Regular Mindful Yoga Practice as a Method to Improve Androgen Levels in Women With Polycystic Ovary Syndrome: A Randomized, Controlled Trial

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Background: Holistic approaches are needed to complement existing therapies for polycystic ovary syndrome (PCOS), a common disorder affecting the health of reproductive-aged females.

Objective: To determine whether thrice-weekly mindful yoga practice improves endocrine, cardiometabolic, or psychological parameters in women with PCOS.

Methods: Thirty-one women with PCOS between the ages of 23 and 42 years and living in Erie County, Pennsylvania, were recruited for this randomized, controlled study arm, which was part of a larger 3-part investigation. Women were randomly assigned to either a mindful yoga intervention group or no intervention (control) group. Group classes were 1 hour, thrice weekly. Initial endocrine, cardiometabolic, and psychological measurements were compared with measurements taken after the 3-month intervention period. Measurements included free testosterone, dehydroepiandrosterone, androstenedione, body mass index, waist-to-hip ratio, fasting blood glucose and insulin levels, and anxiety and depression scores.

Results: Twenty-two women completed the 3-month intervention period, 13 in the mindful yoga group and 9 in the control group. Paired comparisons of pre- and post-intervention parameters indicated that women who completed the mindful yoga intervention had significantly lower free testosterone levels (5.96 vs 4.24 pg/mL; $P<.05$) and dehydroepiandrosterone levels that trended lower. Improved testosterone may persist for several months after completion of a 3-month, thrice-weekly mindful yoga intervention. Additionally, improvements were seen in measures of anxiety and depression.

Conclusion: The improvements observed suggest that regular mindful yoga practice can be a useful complementary therapeutic option for women with PCOS, particularly for improving serum androgen levels, a hallmark feature of PCOS. This improvement occurred in the absence of weight loss and may persist even if there is a lapse in practice. (ClinicalTrials.gov No. NCT03383484)

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The most common endocrine and metabolic disorder in women, polycystic ovary syndrome (PCOS), affects 5% to 15% of women of reproductive age and is the most common cause of anovulatory infertility.[1,2] The triad of defining PCOS features includes hyperandrogenism (clinical or biochemical), menstrual irregularity secondary to oligo-ovulation or anovulation, and polycystic ovary morphology. The Rotterdam criteria, most often used for diagnosis, include the presence of at least 2 of the above criteria, along with exclusion of other diseases and conditions that may produce similar features, including but not limited to disorders involving adrenal hormones, thyroid hormone, or prolactin.[3] Women with PCOS may present with hirsutism, acne, male-pattern hair loss, subfertility, and greater incidence of miscarriage.[4,5]

Cardiometabolic and Psychological Impact of PCOS

Polycystic ovary syndrome can affect women's health beyond the reproductive years. Women with PCOS commonly exhibit excessive weight gain, glucose intolerance, and insulin resistance, abnormal adipokine secretion, and are more likely to develop type 2 diabetes mellitus and cardiovascular sequelae.[6-8] Insulin and androgens are reported to have a reciprocal relationship in PCOS, with an elevation in either hormone stimulating an increase in the other, further perpetuating the pathogenesis of the disorder.[9-11] Obesity exacerbates the severity of PCOS and increases the risk of related sequelae, although lean women with PCOS are also reported to have insulin resistance and altered adipokine secretion, indicative of metabolic dysfunction even in the absence of obesity in this population.[12-16] Women with PCOS are also reported to be more likely to experience anxiety and depression.[17,18] Taken together, PCOS has the potential to affect long-term health and quality of life.[19]

Therapies for PCOS

Despite its prevalence and impact on female health, the cause of PCOS remains unknown. Weight loss of 5% to 10% can improve menstrual regularity, androgen levels, and possibly fertility in obese young adult women with PCOS, and is the first-line therapy.[14,20,21] However, there are often hurdles to achieving and maintaining weight loss. Current pharmacologic therapies typically target individual symptoms, such as reducing elevated androgens with anti-androgenic medications, regulating the menstrual cycle with hormonal contraceptives, and using ovulation inducers to increase the likelihood of conception.[22,23] However, pharmacologic interventions are limited in their scope and may result in adverse effects as well as increased risk for developing complications such as thrombosis and breast and cervical cancer (although ovarian and endometrial cancer risk is lower).[24,25] Recent surveys of women with PCOS indicated that these women are interested in complementary or alternative options for treating their symptoms.[26,27] Reasons cited include strong dissatisfaction with pharmaceutical therapies, desire for an effective and safe alternative to hormonal contraception and fertility drugs, and desire for more than single symptom management. Existing nonpharmacologic options for women with PCOS are dietary modification (including reduced carbohydrate intake) to promote a reduction in serum insulin levels,[28,29] nutritional and herbal supplements,[26,30] acupuncture,[31,32] and aerobic exercise to promote weight loss.[14,29,33-35]

