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Evaluation of a functional medicine approach to treating fatigue, stress, and digestive issues in women

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ABSTRACT

Fatigue, stress, and digestive disorders are common among adults, especially women. We conducted a 28-week pilot study to assess the efficacy of a functional medicine approach to improving stress, energy, fatigue, digestive issues, and quality of life in middle-aged women. Findings showed significant improvements in many stress, fatigue, and quality-of-life measures. The treatment program increased mean salivary dehydroepiandrosterone levels and the cortisol-dehydroepiandrosterone ratio. Stool sample analyses suggested that these treatments reduced *Helicobacter pylori* infections. This study suggests that functional medicine may be an effective approach to managing stress and gastrointestinal symptoms.

1. Introduction

Fatigue and stress are common in the United States, especially among women [1]. Digestive disorders are also commonly reported among women, and stress is a contributor [2]. One type of treatment approach, functional medicine, may be useful for addressing these common conditions.

Functional medicine is a systems approach to chronic illness which addresses the whole person rather than an isolated set of symptoms [3]. The functional medicine model is focused on restoring optimal functioning of 3 body systems: hormonal, digestive, and detoxification. Restoring these 3 body systems has positive effects on stress, energy, fatigue, digestive issues, and quality of life. Laboratory assessments in functional medicine include measurement of salivary cortisol and dehydroepiandrosterone (DHEA) to assess the hypothalamus-pituitary-adrenal (HPA) axis. "Dysregulation of the HPA axis resulting in hypercortisolism has been proposed as a mechanism by which depression may evolve from chronic stress" [4]. Functional medicine testing may also include stool analysis to evaluate the possible presence of pathogenic organisms; stool analysis to determine the proper functioning of the gastrointestinal tract may be used but is considered unconventional [5].

This functional medicine study focused on the hormonal and gastrointestinal systems. The primary purpose of this 28-week pilot study was to assess the efficacy of a specific functional medicine approach for improving stress, energy, fatigue, digestive issues, and quality of life in middle-aged women exposed to high-stress work environments. The approach included lifestyle factors coupled with specific nutritional supplement protocols to treat HPA axis dysregulation and gastrointestinal infections. Changes in gastrointestinal health over the course of the program, in addition to the participants' satisfaction with the functional medicine program, were also evaluated.

2. Methods

2.1. Participants

The study protocol was approved by MaGil IRB, Inc, review board. Participants screened included women aged 30–55 years living in Northern California. Participants were recruited from Internet advertising on social networks and flyers in the local area; they were enrolled in August 2014, and the study was conducted from September 2014 through April 2015. All participants self-reported that they experienced stress from their work and/or home lives. Inclusion criteria were providing written consent to

Abbreviations: DHEA, dehydroepiandrosterone; HPA, hypothalamus-pituitary-adrenal; POMS, profiles of mood states; SF-36, short Form Health Survey; VAS, visual analog scale.

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participate, allowing the use of their data for the study and for contact by the study personnel, and having access to a home computer. Exclusion criteria were: a history of cancer; current use of thyroid medication; a history of thyroid or pituitary disorder or adrenal disorder other than adrenal fatigue; diabetes mellitus; a diagnosis of hypertension; pregnant or breastfeeding; childbearing potential but not using acceptable methods of birth control (eg, spermicide with condom, diaphragm, or cervical cap; intrauterine device; hormonal contraception; vasectomy; or abstinence—Plan B or rhythm methods were not considered reliable methods); current smokers; current participation in another clinical trial; active drug or alcohol abuse or dependence; and other conditions that, in the opinion of the investigator, would interfere with adherence to study requirements.

Upon enrollment, demographic data were collected, a medical history was obtained, and a physical examination was performed by the functional medicine provider. A negative pregnancy test was required before enrollment. Vital signs and anthropometrics were obtained at enrollment and at the end of the study. Responsibilities regarding study guidelines and requirements were outlined, and informed consent was obtained.

2.2. Clinical measurements

2.2.1. Assessment of mood, quality of life, fatigue, stress, and satisfaction

The Profiles of Mood States (POMS) questionnaire, Visual Analog Scale (VAS), Short Form Health Survey (SF-36) quality of life questionnaire, and the global satisfaction questionnaire were administered at enrollment, week 4, week 8, and the end of the study (week 28).

