

Effects of exercise and nutritional counseling in women with polycystic ovary syndrome

Brenda Bruner, Karen Chad, and Donna Chizen

Abstract: This pilot study assessed the effects of exercise and nutritional counseling on hormonal, menstrual, and reproductive function in women with polycystic ovary syndrome (PCOS). Twelve females with a clinical, biochemical, and ultrasonographic diagnosis of PCOS were randomly assigned to endurance and resistance exercise plus nutritional counseling (EN) or nutritional counseling only (N) for a period of 12 weeks. Anthropometry, resting metabolic rate (RMR), selected hormones, and ovarian follicle population were measured pre and post-intervention. Following the 12 week intervention, greater decreases in sum of 2 skinfolds ($p = 0.002$) and a greater increase in estimated $\text{VO}_2 \text{ max}$ ($p = 0.017$) occurred in the exercise group. Significant decreases in waist girth ($p = 0.001$) and insulin levels ($p = 0.03$) occurred in both groups. Hormonal changes were not statistically significant; however, a trend towards an improved hormonal profile, specifically sex-hormone binding globulin (EN, 39% increase; N, 8% increase) and luteinizing hormone : follicle-stimulating hormone (LH:FSH) (EN, 9% decrease; N, 27% decrease) occurred in the absence of weight loss. These findings suggest exercise and nutritional counseling may benefit the metabolic and reproductive abnormalities associated with PCOS.

Key words: physical activity, endurance exercise, resistance training, overweight, polycystic ovary syndrome.

Résumé : Cette étude pilote analyse les effets de l'exercice physique et du counseling nutritionnel sur les fonctions hormonales, menstruelles et reproductrices de femmes atteintes du syndrome des ovaires polykystiques (PCOS). Douze femmes avec un diagnostic de PCOS sur un plan clinique, biochimique et ultrasonographique sont réparties aléatoirement dans deux groupes, l'un (EN) comprenant des exercices de force et d'endurance combinés à du counseling nutritionnel et l'autre (N) comprenant seulement le counseling, les deux sur une période de 12 semaines. Les variables suivantes sont mesurées avant et après les 12 semaines d'intervention : caractéristiques anthropométriques, métabolisme de repos (RMR), des hormones spécifiques et un ensemble de follicules ovariens. Après les 12 semaines d'intervention, on observe une plus grande diminution de la somme de l'épaisseur de deux plis cutanés ($p = 0.002$) et une plus grande augmentation du $\text{VO}_2 \text{ max}$ estimé dans le groupe soumis à l'effort ($p = 0.017$). On observe aussi dans les deux groupes une diminution significative du tour de taille ($p = 0.001$) et des concentrations d'insuline ($p = 0.03$). Les variations hormonales ne sont pas statistiquement significatives même si le profil hormonal semble amélioré, notamment en ce qui concerne les globulines spécifiques (EN, augmentation de 39 %; N, augmentation de 8 %) et le ratio LH-FSH (EN, diminution de 9 %; N, diminution de 27 %), et ce, sans perte de poids. Il semble d'après ces observations, qu'un programme d'entraînement et de counseling nutritionnel profitent aux femmes présentant le syndrome du PCOS.

Mots clés : activité physique, exercice d'endurance, entraînement à la force, excès de poids, syndrome des ovaires polykystiques.

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Introduction

Currently, polycystic ovary syndrome (PCOS) is described as the most frequent cause of anovulation resulting in infertility in adult women (Knochenhauer et al. 1998; Ehrmann et al. 1999; Sozen and Arici 2000). Researchers agree that it is one of the most common reproductive endocrinological disorders, affecting approximately 4%–12% of women (Kno-

chenhauer et al. 1998). In addition to the role PCOS plays in the reproductive potential and fertility status of women, many other health risks are associated with this syndrome, including features of metabolic syndrome such as obesity, insulin resistance, and hyperlipidemia (Norman et al. 2004), as well as an increased risk of developing type 2 diabetes and hypertension, and a subsequent risk of cardiovascular disease (Solomon 1999). Approximately 50% of women with PCOS are overweight or obese, with the pattern of body fat primarily centrally located (Norman et al. 2004). Previous research has found that obese women with PCOS have a more rapid progression from normal glucose function to impaired glucose tolerance and diabetes compared with age- and weight-matched controls without PCOS (Ehrmann et al. 1999; Norman et al. 2001). From a health perspective, treating women for PCOS may not only result in the restoration of reproductive potential, but may also reduce their risk of developing the associated non-reproductive conditions.

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Table 1. Baseline and post-intervention anthropometric subject characteristics.

Characteristic	EN Group (<i>n</i> = 7; mean age 32.3±1.0)		N Group (<i>n</i> = 5; mean age 28.4±2.7)	
	Pre	Post	Pre	Post
Body mass (kg)	100.5±6.7	99.7±7.5	94.8±6.2	91.7±4.9
BMI (kg/m ²)	36.2±2.0	35.9±2.2	37.1±3.4	35.9±3.0
Waist Girth (cm)	98.3±5.0	93.1±4.8 ^a	99.8±5.0	94.8±5.4 ^a
SO2S (mm)	75.0±3.0	65.0±3.1 ^{a, b}	73.9±5.8	75.2±5.3

Note: All values are means ± SE. BMI, body mass index; SO2S, sum of 2 skinfolds (subscapular, iliac crest).

^aSignificantly different from baseline.

^bSignificantly different between groups.