Yoga is a low-impact exercise that does not require the individual to have a specific level of fitness or flexibility to participate or benefit from the practice. It has been used as a therapy for many different conditions, including hypertension, multiple sclerosis, asthma, low back pain, arthritis, and for pain and stress management; its therapeutic mechanism has been attributed to decreased sympathetic tone, cortisol, and stress levels.[36-42] While moderate aerobic exercise improves cardiometabolic and reproductive parameters in women with PCOS, a major benefit of yoga is that it is accessible to individuals of varying fitness levels who may be uncomfortable with

more intense aerobic activity. In addition, yoga promotes mindfulness in the participant, including awareness of the body's posture and breathing.[43] Elements of mindfulness can be applied not only in yoga practice, but may also be reinforced in daily activities to promote relaxation and focus. Studies[44,45] on the effects of yoga on females with PCOS have reported improved insulin sensitivity and lipid profiles, but were limited to a study population of adolescent females without biochemical hyperandrogenism. In addition, these studies required daily yoga for 1 hour over a 3-month period. While these results were promising, the more realistic practice of yoga several times per week or by women with PCOS were not explored. In the current study, we examined the effects of 3 months of thrice-weekly mindful yoga practice on the metabolic, endocrine, and reproductive health of women with PCOS. The primary aim was to determine whether regular mindful yoga practice would decrease androgen levels, with a primary outcome measure of serum testosterone level. The secondary aim was to determine whether regular mindful yoga practice would decrease other common reproductive, metabolic, and psychological factors associated with PCOS; thus, the secondary outcome measures included menstrual cycle length, Ferriman-Gallwey score, weak androgens, fasting blood glucose and insulin, adiponectin, waist-to-hip ratio, body mass index (BMI), and scores for anxiety and depression. Furthermore, we investigated whether the benefits observed with the regular mindful yoga practice persisted beyond the completion of the 3-month intervention period.

Methods

All protocols were approved by the Lake Erie College of Osteopathic Medicine institutional review board (protocol #23-156). This was a separate arm of a larger study, results from which are also reported in the May issue of *The Journal of the American Osteopathic Association* and participant recruitment for which occurred during the same time period.[46] (ClinicalTrials.gov No. NCT03383484)

Participant Recruitment and Consent

Study participants were recruited from the Erie, Pennsylvania, area by direct advertising through radio, billboards, website, newspaper, and magazine ads. Physician referrals from Medical Associates of Erie providers were also used to recruit potential participants. Recruitment lasted 4 months, from October 2016 through January 2017. Potential participants signed a consent form to have relevant medical records released to confirm PCOS diagnosis, as well as informed consent to participate in the study.

Participant Inclusion and Exclusion

A participant questionnaire was given at the time of consent to supplement the medical records in order to determine eligibility. Participants were premenopausal women between the ages of 22 and 43 years, with a BMI of 20 to 48, who had a confirmed diagnosis of PCOS, and exhibited the 2003 Rotterdam criteria for PCOS diagnosis, defined as at least 2 of the following 3 features: clinical or biochemical hyperandrogenism (moderate acne or a modified Ferriman-Gallwey [mFG] score >8 or free testosterone >5 pg/mL), polycystic ovaries (≤12 cysts on 1 ovary by ultrasonography or ovarian volume >10 mL for 1 ovary), and menstrual irregularity (defined as ≤8 menstrual periods per year or cycles averaging >35 days).[47] Exclusion criteria included smoking, use of hormone-based medications within the past 3 months (hormonal contraception, ovulation inducers, antiandrogens) or insulin-sensitizing agents, presence of another endocrine disorder diagnosis, pregnancy or breastfeeding within the past 6 months, or diagnosis of a major psychiatric disorder or use of antipsychotic medication. None of the participants practiced yoga or received osteopathic manipulative treatment or acupuncture within the 6 months before the study.

