. Foda AA, Foda EA, Abel-Aal I. Serum Irisin levels as a marker in some phenotypes of PCOS. Middle East Fertility Society Journal. 2017 Sep 22.

[4]. Mihailidis J, Dermesropian R, Taxel P, Luthra P, Grant-Kels JM. Endocrine evaluation of hirsutism. International journal of women's dermatology. 2017 Mar 1;3(1):S6-10.

[5]. Sachdeva S. Fitzpatrick skin typing: applications in dermatology. Indian Journal of Dermatology, Venereology, and Leprology. 2009 Jan 1;75(1):93.

[6]. Schmidt TH, Khanijow K, Cedars MI, Huddleston H, Pasch L, Wang ET, Lee J, Zane LT, Shinkai K. Cutaneous findings and systemic associations in women with polycystic ovary syndrome. JAMA dermatology. 2016 Apr 1;152(4):391-8.

[7]. Khomami MB, Tehrani FR, Hashemi S, Farahmand M, Azizi F. Of PCOS symptoms, hirsutism has the most significant impact on the quality of life of Iranian women. PloS one. 2015 Apr 15;10(4):e0123608.

[8]. Uysal G, Sahin Y, Unluhizarci K, Ferahbas A, Uludag SZ, Aygen E, Kelestimur F. Is acne a sign of androgen excess disorder or not?. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2017 Apr 1;211:21-5.

[9]. Hacivelioglu S, Gungor AN, Gencer M, Uysal A, Hizli D, Koc E, Cosar E. Acne severity and the Global Acne Grading System in polycystic ovary syndrome. International Journal of Gynecology & Obstetrics. 2013 Oct 1;123(1):33-6.

[10]. Özdemir S, Özdemir M, Görkemli H, Kiyici A, Bodur S. Specific dermatologic features of the polycystic ovary syndrome and its association with biochemical markers of the metabolic syndrome and hyperandrogenism. Acta obstetricia et gynecologica Scandinavica. 2010 Feb 1;89(2):199-204..

[11]. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. The Journal of Clinical Endocrinology & Metabolism. 2004 Jun 1;89(6):2745-9.

[12]. Eleftheriadou M, Stefanidis K, Lykeridou K, Iliadis I, Michala L. Dietary habits in adolescent girls with polycystic ovarian syndrome. Gynecological Endocrinology. 2015 Apr 3;31(4):269-71.

[13]. Marzouk TM, Ahmed WA. Effect of dietary weight loss on menstrual regularity in obese young adult women with polycystic ovary syndrome. Journal of pediatric and adolescent gynecology. 2015 Dec 1;28(6):457-61.

[14]. Moran LJ, Brinkworth GD, Norman RJ. Dietary therapy in polycystic ovary syndrome. InSeminars in reproductive medicine 2008 Jan (Vol. 26, No. 01, pp. 085-092). © Thieme Medical Publishers.

[15]. Harris JA, Benedict FG. A biometric study of human basal metabolism. Proceedings of the National Academy of Sciences. 1918 Dec 1;4(12):370-3.

[16]. Fauser BC, Tarlatzis B, Chang J, Azziz R, Legro R, Dewailly D, Franks S, Balen AH, Bouchard P, Dahlgren E. The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19(1):41-7.

[17]. Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R, Carmina E, Chang J, Yildiz BO, Laven JS, Boivin J. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Fertility and sterility. 2012 Jan 1;97(1):28-38.

[18]. Hoeger K. Obesity and weight loss in polycystic ovary syndrome. Obstetrics and Gynecology Clinics. 2001 Mar 1;28(1):85-97.

[19]. Doshi A, Zaheer A, Stiller MJ. A comparison of current acne grading systems and proposal of a novel system. International journal of dermatology. 1997 Jun 1;36(6):416-8.

[20]. Lim AJ, Huang Z, Chua SE, Kramer MS, Yong EL. Sleep duration, exercise, shift work and polycystic ovarian syndrome-related outcomes in a healthy population: A cross-sectional study. PloS one. 2016 Nov 21;11(11):e0167048.

[21]. Martinez-Bermejo E, Luque-Ramirez M, Escobar-Morreale HF. Obesity and the polycystic ovary syndrome. Minerva endocrinologica. 2007 Sep;

[22]. Panidis D, Farmakiotis D, Rousso D, Kourtis A, Katsikis I, Krassas G. Obesity, weight loss, and the polycystic ovary syndrome: effect of treatment with diet and orlistat for 24 weeks on insulin resistance and androgen levels. Fertility and sterility. 2008 Apr 1;89(4):899-906.

[23]. Omar AN, Habib F, Mojaddidi M, El-Bab MF. Body weight reduction and metformin: Roles in polycystic ovary syndrome. Pathophysiology. 2013 Apr 1;20(2):131-7.