It is accepted that lifestyle modifications in the form of exercise and proper nutrition decrease the risk of developing the aforementioned non-reproductive conditions, namely type 2 diabetes (Pan et al. 1997; Tuomilehto et al. 2001; Diabetes Prevention Program Research Group 2002). This is of particular relevance for overweight and obese women with PCOS and insulin resistance, given their risk of developing type 2 diabetes is 7–10 times greater compared with women of normal mass who also have PCOS (Norman et al. 2001). Previous research aimed at improving the reproductive potential of women with PCOS has primarily involved pharmacological therapy aimed at improving insulin sensitivity and inducing ovulation (Casimirri et al. 1997; Ehrmann et al. 1997; Nestler 1998). The most commonly used treatments have consisted of fertility drugs such as clomiphene citrate and insulin-sensitizing drugs such as metformin, used either alone or in combination. Although some studies report varying success rates with these therapies (Opsahl et al. 1996; Ehrmann et al. 1999; Nestler 1998), a meta-analysis suggests that metformin is effective for improving ovulation rates and reducing fasting insulin levels in women with PCOS; however, it was ineffective in decreasing body mass or fatness (Lord et al. 2003). In addition, the authors could find no literature reporting the safety of long-term use of metformin in young women (Lord et al. 2003).

Non-pharmacological therapies have also been explored in this population and have largely consisted of dietary restriction (Hollmann et al. 1996; Pasquali et al. 1997; Clark et al. 1998). Although dietary control has been shown to produce favorable reproductive outcomes, long-term dietary restriction is generally difficult to maintain. Because there tends to be a poor compliance to diet restriction over time, weight loss is rarely sustained (Ross et al. 2000). In addition, very low calorie diets have been shown to adversely alter the body's metabolism by decreasing the resting metabolic rate (RMR) (Leibel et al. 1995). It is theorized that the decrease in RMR may occur because of the decrease in fat-free mass (FFM), which is associated with diet-induced weight loss (Ross et al. 2000). Since exercise training increases RMR by promoting an increase in FFM, the addition of chronic exercise as an adjunct to dietary treatment has the potential to decrease fat mass while preserving fat-free mass, the goal of any weight-loss program (Ross et al. 2000).

There are limited studies exploring exercise therapy as a treatment option for women with PCOS (Clark et al. 1995; Clark et al. 1998). It is well known that exercise is one of

the cornerstones in the treatment of type 2 diabetes, primarily because of its beneficial effects on improving insulin sensitivity (Hamdy et al. 2001). Chronic exercise also has a favorable affect on body composition by contributing to the decrease of fat mass and the preservation of fat-free mass (Ryan et al. 1995; Lemmer et al. 2001). As there are strong associations between obesity, insulin resistance, PCOS, and the development of type 2 diabetes, this pilot study was designed to observe the effects of a supervised exercise program (endurance and resistance training) combined with nutritional counseling on the metabolic and reproductive abnormalities associated with PCOS in obese woman.

Materials and methods

Participants

Twelve sedentary, untrained, adult females in their reproductive years, with a clinical and biochemical diagnosis of PCOS were recruited through a local newspaper advertisement and by notices placed in the local hospitals. The participants were moderately obese (mean body mass index (BMI) = 36.6 kg/m²) and displayed central obesity as determined by waist girth (WG) (mean WG = 98.9 cm). All individuals gave informed written consent according to the guidelines established by the participating University's Advisory Committee on Ethics in Human Experimentation. Before initiating the study, all participants were assessed to confirm the diagnosis of PCOS. During this initial consultation, each woman completed a questionnaire regarding menstrual history, medical history, physical activity habits, and weight-loss history. A complete assessment was then carried out by the same gynecologist, which included a complete physical examination, transvaginal ultrasound, and hematological assessment that included pregnancy testing and ruling out the presence of thyroid disease or increased prolactin and dehydroepiandrosterone sulfate (DHEAS) levels. According to the Rotterdam criteria, 2 of the following 3 symptoms or signs are required for a diagnosis of PCOS: (i) anovulation or oligo-ovulation; (ii) clinical and (or) biochemical signs of hyperandrogenism; (iii) the presence of polycystic ovaries, along with the exclusion of other etiologies such as Cushing's syndrome, congenital adrenal hyperplasia, and androgen-secreting tumors (Rotterdam PCOS Consensus Workshop 2004). All women in the study were confirmed to have PCOS, as each participant met all 3 of the criteria outlined above. Although an elevation of luteinizing hormone (LH) is not considered a

Table 2. Baseline and post-intervention hormone and androgen assays.

Characteristic	EN Group (<i>n</i> = 7)		N Group (<i>n</i> = 5)	
	Pre	Post	Pre	Post
QUICKI	0.32±0.01 (0.33)		0.32±0.02 (0.31)	
LH:FSH (U/L)	2.2±0.7 ^a (1.7)	2.0±0.5 ^a (1.5)	2.0±0.4 ^a (1.7)	1.5±0.3 ^a (1.8)
Fasting insulin (pmol/L)	116.7±42.2 ^b (90.1)	82.5±20.8 ^{b, c} (63.5)	233.8±77.4 ^d (126.3)	105.0±24.6 ^{d, c} (110.5)
SHBG (nmol/L)	26.4±4.3 (30.4)	36.8±13.3 (27.6)	17.1±4.9 ^d (17.0)	18.4±4.0 ^d (14.4)
Testosterone (nmol/L)	3.0±0.3 (3.1)	3.2±0.2 (3.4)	3.1±1.0 ^d (2.5)	3.1±0.4 ^d (2.7)
FAI	13.9±2.6 (11.0)	13.9±2.6 (12.0)	20.3±4.6 ^d (23.0)	19.8±4.1 ^d (19.0)

Note: All values are means ± SE (median value). QUICKI, quantitative sensitivity check index; LH:FSH, ratio of luteinizing hormone to follicle-stimulating hormone; SHBG, sex-hormone-binding globulin; FAI, free androgen index.