Study Design, Participant Attrition, and Protocol Deviations

Participants were enrolled in the study after confirming eligibility according to inclusion and exclusion criteria. All participants were randomly assigned a unique,

sequential number to allow for random assignment to a group (no intervention [control], mindful yoga, or OMT; the latter is reported elsewhere the May issue of *The Journal of the American Osteopathic Association*). After group assignment but before the intervention period began, 10 of the 55 participants withdrew from the study, citing the following reasons: group assigned was not desired (6, most citing desire to be in the yoga group); inability to make the time commitment for attendance of the yoga group class (3); and personal reasons (1). More participants were placed in the mindful yoga intervention group, in anticipation of attrition during the intervention period (**Figure**).[48]

Protocol deviations included participant noncompliance (failure to complete initial or 3-month measurements, failure to attend group mindful yoga classes 3 times per week, and discontinuation of the intervention). No deviation from the mindful yoga methods protocol occurred. No protocol violations occurred.[49]

Data Collection

Participants used their assigned number (above) for identification during data collection. Investigators collecting participant data were blinded to participant intervention group (V.P., C.M., H.M., S.B., C.B.S.).

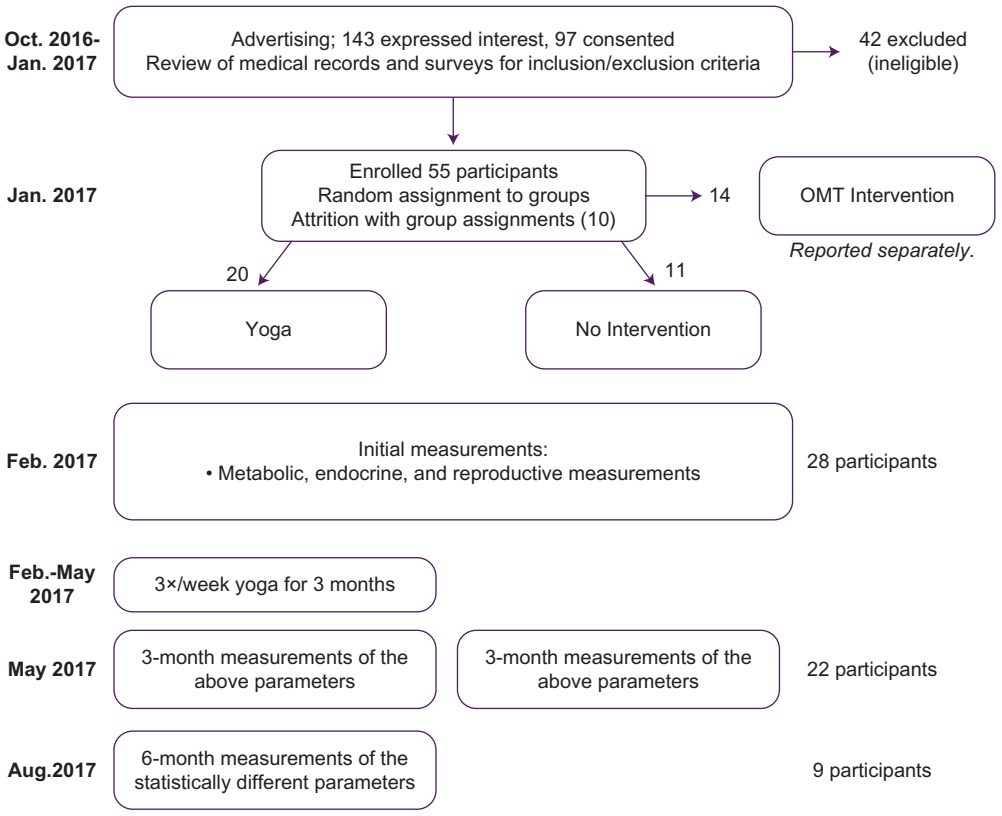

Figure.
Study design overview and timeline. Women with polycystic ovary syndrome (PCOS) were recruited from the Erie, PA, area using media advertising. After informed consent to participate in the study and release medical records, eligibility was determined according to inclusion and exclusion criteria, using Rotterdam criteria, and a questionnaire. Participants (N=13) were randomly assigned to the no intervention (control) or mindful yoga intervention group. Thirty-one participants were enrolled in the study, and 22 completed the 3-month intervention period and postintervention measurements. An additional 14 participants were included in a separate arm of the study assessing osteopathic manipulative treatment (OMT) for sympathetic tone in women with PCOS.[46]

De-identified participant data were stored in a secure database.