POMS is a widely used questionnaire to assess mood states [6]. All study participants completed the self-administered POMS questionnaire (Educational and Industrial Testing Service). The questionnaire measures 6 mood subscales that include tension-anxiety, depression, anger-hostility, vigor, fatigue, and confusion. Lower scores in the tension-anxiety, depression, anger-hostility, fatigue, and confusion subscales indicate positive mood, whereas higher vigor scores reflect a positive mood.

The VAS is commonly used to measure and compare change in various parameters within individuals [7]. This study used a VAS for fatigue and for stress. The SF-36 is a multipurpose health survey that measures the generic health concepts of physical functioning, role functioning (physical and emotional), vitality, emotional well-being, social functioning, pain, and general health [8].

At the end of the study (28 weeks), patients were asked to rate their experience with a global product satisfaction scale. Questions addressed satisfaction with the overall performance of the study; likelihood of recommending this methodology to family or friends; whether the protocol helped improve stress, energy, fatigue, digestive level, and quality of life; whether the protocol allowed them to feel more energetic; and whether they tolerated the protocol well.

Salivary cortisol and DHEA were measured at weeks 0 and 24. A salivary test kit from Biohealth Laboratory was collected in the morning, noon, evening, and before bed. DHEA was a 1-time salivary measurement.

Fecal specimens were examined for ova and parasites using a commercial, 4-day home stool kit from Biohealth Laboratory. The ova and parasites measured in the stool analysis included protozoa, flatworms, roundworms, *Cryptosporidium parvum*, *Giardia lamblia* antigens, bacteria, fungi (including yeasts), occult blood, *Clostridium difficile* colitis toxins A and B, and the *Helicobacter pylori* antigen measured via stool antigen fecal smear.

2.3. Lifestyle and nutritional counseling

Weekly telephone calls were made to eligible participants during the 4-week run-in period for lifestyle and nutritional counseling. At baseline, a 1-h in-person coaching session with a functional medicine practitioner, including review of saliva and stool sample test results, was performed, and a participant-specific supplementation protocol was issued. Compliance and counseling telephone calls were made at weeks 6, 10, 12, 16, 20, and 24 post screening. In-clinic visits occurred at weeks 8 and 28 post screening. Online group sessions with the nutritionist occurred once per month for nutrition coaching and follow-up with diet compliance.

2.4. Study treatment protocol

Participant-specific supplementation protocols were issued after the in-person coaching session. The personalized program involved a combination of adrenal and digestive cleanse protocols. The protocols are detailed in the Appendix.

Compliance with the supplemental protocol was measured using a supplement diary. Participants were required to complete a daily dosing diary to determine if they followed their designated protocol. In addition, participants were required to return their empty supplement bottles at the end of the study as an additional measure of compliance.

2.5. Statistical analysis

We expected to recruit 25 participants and anticipated a small attrition rate, allowing the study to reach an anticipated minimum of 20 participants. Because this was a pilot study, there was no formal sample size calculation. All variables under investigation were summarized by time point. End points measured in interval/ratio scales and their changes from baseline were presented as mean (SD) or median (range). All missing values of efficacy variables were imputed with the most recent previously available value (last value carried forward imputation). All interval/ratio scale end points were tested for normality and log normality. Log-normally distributed variables were analyzed in the logarithmic domain. Variables that were intractably non-normal were analyzed by an appropriate nonparametric test. The changes from baseline of interval/ratio-scaled variables were tested using the paired Student *t*-test. In cases of intractable non-normality, the Wilcoxon signed-rank test was used. $P < 0.05$ was considered statistically significant. All evaluations were carried out using the software package R, version 3.03.

3. Results

3.1. Demographics, screening characteristics, and compliance

A total of 25 women were screened; 24 participants were enrolled in the study, and 21 completed the trial. Most participants had demanding professional schedules that included running their own businesses, managing large companies, and frequent travel. A modified per-protocol population was used for the analysis of efficacy end points, which consisted of all participants receiving a functional medicine treatment and completing at least 1 postdose visit, regardless of compliance, protocol deviations, or withdrawal (Fig. 1).

The mean (SD) age of enrolled participants was 44.9 [5] years (Table 1). No screening characteristics were outside clinically acceptable ranges. The average compliance exhibited by participants was more than 80% for the adrenal and gastrointestinal protocols. However, individual compliance varied, with 1 participant having a