^a*n* = 5

^b*n* = 6

^cSignificantly different from baseline.

^d*n* = 4

diagnostic criterion for PCOS, it is a plausible part of a multifactorial mechanism for the expression of hyperandrogenism (hirsutism) and therefore we included it in this study. The LH – follicle-stimulating hormone (FSH) ratio was consistently > 1.0 for all the participants. In addition, we were interested in examining obese women, therefore participants who met the diagnostic criteria for PCOS and had a BMI > 27 kg/m² were invited to participate in the study. Exclusion criteria included type 1 or type 2 diabetes, the presence of thyroid disease, increased prolactin levels, increased DHEAS levels, and a positive pregnancy test, all of which were measured during the pre-screening assessment. Potential participants reporting a current smoking history were also excluded from the study. In addition, any other cardiovascular, respiratory, or endocrinological diseases that required the use of prescribed medication resulted in participant exclusion. After acceptance into the study, the women were asked to refrain from taking oral contraceptive pills and counseled on barrier methods of contraception. Before initiation of the intervention, each woman was prescribed oral medroxyprogesterone acetate (10 mg) for 12 d to induce withdrawal bleeding as a medical means to prevent dysfunctional uterine bleeding and endometrial hyperplasia. The eligible participants were then randomly allocated by having the researcher choose a sealed envelope for each participant indicating which treatment they would receive: exercise and nutritional counseling (EN, *n* = 7) or nutritional counseling only (N, *n* = 5).

Measurements

Pre- and post-testing were conducted on all participants. This included body composition analyses (BMI, WG, sum of 2 skinfolds); tests for insulin sensitivity, androgen levels, fasting lipid levels, cardiorespiratory fitness, resting metabolic rate, ovarian follicle population; and documentation of menstrual history and nutritional practices.

Anthropometry

Skinfold measurements were taken from 2 sites (subscapular and iliac crest) and were measured as outlined by the Canadian Society for Exercise Physiology 1996a. The measurements were taken on the right side of the body and were recorded to the nearest 0.2 mm. The procedure was repeated to obtain a second measurement at both sites and the mean

of the 2 measurements were recorded. When the difference between the 1st and 2nd measurement of a particular skinfold was greater than 0.4 mm, a 3rd measurement was taken. From the 3 measurements, the 2 that were more closely matched in value were used. When all 3 measurements showed equal variation, the mean of all 3 was used. The final measurements from each skinfold site were then summed. WG was measured by positioning a tape measure horizontally at the level of the noticeable waist narrowing. The measurement was read at the end of a normal expiration. When the point of narrowing could not be found, an indeterminate waist was approximated by finding the lateral level of the 12th or lower floating rib and the girth was recorded at that site (Canadian Society for Exercise Physiology 1996a; American College of Sports Medicine 2001). WG measurements were taken twice and recorded to the nearest 0.5 cm. When the difference between the 1st and 2nd girth measurement was greater than 0.5 cm, a 3rd measurement was taken and the average was determined from all 3 measurements. All anthropometric measurements were taken by the same tester.

Blood samples

After a minimum 12 h fast, blood samples were drawn from each subject in the morning at approximately the same time of day and were analyzed immediately for determination of fasting and insulin and lipid profiles. Fasting insulin levels were analyzed using the Immulite 2000 chemiluminescent immunoassay system (Diagnostic Product Corporation, Los Angeles, Calif.). Blood samples were also drawn to determine FSH and LH levels, as well as total testosterone level, sex-hormone-binding globulin (SHBG) level, and free androgen index (FAI). The FSH and LH levels were measured by microparticle enzyme immunoassay (MEIA) technology using the AxSYM System (Abbott Laboratories, Abbott Park, Ill.). Total testosterone was analyzed using the Abbott Architect (Abbott Laboratories). SHBG was analyzed using the Immulite 2000 chemiluminescent immunoassay system (Diagnostic Product Corporation, Los Angeles, Calif.). The formula for the free androgen index (FAI) was obtained from the provincial lab where the blood samples were analyzed and was calculated from the results of the total testosterone and SHBG (testosterone/SHBG). Lipid analysis included total cholesterol (TC), high-density lipoprotein

Table 3. Baseline and post-intervention cardiovascular fitness scores, resting energy expenditure values, and ovarian follicle population.

Characteristic	EN Group (<i>n</i> = 7)		N Group (<i>n</i> = 5)	
	Pre	Post	Pre	Post
VO ₂ (mL·kg ⁻¹ ·min ⁻¹)	22.6±2.1 (20.3)	32.0±2.9 ^{a, b} (31.5)	23.9±2.5 (22.1)	25.0±4.1 (22.7)
REE (kcal/d)	1485±177 (1469)	1610±146 (1452)	1596±107 (1653)	1586±103 (1530)
PCO-R	49±7 (48)	44±5 (42)	47±8 (47)	46±8 (38)
PCO-L	35±5 (33)	39±6 (38)	33±4 ^c (32)	39±7 ^c (35)

Note: All values are means ± SE (median value). VO₂, oxygen consumption; RMR, resting energy expenditure; PCO-R, number of ovarian follicles on the right ovary; PCO-L, number of ovarian follicles on the left ovary.