Clinical Assessment

In January 2017, before the intervention period, a gynecologist (C.B.S.) who was blinded to the assigned intervention group assessed participants' weight, height, BMI, blood pressure, heart rate, waist and hip circumference, hirsutism (mFG score), and acne (face, chest, and back) in a physicians' office. Patients were asked about their menstrual cycle history and pattern (<25 days, 25-35 days, or >35 days), pregnancies, and any medications that they had taken within the past 6 months. Participants had peripheral venous blood collected while fasting to measure the following: glucose, insulin, adiponectin, free testosterone, dehydroepiandrosterone (DHEA), DHEA sulfate (DHEA-S), androstenedione (A4), follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, thyroid-stimulating hormone, and human chorionic gonadotropin (hCG) levels. Patients completed secure online questionnaires for anxiety (Beck Anxiety Inventory [BAI], Pearson Global) and depression (Beck Depression Inventory-II [BDI-II], Pearson Global).

Postintervention measurements were taken in May 2017 for participants in both the control group and the mindful yoga intervention group (for those who regularly attended, defined as ≤2 classes each week), within 1 week after conclusion of the 3-month intervention. The mindful yoga intervention group participants also had their free testosterone, DHEA, and adiponectin measured again in August 2017, 3 months after conclusion of the 3-month intervention, to determine whether significant postintervention changes persisted over time.

Serum Analysis

All participants had pre- and postintervention fasting venous blood draws. All whole blood samples were collected by Associated Clinical Laboratories and analyzed by Associated Clinical Laboratories or Quest Diagnostics. Fasting blood glucose was measured by spectrophotometry; adiponectin was determined by an enzyme-linked immunosorbent assay; free testosterone was calculated from a mathematical model using sex hormone binding globulin, albumin, and total testosterone (quantified by liquid chromatography-mass spectrometry); A4 and DHEA were quantified by liquid chromatography-mass spectrometry; and serum insulin, DHEA-S, FSH, LH, prolactin, thyroid-stimulating hormone, serum hCG, and progesterone were determined by immunoassay. The homeostatic model assessment of insulin resistance (HOMA-IR) was calculated from the fasting blood glucose and serum insulin (HOMA-IR=fasting insulin x fasting glucose / 405).[50]

Assessment of Anxiety and Depression

All participants were provided unique website links to complete the BAI and BDI-II before the 3-month intervention and within 1 week of the completion of the intervention period. These surveys have documented validity, and reviews of multiple studies have indicated high reliability.[51,52] Surveys were automatically scored online. The BAI scores were reported on a range of 0 to 63, with total scores interpreted as follows: 0 to 7, minimal anxiety; 8 to 15, mild anxiety; 16 to 25, moderate anxiety; and 26 to 63, severe anxiety. The BDI-II scores were reported on a range of 0 to 63, with total scores interpreted as follows: 0 to 13, minimal depression; 14 to 19, mild depression; 20 to 28, moderate depression; and 29 to 63, severe depression.

Mindfulness Training

All women in the mindful yoga intervention group participated in a 3-hour workshop on the principles and practice of mindfulness, as this was an integral component of the mindful yoga group practice. Topics covered included the Benson breathing exercise, slow walking meditation, positive self-talk, tapping, guided imagery, and appreciative inquiry. The workshop was conducted by 2 registered nurses, each with over 40 years' experience in women's health, as well as certification in specialties involving meditation and mindfulness practice (certified hypnotist instructors and appreciative inquiry

practitioner). The workshop was also attended by the yoga instructor for the intervention group, who incorporated elements of mindfulness throughout the 3-month mindful yoga class, including breathing exercises and guided imagery.

