ORIGINAL ARTICLE: MENTAL HEALTH

Cognitive-behavioral therapy improves weight loss and quality of life in women with polycystic ovary syndrome: a pilot randomized clinical trial

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Objective: To compare the effects of cognitive-behavioral therapy (CBT) and lifestyle modification (LS) versus LS alone on weight, depressive and anxiety symptoms, and stress response in women with polycystic ovary syndrome (PCOS), overweight/obesity, and depressive symptoms.
Design: A 16-week pilot randomized clinical trial.
Setting: Tertiary-care PCOS center.
Patient(s): Overweight/obese women with PCOS and depressive symptoms.
Intervention(s): Weekly CBT (n = 7) or contact only/no therapy (n = 8) for 8 weeks. Both groups received weekly LS for 16 weeks.
Main Outcome Measure(s): Changes in weight, depression (Center for Epidemiologic Studies Depression Scale [CES-D]), anxiety (State-Trait Anxiety Inventory [STAI]), quality of life (Polycystic Ovary Syndrome Health-Related Quality of Life Questionnaire [PCOSQ]), laboratory tests, and response to a Trier Social Stress Test (TSST).
Result(s): The CBT+LS group lost more weekly weight (−0.35 kg/wk vs. −0.16 kg/wk) compared with the LS group. Overall, the CBT+LS group lost 3.2 kg versus 1.8 kg for the LS group. The CBT+LS group had greater improvement in PCOSQ at 8 weeks (+3.7 vs. +1.2 points). In the overall cohort, STAI and CES-D decreased by −0.27 points per week and −0.31 points/wk, respectfully, and total and free T decreased at week 8. Heart rate response to TSST was lower at 15 minutes after stressor in the CBT+LS group.
Conclusion(s): Weekly CBT+LS for 8 weeks compared with LS alone resulted in significant weight loss and improved quality of life in overweight/obese women with PCOS and depressive symptoms. These interventions were associated with a decreased autonomic response to a laboratory stressor, suggesting a potential link between CBT, weight loss, and modulation of the stress response.
Clinical Trial Registration Number: NCT01899001. (Fertil Steril® 2018;■:■–■. ©2018 by American Society for Reproductive Medicine.)
Key Words: PCOS, weight loss, depression, CBT, nutrition

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Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting reproductive-age women worldwide (1). Women with PCOS have higher rates of obesity and an increased prevalence of cardiovascular disease (CVD) risk factors, such as insulin resistance, dyslipidemia, and diabetes (2, 3). Given that women with PCOS often present to health care providers early in their reproductive

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years, there is an opportunity to modify these risk factors. Lifestyle modifications (LS) are recommended as first-line treatment in women with PCOS (4, 5), with a recent study showing that lifestyle interventions associated with weight loss can also improve pregnancy rates (6).

Women with PCOS also have a high prevalence of depression and anxiety. A recent meta-analysis showed median prevalences of depressive symptoms of 36.6% (interquartile range [IQR] 22.3%–50.0%) and anxiety symptoms of 41.9% (IQR 13.6%–52.0%) in women with PCOS. Compared with women without PCOS, these numbers represented a more than threefold increase in odds of depressive symptoms (odds ratio [OR] 3.78–95% CI 3.03–4.72; 18 studies) and a more than fivefold increase in odds of anxiety symptoms (OR 5.62–95% CI 3.22–9.80; 9 studies) (7). Other studies have also shown that women with PCOS have a decreased quality of life (QoL) compared with control women (8). Depression and anxiety are independently associated with CVD (9), as well as CVD risk factors, such as obesity (10), insulin resistance (11), and diabetes (12). In addition, obesity and psychiatric disorders are both associated with hypothalamic-pituitary-adrenal (HPA) axis disturbances and dysregulated inflammatory pathways (13). Studies on the use of LS in women with PCOS have not addressed comorbid depression or anxiety, so we do not know the success of these interventions in women with PCOS who also have depression or anxiety.