^aSignificantly different from baseline.

^bSignificantly different between groups.

^c*n* = 4

(HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides (Tg) and TC:HDL. Total cholesterol, HDL, and Tg were analyzed using the automated SYNCHRON LX System (Beckman Coulter, Inc., Fullerton, Calif.). LDL cholesterol was calculated from values obtained for TC, HDL, and Tg (LDL = TC – HDL – (Tg/2.2)). TC:HDL was also determined from the calculated values for each.

Cardiorespiratory fitness

Cardiorespiratory fitness was determined by the Astrand and Ryhming submaximal cycle ergometer test conducted on a Monark 818E cycle ergometer. The participants pedaled at 50 r/min for 6 min at a work rate that elicited a steady-state heart rate between 120 and 150 beats/min. Maximal oxygen uptake was estimated using the normative data of Astrand and Rodahl (Canadian Society for Exercise Physiology 1996b).

Resting metabolic rate

The resting metabolic rate of each participant was measured by a Sismometrics VMAX 29 series metabolic cart (Sismometrics, Yorba Linda, Calif.). All participants were instructed to fast for at least 12 h before being tested. In addition, they were instructed to avoid any form of exercise training for at least 48 h, attain a minimum of 8 h of sleep the night before, and to avoid any activity requiring excessive movement the morning of the testing. After height and mass were recorded, each subject rested in the supine position for approximately 15 min. A ventilated hood was placed over the participant's head and room air was inhaled and exhaled into the hood, which was attached to the gas analyzers via a collection tube. The baseline RMR measurements continued until the subject reached a "steady state" defined as 5 consecutive readings (separated by at least 1 min) with exhaled volume values within 5% of the previous values (Barsztein et al. 1989). All participants were tested in the morning at approximately the same time of day. Resting energy expenditure was estimated using measured respiratory exchange ratio to establish the caloric equivalent (Barsztein et al. 1989).

Transvaginal ultrasonography

Transvaginal ultrasound was used to determine the presence of a polycystic ovarian population of follicles and to

determine the presence of a corpus luteum. The number of ovarian follicles was assessed in the plane of largest ovarian dimension in both transverse and sagittal planes. Endometrium thickness and pattern (A–D) was also recorded (Fleischer et al. 1986, 1990). The same gynecologist performed each transvaginal ultrasound.

Menstrual history

Menstrual history was taken before acceptance into the study and during the time of the second ultrasound examination. The history included questions relating to the regularity of menstruation, the number of days from the beginning of one menstrual period to the beginning of the next menstrual period (i.e., shortest and longest periods of time between cycles), and the number of days of menses.

Nutrient intake

Individual nutrient intakes were determined using a 3 d food diary before and after completion of the study. The women were asked to recall the types and amounts of food and beverages that they had consumed over the previous 24 h. Three recalls were performed covering 2 weekdays and 1 weekend day. Food consumption data obtained from the 3 d food diaries were analyzed for energy and nutrient content (FUEL Nutrition Software 2.1a; LogiForm International Inc., Saint-Foy, Qué.).

Exercise protocol

The participants in the combined exercise and nutritional counseling (EN) group participated in a 12 week supervised exercise program focusing on weight loss, as this has shown to improve the symptoms of PCOS (Clark et al. 1995; Huber-Buchholz et al. 1999). The exercise program was conducted 3 d/week using a combination of endurance and resistance training. Each exercise consisted of a 10 min warm up period on the treadmill or bicycle, followed by 30 min of cardiorespiratory exercise such as treadmill walking and (or) stationary cycling at a moderate intensity level of 70%–85% of their age-predicted maximum heart rate. To ensure a moderate intensity of exercise was achieved, Polar Heart Rate monitors (Model a1, Polar Electro Canada, Lanco Logistics, Lachine, Que.) were used to monitor heart rates during the endurance exercise sessions. The resistance-training component was composed of 12 exercises: biceps curl, lat pulldown, leg curl, leg extension, shoulder press,

chest press, leg press, hip abduction, hip adduction, hip flexion, hip extension, and back extension. After familiarization with the resistance-training equipment and program, each subsequent session began with 2 sets of 10 repetitions using a comfortable baseline mass. When 3 sets of 15 repetitions of each exercise were completed comfortably, the mass was then increased by approximately 5% or 2.2 kg (whichever was greater). Each exercise session lasted approximately 90 min and all data was recorded in a training log by the participants and the supervisor to ensure the accuracy. The women were also encouraged to participate in a physical activity such as walking on the alternate days when not at the supervised program and were given an activity log to complete with regards to their physical activity outside of the structured program.

Nutritional counseling

Participants in both the exercise (EN) and nutritional-counseling only (N) groups were encouraged to attend 1 h group nutritional seminars each week conducted by the researcher and a registered dietitian. They were counseled on long-term nutritional strategies including (i) determining caloric requirements, (ii) *Canada's Food Guide to Healthy Eating*, (iii) serving sizes and portion sizes, (iv) daily fat consumption targets, (v) diet strategies and goals for weight loss, (vi) shopping tips for healthy food choices, (vii) meal planning, (viii) food preparation and modification, and (ix) other weight-related topics specific to carbohydrate, fat and protein, fiber, water, and key nutrients.

Statistical analysis

A 2 factor (2×2 ; group \times time) repeated measures analysis of variance (ANOVA) was performed for each dependent variable and a 1 way ANOVA was used to assess the significance of differences between groups on the dependent variables assessed. Tukey's post hoc analysis was performed if there was a significant finding. Statistical significance was set at $p < 0.05$. All values are expressed as the mean \pm the standard error.