Mindful Yoga Intervention

Women in the mindful yoga intervention group participated in a 3-times-per-week group class at the Lake Erie College of Osteopathic Medicine Wellness Center with the same experienced and certified yoga instructor and therapist from February 2017 until May 2017 (3 months). Each class was 1 hour and followed a curriculum that began with body awareness through a mental body scan, moving into a practice that included pranayama exercises (3-part yogic breath: ujjayi breath, alternate nostril breathing, and breath of fire), vinyasa flow yoga, restorative yoga asanas, and concluded with meditation that incorporated guided imagery of healing energy and mindful "I am" statements.

Participants in the control group were instructed to complete the initial and 3-month measurements and asked not to change any aspects of their daily routine (eg, no changes to diet, activity level, or therapies). Participants reported no changes to their daily routine.

Statistical Analysis

Power analysis was conducted with the Statistical Decision Tree Power Calculator (QFAB Bioinformatics) to determine the sample size needed to detect a Pearson correlation coefficient of 0.6 with a power of at least .80, with a significance level of .05 (n=8 per group). GraphPad Prism 7.03 software was used for data analysis. Mean values of initial parameters (age, BMI, waist-to-hip ratio) for women in each group were analyzed with unpaired *t* tests to ensure that the groups were comparable. Paired *t* tests (for normally distributed data) or Wilcoxon matched-pair signed rank tests (for data that were not normally distributed) were used to compare participants' preintervention measurements (0 months, January 2017) with their postintervention measurements (3 months, May 2017). Repeated-measures analysis of variance (for normally distributed data) or Friedman test (for data that were not normally distributed) with the post hoc Tukey test was used to determine whether there were any significant differences between participants' initial (January 2017), post intervention (May 2017), and subsequent no intervention for 3 months (6 months, August 2017) measurements. Significance was set at $P<.05$, with P values between .05 and .10 considered trending.

Results

During the intervention period, 2 of the 11 participants assigned to the control group did not complete initial measurements, resulting in 9 participants for data analysis. In the mindful yoga group, 2 of the 20 participants did not complete the initial measurements, 1 participant completed initial measurements but did not attend any classes or complete the 3-month measurements, 1 participant stopped attending yoga classes after 6 weeks and did not return for 3-month measurements, and 3 participants did not complete the 3-month measurements, resulting in 13 participants for data analysis.

Participant Demographics

Table 1 shows the mean values for participant demographics for the initial group assignments, with no significant difference in participant age, BMI, waist-to-hip ratio, or menstrual irregularity.

Androgen Levels

Participants who regularly attended the mindful yoga class and participants in the no intervention (control) group had their blood work and clinical assessments repeated within 2 weeks of the final class (3 months); these values were compared with their initial values (0 months) by paired comparison statistical testing to compare individual participant's pre- and postintervention values (Table 2). While no improvements were observed in androgen levels for participants in the

Table 1.
Demographics for Participants Completing Initial Measurements

Characteristic	No intervention (n=9)	Yoga intervention (n=18)	*P* value[a]
Participants at study start, n	9	18	…
Age, y, mean (SD)	31.2 (2.3)	30.9 (1.2)	.968
BMI, mean (SD) (reference range,18.5-24.9)	35.4 (3.3)	35.1 (1.5)	.948
Waist-to-hip ratio, mean (SD) (reference <0.85)	0.8003 (0.020)	0.8509 (0.014)	.056
Mean menstrual cycle length, d (reference range, 25-34 d)	>35	>35	…

[a]Statistical significance was set at $P<.05$, with P values between .05 and .10 considered trending.

Abbreviation: BMI, body mass index.

control group, there was a significant decrease in free testosterone for participants in the mindful yoga group (5.96 vs 4.24 pg/mL; $P=.0413$), and DHEA levels also trended lower (359.7 vs 316.6 ng/mL; $P=.0574$). No significant improvements were noted in either group for DHEA-S, A4, or mFG score for hirsutism. Some participants reported an improvement in their acne, as well as a shorter menstrual cycle length after the yoga intervention (data not shown).

Metabolic Parameters

Cardiometabolic parameters for participants before- and after intervention are shown in Table 2. No significant changes were noted in either group for fasting blood glucose, insulin, homeostatic model assessment of insulin resistance (HOMA-IR), BMI, or waist-to-hip ratio. However, there was a significant decrease in adiponectin in the mindful yoga group participants (10.6 vs 8.8 µg/mL; $P=.0045$).