A small study in adolescents with PCOS showed improvement in both weight and depression scores after cognitive-behavioral therapy (CBT); however, there was no control group (14). CBT is a psychotherapy that focuses on changing dysfunctional thoughts that lead to negative mood states and maladaptive behaviors (15). CBT is recommended by the American Psychological Association and the American College of Physicians as a first-line treatment for depression (16, 17), and a recent meta-analysis showed moderate to large treatment effects for both major depressive disorder (MDD) and generalized anxiety disorder (18). CBT techniques have also been successful in achieving weight loss in various populations (19–22), although very few studies have included women with concurrent obesity and depression (14, 23, 24). Also, CBT has not been evaluated in adult women with PCOS to improve weight loss or depressive and anxiety symptoms. Therefore, our overall aim was to compare the feasibility and preliminary efficacy of an intervention which combined CBT and LS versus LS alone in the concurrent treatment of overweight/obesity and depressive symptoms in women with PCOS. Our primary outcome was change in weight. Secondary outcomes were changes in depression, anxiety, and quality of life scores. Tertiary outcomes included changes in metabolic risk, inflammation, perceived stress, and autonomic and endocrine response to a laboratory stressor.

MATERIALS AND METHODS

Study Design

We conducted an open-label 16-week randomized clinical pilot study at a single tertiary care center from August 2013 to October 2015 to investigate the use of CBT to treat symptoms of depression and improve cardiovascular risk factors in overweight/obese women with PCOS. The study protocol was approved by the Institutional Review Board at the University of Pennsylvania. The trial was registered at clinicaltrials.gov (NCT01899001).

Participants

Women were eligible if they met National Institutes of Health criteria for PCOS (25), had a body mass index (BMI) of 27–50 kg/m^2 and had a positive screen for depression symptoms, defined as a Center for Epidemiologic Studies Depression Scale (CES-D) score $\geq$14 (26). Subjects with depression and anxiety disorders that were currently being treated were included if their medication had not been changed for $\geq$2 months and their CES-D score was still $\geq$14. Patients with an active eating disorder, currently participating in a weight loss program, or receiving pharmacotherapy for dyslipidemia, hypertension, or diabetes/impaired glucose tolerance, or on hormonal therapy were excluded. The washout period for oral contraceptive pills or metformin was 4 weeks. Given the association between nicotine and cortisol levels (27, 28), which we measured during the Trier Social Stress Test (TSST), women who smoked on average five or more cigarettes per day were excluded. Pregnant women and women who were planning pregnancy within the 16-week period were also excluded.

Lifestyle Modification

All women received in-person individual 30-minute weekly nutrition/exercise counseling by a trained counselor for 16 visits at Penn's Center for Weight and Eating Disorders. Subjects were recommended a self-selected diet of 1,500–1,800 kcal/d of conventional foods based on the Food Guide Pyramid and an exercise goal starting at 50 minutes per week and increasing to 175 minutes per week. Counseling included standard weight loss skills including self-monitoring, problem-solving, enlisting social support, and overcoming negative thoughts. Subjects kept daily food intake and exercise logs which were reviewed at each counseling session. Previous studies have shown significant weight loss after 16 weeks of LS in women with PCOS (6).

Cognitive-Behavioral Therapy

Participants randomized to the CBT group received weekly 30-minute sessions with a CBT-trained clinical psychologist (L.H. or S.K.) from the Penn Center for Women's Behavioral Wellness for the first eight visits. Sessions included behavioral components, such as activity scheduling and homework, and cognitive skills, such as identifying automatic thoughts and cognitive distortions (15, 17). Sessions were highly standardized and followed The Brief Cognitive Therapy Manual (Supplemental Table 1 available online at www.fertstert.org) (29). This 8-week time frame of brief CBT has been successful in other randomized controlled trials (22). To control for contact time during CBT, the subjects randomized to the LS-only arm met with a team member at the