Results

Anthropometric data are presented in Table 1. At baseline, there were no significant differences between the groups on all variables assessed. Following the intervention, no significant differences in body mass ($p = 0.12$) or BMI ($p = 0.12$) were observed between groups. There was a significant decrease in WG in both groups (EN, 5.3%; N, 5%; $p = 0.001$) following the intervention program, although there was no group \times time interaction. The sum of 2 skinfolds data demonstrated a significant group \times time interaction ($p = 0.002$) after the intervention, with a greater decrease in the EN group (12%) than in the N group (3%).

Hormone and androgen assay data are presented in Table 2. There were no significant differences between groups at baseline. Following the intervention, there was no significant difference in LH:FSH ($p = 0.20$). Data on 2 women in the EN group were excluded owing to laboratory error ($n = 1$) and a positive pregnancy test ($n = 1$). There was a significant decrease in fasting insulin levels (EN, 29%; N, 55%) follow-

ing the intervention ($p = 0.03$); however, these differences were not significant between the 2 groups. Data for 2 women (EN = 1, N = 1) were excluded in this analysis owing to laboratory error. There were no significant differences in SHBG ($p = 0.50$), testosterone ($p = 0.61$) or FAI ($p = 0.89$) following the intervention. The lipid profile revealed no significant differences between groups at baseline. Data collected on the lipid profile following the intervention showed no significant differences in HDL ($p = 0.76$), LDL ($p = 0.81$), Tg ($p = 0.84$), TC ($p = 0.96$) or HDL/TC ($p = 0.84$) within or between the 2 groups. The quantitative insulin sensitivity check index (QUICKI) was used to estimate insulin resistance. Before initiating the study, insulin resistance was detected in 5 (41.7%) of the women (EN, 3; N, 2). Fasting glucose was only measured during the initial baseline screening to rule out type 2 diabetes, therefore, post-intervention values are not reported.

All women responded to the medroxyprogesterone acetate therapy to induce menses. Eleven of the 12 participants did not have regular menses during the study; however, 1 participant did ovulate and conceive during the study. It is interesting to note that the 2 previous pregnancies in this individual were achieved by the use of clomiphene citrate.

There was a significant group \times time interaction ($p = 0.02$) in predicted maximal oxygen consumption ($VO_{2\max}$) following the 12 week exercise program. As presented in Table 3, greater increases were observed in the EN group (42%) compared with the N group (5%). There was no significant difference in resting metabolic rate (RMR) observed between the 2 groups ($p = 0.63$), although the EN group increased by 9% and the N group decreased by 1% following the intervention (Table 3). There were no significant differences in ovarian follicle population in either ovary between the groups (Table 3).

Discussion

It has previously been shown that weight loss, independent of exercise, improves insulin resistance (Guzick et al. 1994; Holte et al. 1995) and hyperinsulinemia (Pasquali et al. 1989; Kiddy et al. 1992) in obese women with PCOS. As insulin resistance is now believed to play a key role in the pathogenesis of PCOS, it was important to determine if exercise would exert the same beneficial effects as the diet-induced weight loss previously demonstrated in obese women with PCOS. Specifically, we wanted to determine the effects of exercise on body composition, primarily patterns of body fatness, and resting metabolic rate. Although a limitation to this study is the small sample size, which increases the risk of a type II error, the results of this pilot study are encouraging for obese women with PCOS and the promotion of exercise in the treatment of this condition. Our findings revealed that the combination of exercise and nutritional counseling, as well as nutritional counseling alone, provided favorable effects on WG, body fatness, and fasting insulin levels, as well as a trend towards an increase in resting metabolic rate in the exercise and nutrition (EN) group after completion of the intervention. Although reductions in WG and fasting insulin levels were similar between the groups, there was a greater decrease in body fatness in the EN group, as shown by the significant decrease in sum of 2

skinfolts, which occurred in the absence of a significant weight loss. While these findings may be a reflection of the small sample size, it is worthwhile to note that PCOS is characterized by hyperinsulinemia and worsened by abdominal obesity (Lord et al. 2003), and thus these results offer a promising alternative to drug treatment.

Although we cannot claim unequivocally that the program of exercise and nutritional counseling (EN) was superior to that of nutritional counseling only (N), the literature supports the rationale that exercise may be a more viable option than dietary restriction, and has the potential to provide beneficial effects. For example, previous literature suggests that improvements in the biochemical profile of women with PCOS occurs with a weight loss of 5%–10% of initial body mass (Hamilton-Fairley et al. 1993; Wahrenberg et al. 1999); however, this pilot data has shown a trend towards an improvement, primarily in fasting insulin levels, with a body mass reduction of as little as 1%. Although the N group had a slightly greater weight loss than the EN group (3% vs. 1%, respectively), and although changes in WG were the same for both groups (5%), the EN group also had a significant decrease in SO2S. Given this, factors other than a reduction in body mass, such as a decrease in body fat, may be more important in this population. Therefore, using total body mass as an assessment of the effectiveness of exercise may underestimate the loss of fat mass (Prentice and Jebb 2001), as may have been the case in this study.