Anxiety and Depression

Scores for anxiety (14.4 vs 11.3; $P=.0365$) and depression (16.0 vs 7.25; $P<.001$) significantly improved after the 3-month mindful yoga intervention (Table 2). In the control group, scores for depression also trended lower (18.0 vs 12.0; $P=.06$).

Free Testosterone

To determine whether improvements in serum free testosterone or DHEA level or the change in adiponectin would persist without continued participation in mindful yoga, we reassessed these parameters for women in the mindful yoga group who did not continue practicing yoga for 3 months after the completion of the intervention (6-month follow-up). Participants who reported that they practiced yoga during this postintervention period were not included in this 6-month follow-up. For the participants who completed this final assessment (9 of the 13 who completed the 3-month mindful yoga intervention), we found that free testosterone levels remained similar to the improved levels observed after the 3-month mindful yoga intervention (Table 3), with significant improvement after yoga intervention (7.1 vs 4.3 vs 4.9; $P=.0201$), although the difference between the 0 months and 6 months values trended toward but did not reach significance ($P=.06$). No significant difference was found in DHEA levels, although the median value did remain lower compared with the initial value for this group of 9 participants (277 vs 205 vs 216). The mean adiponectin level did increase compared with the postintervention value, but did not reach the level initially observed in this group of 9 participants (10.3 vs 8.2 vs 9.1; $P=.0508$).

Table 2.
Participant Parameters Before and After the 3-Month Intervention (N=13)[a,b]

Test	Control (0 mo) (n=9)	Control (3 mo) (n=9)	*P* value[b]	Yoga (0 mo) (n=13)	Yoga (3 mo) (n=13)	*P* Value[b]
Free T, pg/mL, (reference range, 0.2-0.5 pg/mL)	7.39 (1.61)	7.36 (1.29)	.967	5.96 (1.2)	4.24 (0.6)	.0413
DHEA ng/dL (reference range, 102-1185)	382.7 (56-713)	368.3 (65-541)	.742	359.7 (109-892)	316.6 (114-914)	.0574
DHEAS (μg/dL) (reference range, 45-320)	197.4 (30.7)	224.4 (34.1)	.0038	177.2 (22.5)	167.7 (19.1)	.501
A4 (ng/dL) (reference range, 30-250)	209.2 (56.0)	246.2 (45.9)	.147	175.8 (22.1)	158.3 (16.3)	.224
mFG score (>6)	4.0 (0.6)	4 (0.6)	.999	3.3 (0.6)	3.3 (0.6)	.950
Fasting BG, mg/dL, (reference range, 65-99)	89.2 (4.5)	92.1 (2.7)	.403	87.9 (1.9)	86.3 (1.9)	.387
Fasting insulin, μIU/mL (reference range, <23)	14.8 (3.9)	12.7 (2.7)	.328	mean (range), 11.0 (2-33)	mean (range), 10.0 (2-47)	.824
HOMA-IR (reference range, 0.5-1.4)	3.48 (1.02)	3.00 (0.66)	.382	mean (range), 2.3 (0.4-0.7)	mean (range), 2 (0.4-11.3)	.693
Adiponectin, μg/mL, (reference range, 5-28)	8.1 (1.3)	9.0 (1.7)	.252	10.6 (1.1)	8.8 (1.2)	.0045
BMI (reference range, 18.5-24.9)	35.4 (3.3)	35.6 (3.3)	.403	35.0 (1.9)	34.7 (2.0)	.375
Waist-to-hip ratio	0.8003 (0.020)	0.8114 (0.020)	.344	0.8449 (0.017)	0.8319 (0.015)	.319
BAI score	12.0 (2.9)	10.9 (2.2)	.633	14.4 (3.0)	11.3 (2.1)	.0365
BDI-II score	18.0 (2.1)	12.0 (1.7)	.06	16.0 (2.8)	7.25 (2.1)	<.0001

[a]Data are given as mean (SD) unless otherwise indicated.
[b]*P* value was used to evaluate endocrine, metabolic, and psychologic differences between the group that completed regular yoga intervention and the group that did not (control). Statistical significance was set at $P<.05$, with *P* values between .05 and .10 considered trending.