[24]. Douglas CC, Gower BA, Darnell BE, Ovalle F, Oster RA, Azziz R. Role of diet in the treatment of polycystic ovary syndrome. Fertility and sterility. 2006 Mar 1;85(3):679-88.

[25]. Stamets K, Taylor DS, Kunselman A, Demers LM, Pelkman CL, Legro RS. A randomized trial of the effects of two types of short-term hypocaloric diets on weight loss in women with polycystic ovary syndrome. Fertility and sterility. 2004 Mar 1;81(3):630-7.

[26]. Moran LJ, Noakes M, Clifton PM, Tomlinson L, Norman RJ. Dietary composition in restoring reproductive and metabolic physiology in overweight women with polycystic ovary syndrome. The Journal of Clinical Endocrinology & Metabolism. 2003 Feb 1;88(2):812-9.

[27]. Moran LJ, Noakes M, Clifton PM, Wittert GA, Williams G, Norman RJ. Short-term meal replacements followed by dietary macronutrient restriction enhance weight loss in polycystic ovary syndrome–. The American journal of clinical nutrition. 2006 Jun 1;84(1):77-87..

[28]. Marsh KA, Steinbeck KS, Atkinson FS, Petocz P, Brand-Miller JC. Effect of a low glycemic index compared with a conventional healthy diet on polycystic ovary syndrome–. The American journal of clinical nutrition. 2010 May 19;92(1):83-92.

[29]. Anwar S, Shikalgar N. Prevention of type 2 diabetes mellitus in polycystic ovary syndrome: A review. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2017 Jul 8.

[30]. Bako AU, Morad S, Atiomo WA. Polycystic ovary syndrome: An overview. Reviews in Gynaecological Practice., 2005; 5: 115-122.

[31]. Goodman NF, Cobin RH, Futterweit W, Glueck JS, Legro RS, Carmina E. American Association of Clinical Endocrinologists, American College of Endocrinology, and Androgen Excess and PCOS Society disease state clinical review: guide to the best practices in the evaluation and treatment of polycystic ovary syndrome-part 1. Endocrine Practice. 2015 Nov;21(11):1291-300.

[32]. Rondanelli M, Perna S, Faliva M, Monteferrario F, Repaci E, Allieri F. Focus on metabolic and nutritional correlates of polycystic ovary syndrome and update on nutritional management of these critical phenomena. Archives of gynecology and obstetrics. 2014 Dec 1;290(6):1079-92.

[33]. Farrell K, Antoni MH. Insulin resistance, obesity, inflammation, and depression in polycystic ovary

syndrome: biobehavioral mechanisms and interventions. Fertility and sterility. 2010 Oct 1;94(5):1565-74.

[34]. Kumarapeli VL, Seneviratne RD, Wijeyaratne CN. Health related quality of life and psychological distress in polycystic ovary syndrome: a hidden facet in South Asian women. BJOG: An International Journal of Obstetrics & Gynaecology. 2011 Feb 1;118(3):319-28.

[35]. Nakanishi N, Shiraishi T, Wada M. Association between C-reactive protein and insulin resistance in a Japanese population: the Minoh Study. Internal medicine. 2005;44(6):542-7.

[36]. El-Mesallamy HO, El-Razek RA, El-Refaie TA. Circulating high-sensitivity C-reactive protein and soluble CD40 ligand are inter-related in a cohort of women with polycystic ovary syndrome. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2013 Jun 1;168(2):178-82.

[37]. Legro RS, Kunselman AR, Dunaif A. Prevalence and predictors of dyslipidemia in women with polycystic ovary syndrome. The American journal of medicine. 2001 Dec 1;111(8):607-13.

[38]. Heymsfield SB, Segal KR, Hauptman J, Lucas CP, Boldrin MN, Rissanen A, Wilding JP, Sjöström L. Effects of weight loss with orlistat on glucose tolerance and progression to type 2 diabetes in obese adults. Archives of Internal Medicine. 2000 May 8;160(9):1321-6.

[39]. Jayagopal V, Kilpatrick ES, Holding S, Jennings PE, Atkin SL. Orlistat is as beneficial as metformin in the treatment of polycystic ovarian syndrome. The Journal of Clinical Endocrinology & Metabolism. 2005 Feb 1;90(2):729-33.

How to cite this article:

Noha F. Mahmoud. EFFECT OF DIET CONTROL THERAPY ON THE DERMATOLOGICAL SYMPTOMS OF OBESE POLYCYSTIC OVARIAN SYNDROME WOMEN: REPEATED MEASURE DESIGN. Int J Physiother Res 2018;6(3):2740-2747. **DOI:** 10.16965/ijpr.2018.128