A decrease in abdominal obesity may not only be effective at improving insulin sensitivity, but may also improve (increase) levels of SHBG in women with PCOS. Increased abdominal fat deposition is associated with decreased levels of SHBG and increased synthesis of androgens (Speroff et al. 1999); however, following the intervention, SHBG increased 39% in the EN group compared with an 8% increase in the N group. Although these results were not significant, the trend suggests that the change in SHBG may have been due to changes in body fatness, characterized by decreases in WG and SO2S, particularly in the EN group where significant changes in body fatness were observed. It should also be mentioned that increased free androgen levels have previously been shown to be associated with decreased levels of SHBG (Yen et al. 1999), and although it is speculated that with a rise in SHBG comes a subsequent decrease in free testosterone, any associations between an increase in SHBG and decrease in free-testosterone levels cannot be reported; unfortunately, these measurements were not available owing to a change in hospital laboratory policy.

As mentioned previously, the women in the EN group had little change in their body mass but showed a decrease in body fat. Indeed, exercise levels typically prescribed for weight loss (i.e., moderate activity performed 3–5 h/week) may have modest effects on decreasing body mass alone, but increases fat loss and preserves fat free mass (FFM). While dieting alone can result in loss of fat mass, it can also result in loss of FFM. Resting metabolic rate (RMR) has also been found to be lowered during dieting, which is in part due to the loss of FFM (Welle et al. 1984). Given the close association between RMR and FFM, the 10% increase in RMR in the EN group following the intervention suggests that the addition of the resistance-training component (which tends to increase FFM) may have been benefi-

cial in increasing the RMR by increasing FFM. Although this assumption cannot be definitively confirmed because a direct measurement of FFM was not obtained, future research should consider using a direct measure of body fatness, particularly as previous research has suggested that body fatness plays a key role in decreasing metabolic risk (Depres and Lamarche 2000). Although waist girth and skinfold measurements can be used to assess body composition and are relatively inexpensive, imaging techniques such as dual-energy X-ray absorptiometry or air-displacement plethysmography may provide a more accurate method for assessing body composition and metabolic risk in women with PCOS.

Apart from the positive changes in body composition attributable to exercise, an increased fitness level may also prove beneficial for women with PCOS, as endurance exercise training has been shown to improve insulin action in obese individuals (Depres and Lamarche 2000), whereas low cardiorespiratory fitness has been associated with metabolic abnormalities (Whaley et al. 1999). Our results showed an increase in relative and absolute $\text{VO}_{2\text{max}}$ in the EN group, and this may serve to reduce metabolic abnormalities such as insulin resistance and compensatory hyperinsulinemia, which are associated with PCOS. Despite our hypothesis that exercise training would have more pronounced effects on the fasting insulin levels in the EN group, there are additional benefits of endurance training, such as the reduction of cardiovascular disease risk factors associated with PCOS.

With regards to polycystic ovary morphology, although there were no significant differences in ovarian follicle population, it is interesting to note the number of follicles detected. Although the presence of 12 or more follicles is consistent with the Rotterdam criteria for polycystic ovaries (Rotterdam PCOS Consensus Workshop 2004), we found that women had a mean of 40 follicles per ovary (range, 25–66 follicles). It is the opinion of the Imaging Group at the Women's Health Imaging Research Laboratory in the Department of Reproductive Medicine at the University of Saskatchewan that this large number of ovarian follicles is the norm for women with polycystic ovaries, and other research done in our laboratory has shown that normal (non-PCOS) ovulating women have a mean of 14 follicles per ovary (Baerwald et al. 2003). It is our clinical experience that women with PCOS typically have over 25 follicles per ovary, but we have seen between 30 and 60 follicles in each ovary. To elucidate the number of follicles seen in women with PCOS and to delineate a more useful criterion to diagnose a polycystic ovary, an observational study is currently being completed at the Women's Health Imaging Research Laboratory.

Conclusions

Although the results of this study are unable to claim that one treatment was superior to another, the results from this pilot study provide some information to suggest that lifestyle modifications in the form of endurance and resistance exercise may provide beneficial effects with regards to the biochemical profile of obese women with PCOS. The preliminary findings of a significant decrease in fasting insulin levels, as well as the tendency towards improved sex

hormones, in the absence of significant weight loss suggests that changes in body composition, specifically a decrease in body fatness, independent of changes in body mass, may be beneficial in reducing the metabolic abnormalities associated with obese women with PCOS, and that this should be investigated further in this population. It is recommended that future research in this area be of longer duration and directed towards obtaining a larger sample size to confirm the findings observed in the present pilot study.

Individuals who embark on an exercise program in an effort to substantially reduce body mass often become discouraged because of the time involved to induce aesthetic changes. It may be encouraging to obese women with PCOS that although a decrease in body mass may initially be most desirable, a decrease in body fatness, primarily in the abdominal region, may improve their metabolic and hormonal profiles with only minimal losses in body mass. These findings may therefore be beneficial in motivating these individuals to continue with positive lifestyle modifications on a long-term basis.