Abbreviations: A4, androstenedione; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory BG, blood glucose; BMI, body mass index; HOMA-IR, homeostatic model assessment for insulin resistance; T, testosterone; mFG, modified Ferriman-Gallwey.

Discussion

We found that thrice-weekly yoga practice significantly improved free testosterone levels, a major criterion used for the diagnosis of PCOS, with DHEA levels trending lower as well. Furthermore, these benefits were observed without daily yoga practice, but rather with a more feasible 3-times-per-week practice. Scores for anxiety and depression were also improved with this intervention.

Table 3.
Persistent Improvement in Serum Testosterone Level After Yoga Intervention

Test	Yoga (0 mo) (n=9)	Yoga (3 mo) (n=9)	Yoga (6 mo) (n=9)	*P* value*
Free T, pg/mL (reference range, 0.2-5.0 pg/mL)	7.1 (4.4)	4.3 (2.2)	4.9 (2.6)	.0201
DHEA, ng/dL (reference range, 102-1185 ng/dL)	277 (109-892)	205 (114-914)	216 (113-481)	.569
Adiponectin, μg/mL, mean (SD) (reference range, 5-28 mg/mL)	10.3 (4.2)	8.2 (3.9)	9.1 (4.9)	.0508

*Statistical significance was set at $P<.05$, with P values between .05 and .10 considered trending.

Abbreviations: BMI, body mass index; DHEA, dehydroepiandrosterone; T, testosterone.

Mindful Yoga as Therapy for PCOS

Women with PCOS have expressed a desire for more natural and holistic therapies to manage their symptoms.[26,27] Unlike some other forms of exercise, yoga is very accessible to a variety of individuals in that it can be practiced by people of all ages and body types, does not require a specific fitness or skill level, does not require equipment, and may be performed in a studio with an instructor or at home. Yoga practice has become increasingly popular as a complementary health approach,[53] and it has been reported to be useful in patients with a variety of conditions.[36-40] In line with osteopathic philosophy, yoga practice embraces the relationship between mind, body, and spirit, and produces measurable physiologic effects. Because of its accessibility and success in helping with other chronic disorders as well as previous reports demonstrating its utility in adolescents with PCOS,[44,45] mindful yoga has potential as a complementary or alternative therapy option for women with PCOS. Our findings support the effectiveness of this type of therapy for this population.

Mindful Yoga in Women With Established PCOS

The women in our study had an mean age of 31 years (range, 23-42 years), indicating that their PCOS diagnosis was established and their health potentially affected by the disorder for a decade or more.[19] Women in this study group exhibited aspects of reproductive dysfunction, such as menstrual cycles longer than 5 days and difficulty conceiving, as well as metabolic dysfunction, such as elevated HOMA-IR (an indicator of insulin resistance), BMI, and waist-to-hip ratio. Despite having PCOS for many years and experiencing some of the associated reproductive and metabolic dysfunction, our results indicate that women with established PCOS and metabolic dysfunction can benefit from regular mindful yoga practice, with potential improvement in androgen profile. That these results can be achieved with a feasible thrice-weekly practice rather than daily practice is an additional benefit.

A4 and DHEA Levels

Diagnosis of PCOS often includes hyperandrogenism, which may be clinical or biochemical. Biochemical hyperandrogenism is usually assessed by serum free testosterone levels, although the weak androgens DHEA and A4 may also be elevated in women with PCOS.[54] Androstenedione has recently been reported to correlate with hirsutism and risk for metabolic disease in women with PCOS, sometimes even in the presence of normal testosterone levels.[55] Furthermore, A4 may be associated with a more severe PCOS

phenotype, including elevated LH, LH:FSH ratio, testosterone, DHEA-S, and free androgen index, as well as increased ovarian volume and greater mean number of follicles in hyperandrogenic women with PCOS.[56] The average initial A4 concentration in our study participants was at the high end but still within normal range, with some participants exhibiting normal A4 levels, which may explain why the decrease did not reach significance with our small sample size. Similarly, the DHEA levels in our study participants were within normal limits, with a trending decrease after intervention.