References

- American College of Sports Medicine. 2001. ACSM's resource manual for guidelines for exercise testing and prescription. Human Kinetics, Champaign, Ill. pp. 101–104.
- Baerwald, A.R., Adams, G.P., and Pierson, R.A. 2003. A new model for ovarian follicular development during the human menstrual cycle. *Fertil. Steril.* **80**: 116–122. doi:10.1016/S0015-0282(03)00544-2. PMID: 12849812.
- Barsztein, S., Elwynn, D.H., Askanazi, J., and Kinney, J.M. 1989. Energy metabolism, indirect calorimetry and nutrition. Williams & Wilkins, New York, N.Y.
- Canadian Society for Exercise Physiology. 1996a. The Canadian physical activity, fitness and lifestyle appraisal resource manual. Canadian Society for Exercise Physiology, Ottawa, Ont. pp. 7.12–7.18.
- Canadian Society for Exercise Physiology. 1996b. Professional fitness and lifestyle consultant resource manual. Canadian Society for Exercise Physiology, Ottawa, Ont. pp. 2.20–2.22.
- Casimirri, F., Biscotti, M., Gambineri, A., Calzoni, F., Eliana, B., and Pasquali, R. 1997. Metformin improves insulin, body fat distribution and androgens in obese women with and without the polycystic ovary syndrome. *Int. J. Obes.* **21**(Suppl. 2): 61.
- Clark, A.M., Ledger, W., Galletly, C., Tomlinson, K., Blaney, F., Wang, X., and Norman, R.J. 1995. Weight loss results in significant improvement in pregnancy and ovulation rates in anovulatory obese women. *Hum. Reprod.* **10**: 2705–2712. PMID: 8567797.
- Clark, A.M., Thornley, B., Tomlinson, L., Galletley, C., and Norman, R.J. 1998. Weight loss in obese infertile women results in improvement in reproductive outcome for all forms of fertility treatment. *Hum. Reprod.* **13**: 1502–1506. doi:10.1093/humrep/13.6.1502. PMID: 9688382.
- Depres, J.P., and Lamarche, B. 2000. Physical activity and the metabolic complications of obesity. In *Physical activity and obesity*. Edited by C. Bouchard. Human Kinetics, Champaign, Ill. pp. 331–354.
- Diabetes Prevention Program Research Group. 2002. The Diabetes prevention program: description of lifestyle intervention. *Diabetes Care*, **25**: 2165–2171. PMID: 12453955.
- Ehrmann, D.A., Schneider, D.J., Sobel, B.E., Cavaghan, M.K., Imperial, J., Rosenfield, R.L., and Polonsky, K.S. 1997. Troglitazone improves defects in insulin action, insulin secretion, ovarian steroidogenesis, and fibrinolysis in women with polycystic ovary syndrome. *J. Clin. Endocrinol. Metab.* **82**: 2108–2116. doi:10.1210/jc.82.7.2108. PMID: 9215280.
- Ehrmann, D.A., Barnes, R.B., Rosenfield, R.L., Cavaghan, M.K., and Imperial, J. 1999. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. *Diabetes Care*, **22**: 141–146. PMID: 10333916.
- Fleischer, A.C., Herbert, C.M., Sacks, G.M., Wentz, A.C., Entman, S.S., and James, A.E. 1986. Sonography of the endometrium during conception and non-conception cycles of in vitro fertilization and embryo transfer. *Fertil. Steril.* **46**: 442–447. PMID: 3091409.
- Fleischer, A.C., Herbert, C.M., Hill, G.A., and Kepple, D.M. 1990. Transvaginal sonography: applications in infertility. *Semin. Ultrasound CT MR*, **11**: 71–81. PMID: 2184868.
- Guzick, D.S., Wing, R., Smith, D., Berga, S., and Winters, S.J. 1994. Endocrine consequences of weight loss in obese, hyperandrogenic, anovulatory women. *Fertil. Steril.* **61**: 598–604. PMID: 8150098.
- Hamdy, O., Goodyear, L.J., and Horton, E.S. 2001. Diet and exercise in type 2 diabetes mellitus. *Endocrinol. Metab. Clin. North Am.* **30**: 883–907. PMID: 11727404.
- Hamilton-Fairley, D., Kiddy, D., Anyaoku, V., Koistinen, R., Sepala, M., and Franks, S. 1993. Response of sex hormone binding globulin and insulin-like growth factor binding protein-1 to an oral glucose tolerance test in obese women with polycystic ovary syndrome before and after calorie restriction. *Clin. Endocrinol. (Oxf.)*, **39**: 363–367. PMID: 7693380.
- Hollmann, M., Runnebaum, B., and Gerhard, I. 1996. Effects of weight loss on the hormonal profile in obese, infertile women. *Hum. Reprod.* **11**: 1884–1891. PMID: 8921059.
- Holte, J., Bergh, T., Berne, C., Wide, L., and Lithell, H. 1995. Restored insulin sensitivity but persistently increased early insulin secretion after weight loss in obese women with polycystic ovary syndrome. *J. Clin. Endocrinol. Metab.* **80**: 2586–2593. doi:10.1210/jc.80.9.2586. PMID: 7673399.
- Huber-Buchholz, M.M., Carey, D.G.P., and Norman, R.J. 1999. Restoration of reproductive potential by lifestyle modification in obese polycystic ovary syndrome: Role of insulin sensitivity and luteinizing hormone. *J. Clin. Endocrinol. Metab.* **84**: 1470–1474. doi:10.1210/jc.84.4.1470. PMID: 10199797.
- Kiddy, D.S., Hamilton-Fairley, D., Busch, A., Short, F., Anyaoku, V., Reed, M.J., and Franks, S. 1992. Improvement in endocrine and ovarian function during dietary treatment of obese women with polycystic ovary syndrome. *Clin. Endocrinol. (Oxf.)*, **36**: 105–111. PMID: 1559293.
- Knochenhauer, E.S., Key, T.J., Kahsar-Miller, M., Waggoner, W., Boots, L.R., and Azziz, R. 1998. Prevalence of the polycystic ovary syndrome in unselected black and white women of the southeastern United States: A prospective study. *J. Clin. Endocrinol. Metab.* **83**: 3078–3082. doi:10.1210/jc.83.9.3078. PMID: 9745406.
- Leibel, R.L., Rosenbaum, M., and Hirsch, J. 1995. Changes in energy expenditure resulting from altered body weight. *N. Engl. J. Med.* **332**: 621–628. doi:10.1056/NEJM199503093321001. PMID: 7632212.
- Lemmer, J.T., Ivey, F.M., Ryan, A.S., Martel, G.F., Hurlbut, D.E., Metter, J.E., et al. 2001. Effect of strength training on resting metabolic rate and physical activity: Age and gender comparisons. *Med. Sci. Sports Exerc.* **33**: 532–541. PMID: 11283427.
- Lord, J., Flight, I.H.K., and Norman, R.J. 2003. Metformin in polycystic ovary syndrome: systematic review and meta-analysis. *Brit. Med. J.* **327**: 951–955.
- Nestler, J.E. 1998. The role of hyperinsulinemia in the pathogen-

- esis of the polycystic ovary syndrome and its clinical implications. *Semin. Reprod. Endocrinol.* **15**: 111–122.
- Norman, R.J., Masters, L., Milner, C.R., Wang, J.X., and Davies, M.J. 2001. Relative risk of conversion from normoglycemia to impaired glucose tolerance or non-insulin dependent diabetes mellitus in polycystic ovarian syndrome. *Hum. Reprod.* **16**: 1995–1998. doi:10.1093/humrep/16.9.1995. PMID: 11527911.
- Norman, R.J., Wu, R., and Stankiewicz, M.T. 2004. Polycystic ovary syndrome. *Med. J. Aust.* **180**: 132–137. PMID: 14748678.
- Opsahl, M.S., Robins, E.D., O'Connor, D.M., Scott, R.T., and Fritz, M.A. 1996. Characteristics of gonadotrophin response, follicular development, and endometrial growth and maturation across consecutive cycles of clomiphene citrate treatment. *Fertil. Steril.* **66**: 533–539. PMID: 8816613.
- Pan, X.-R.L.G.W., Hu, Y.H., Wang, J.X., Yang, W.Y., An, Z.X., Hu, Z.X., et al. 1997. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: The Da Qing IGT and diabetes study. *Diabetes Care*, **20**: 537–544. PMID: 9096977.
- Pasquali, R., Antenucci, D., Casimirri, F., Venturoli, S., Paradisi, R., Fabbri, R., et al. 1989. Clinical and hormonal characteristics of obese amenorrheic hyperandrogenic women before and after weight loss. *J. Clin. Endocrinol. Metab.* **68**: 173–178. PMID: 2642485.
- Pasquali, R., Casimirri, F., and Vicennati, V. 1997. Weight control and its beneficial effect on fertility in women with obesity and polycystic ovary syndrome. *Hum. Reprod.* **12**: Suppl. 1, 82–87. PMID: 9403324.
- Prentice, A.M., and Jebb, S.A. 2001. Beyond body mass index. *Obes. Rev.* **2**: 141–147. doi:10.1046/j.1467-789x.2001.00031.x. PMID: 12120099.
- Ross, R., Janssen, I., and Tremblay, A. 2000. Obesity reduction through lifestyle modification. *Can. J. Appl. Physiol.* **25**: 1–18. PMID: 10683597.
- Ryan, A.S., Pratley, R.E., Elahi, D., and Goldberg, A.P. 1995. Resistance training increases fat-free mass and maintains RMR despite weight loss in postmenopausal women. *J. Appl. Phys.* **79**: 818–823.
- Solomon, C.G. 1999. The epidemiology of polycystic ovary syndrome: prevalence and associated disease risks. *Endocrinol. Metab. Clin. North Am.* **28**: 247–263. PMID: 10352918.
- Sozen, I., and Arici, A. 2000. Hyperinsulinism and its interaction with hyperandrogenism in polycystic ovary syndrome. *Obstet. Gynecol. Surv.* **55**: 321–328. doi:10.1097/00006254-200005000-00026. PMID: 10804539.
- Speroff, L., Glass, R.H., and Kase, N.G. 1999. *Clinical Gynecological Endocrinology and Infertility*; 6th Ed., Baltimore: Lippincott Williams & Wilkins, pp. 492–507.
- Tuomilehto, J., Lindstrom, J., Eriksson, J.G., Valle, T.T., Hamalainen, H., Ilanne-Parikka, P., et al. 2001. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N. Engl. J. Med.* **344**: 1343–1350. doi:10.1056/NEJM200105033441801. PMID: 11333990.
- Wahrenberg, H., Ek, I., Reynisdottir, S., Carlstrom, K., Bergqvist, A., and Arner, P. 1999. Divergent effects of weight reduction and oral contraception treatment on adrenergic lipolysis regulation in obese women with the polycystic ovary syndrome. *J. Clin. Endocrinol. Metab.* **84**: 2182–2187. doi:10.1210/jc.84.6.2182. PMID: 10372729.
- Welle, S.L., Amatruda, J.M., Forbes, G.B., and Lockwood, D.H. 1984. Resting metabolic rates of obese women after rapid weight loss. *J. Clin. Endocrinol. Metab.* **59**: 41–44. PMID: 6725523.
- Whaley, M.H., Kampert, J.B., Kohl, H.W., 3rd, and Blair, S.N. 1999. Physical fitness and clustering of risk factors associated with the metabolic syndrome. *Med. Sci. Sports Exerc.* **31**: 287–293. PMID: 10063819.
- Yen, S.S.C., Jaffe, R.B., and Barbieri, R.L. 1999. *Reproductive endocrinology: physiology, pathophysiology and clinical management*. 4th ed. W.B. Saunders Co., Philadelphia, Pa.