Cardiometabolic Measurements

While the 3-month mindful yoga intervention improved the androgen profile of women with PCOS, it did not result in a significant improvement in the metabolic parameters assessed in this study. Similar to the findings reported by Nidhi et al,[44] there was no significant change in BMI or WHR in women completing the 3-month intervention. However, in contrast with their findings, we did not find improvements in fasting insulin, glucose, or HOMA-IR. This may be because their study employed daily yoga for 1 hour for 12 weeks, which is a more rigorous program than our thrice-weekly class. The difference may also be attributed to the participant demographics; our study included women with a history of PCOS and measurements reflective of chronic metabolic dysfunction, including an average BMI of 35 and a higher HOMA-IR score, whereas Nidhi et al[44] included female adolescents with an average BMI of 20.3 and a lower HOMA-IR (near 3.0 in the current study vs 1.7 in their population). With a population of women who have had PCOS for a decade or longer, the effects of the underlying pathophysiology and the associated metabolic dysfunction may be more pervasive, which could explain the lack of significant improvement in metabolic parameters for the women in our study. By contrast, a population of young, lean women with PCOS might be more pliable with respect to their metabolic parameters, as observed in the study by Nidhi et al.[44] If this is the case, it underscores the importance of implementing this type of therapy as soon as possible after diagnosis in order to achieve maximum benefits, both in terms of endocrine as well as metabolic health.

Adiponectin Levels

Surprisingly, there was a significant decrease in adiponectin levels with completion of the mindful yoga intervention. Adiponectin is an adipose-derived hormone that is associated with insulin sensitivity and anti-inflammatory effects.[57] Most reports indicated that higher adiponectin levels were beneficial, whereas lower adiponectin levels have been associated with insulin resistance, type 2 diabetes, metabolic syndrome, and PCOS.[57-60] In the current study, it is unclear why adiponectin levels would decrease after the intervention. One possibility is that there was a change in the ratio of high molecular weight adiponectin to total adiponectin. This ratio is reported to better predict insulin resistance, as a decrease correlates with greater insulin resistance.[61] The immunoassay used in our study was not able to distinguish between the different molecular weight forms, but it is possible that there was a change in the ratio of high molecular weight to total adiponectin despite lower total adiponectin. Another possibility is that there could have been an increase in adiponectin receptor expression in these women, potentially improving responsiveness to adiponectin but resulting in a decrease in circulating adiponectin levels. Further investigation in a larger study population could help to determine whether lower adiponectin levels are consistently found in association with yoga practice and help to determine the mechanism underlying the decrease.

Psychological Improvements

Women completing the mindful yoga intervention experienced significant improvements in both anxiety and depression. This may be partially attributed to seasonal changes, as a trend toward lower depression scores was also seen in the control group. It is worth noting that the women in the mindful yoga intervention group reported a sense of community by participating

in this study together, which itself could result in improved stress levels and potentially provide therapeutic benefit. In addition, incorporation of mindfulness practice in everyday life may have also contributed to the observed therapeutic benefit in this group, particularly with respect to anxiety and depression.

Limitations

One limitation of this study was the small sample size for each group, which could affect the statistical significance of our findings. The participants in this study were of varying BMIs and ages; in addition to larger randomized controlled studies, future studies could also focus on determining whether this type of yoga practice has a greater impact on women in a specific age group or within a specific BMI range. It is noteworthy that the intervention group used mindfulness as part of their group yoga practice, and they may have incorporated aspects of the mindfulness practice in their daily lives; beyond the yoga practice itself, this factor also may have contributed to the therapeutic benefits observed in this study. Despite these limitations, the results suggest that mindful yoga practice can provide therapeutic benefit to women with PCOS. Furthermore, the improvements in androgen levels are a promising finding, as these hormones may contribute to the pathogenesis of the disorder itself.

Conclusion

We found that thrice-weekly mindful yoga practice improved serum androgen levels, a hallmark feature of PCOS, in women with PCOS. This improvement was observed in the absence of weight loss, and may persist even if there is a lapse in yoga practice. These findings suggest that regular mindful yoga can be a useful complementary therapeutic option, in conjunction with improved diet, to lead to better health in women with PCOS.

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Author Contributions

All authors provided substantial contributions to the conception and design, acquisition of data, or analysis and interpretation of the data; all authors drafted or revised the article critically for important intellectual content; all authors gave final approval of the version of the article to be published; and all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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