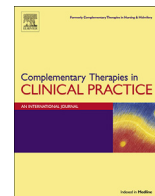




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Letter to the editor

Correspondence regarding Cutshall, Bergstrom, Kalish's "Evaluation of a functional medicine approach to treating fatigue, stress, and digestive issues in women" in *Complement Ther Clin Pract* 2016 May

Keywords:

Nutrition
 Functional medicine
 Fatigue
 Stress
 Dehydroepiandrosterone
 Pregnenolone

Dear Editor,

In the May 2016 issue of this Journal, authors Cutshall, Bergstrom, Kalish [1] report 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" and claim "significant improvements in many stress, fatigue, and quality-of-life measures." To improve future studies, areas for improvement are described in the following paragraphs.

1. Description of treatments

The authors state that treatments were "personalized" but provide little data on how or why the treatment was allocated other than to divide patients into two groups for the "adrenal protocols" which are faintly outlined in the footnotes; no dosages are provided as all of the product formulations appear to be proprietary. Table 1 which outlines the "adrenal protocols" shows the treatments to be remarkably similar between the high and low salivary cortisol groups. The authors administered "DHEA drops" and "pregnenolone drops" but the varying dosages of the hormones, administered three times each per day, are not provided. Authors need to provide the actual dosages of all treatments, including hormones. When new and innovative treatments are used, the scientific rationale and clinical justification should be provided.

2. Use of hormonal therapy

With regard to the salivary testing used in this study, the authors need to have described the laboratory methodology. The authors state, "A **significant increase was seen in mean salivary DHEA concentration**, with an initial value of 4.7 (4.8) ng/mL and an end-of-study value of 5.7 (15.4) ng/mL. However, **the median DHEA concentration decreased** from baseline to end of study

(3.1–2.2 ng/mL), which suggests that the mean value may not accurately reflect the effect of the protocol on DHEA levels. In addition, 1 participant had a **36-fold increase in salivary DHEA level**, which affected the mean." Thus, the same marker was found to increase, decrease, and change unreliably. Table 5 of the results shows that Cortisol/DHEA ratio started at 5.2 and resulted at 12 at the end of the study. Consistently throughout the medical literature, respectively higher levels of cortisol and lower levels of DHEA are causatively associated with insulin resistance, intra-abdominal obesity, hippocampal atrophy, and bone loss [2] [3]; to the contrary of the bulk of the peer-reviewed literature, these authors present these results as beneficial changes. The "DHEA drops" and "pregnenolone drops" are not described either in dosage or formulation. Pregnenolone is a neurosteroid with clinical benefits including amelioration of fatigue, psychosis, anxiety, and depression [4] [5] DHEA is well-known to alleviate depression, inflammation, fatigue and to improve quality-of-life measures [6]. DHEA administration raises androgens and estrogens [7], both of which are important in the promotion of various cancers including breast cancer. [8] [9] The authors might have described appropriate serologic and clinical follow-up, risk considerations, as well as limits to the duration of treatment.

3. Accurate description of functional medicine

The authors define functional medicine as "The functional medicine model is focused on restoring optimal functioning of 3 body systems: hormonal, digestive, and detoxification." The authors' sweeping statement "Restoring these 3 body systems has positive effects on stress, energy, fatigue, digestive issues, and quality of life" has no citations. The definition of functional medicine provided by these authors is discordant with more authoritative descriptions published by the Institute for Functional Medicine [10] and International College of Human Nutrition and Functional Medicine [11]. The authors use the terminology "adrenal and digestive cleanse protocols" without definition, justification, or citation. In scientific publications, unique statements require substantiation and citation.

4. Controlling for external influences

The authors describe the dates of the study as "September 2014 through April 2015" but did not control for vitamin D levels and sunlight exposure which are known to affect mood and cognition. [12] [13] The severity of depression, pain, and "functional disorders" has been reported to vary seasonally with exacerbations in

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fall and winter and alleviation in spring and summer. [14] [15] The “lifestyle and nutritional counseling” included a 1-h in-person coaching session at the start of the study, followed by various telephone contacts and “online group sessions” including “nutrition coaching and follow-up with diet compliance.” This obviously results in the possibility that the patients felt better simply as a result of social contact and conversation with interested educated health professionals and other suffering patients rather than as a result of any biomedical intervention.

5. Disclosure of commercial interests

The authors deny conflict of interest and that “The study sponsors had no involvement in the study design; in the collection, analysis, and interpretation of data; in the writing of the manuscript; or in the decision to submit the manuscript for publication.” However, the authors do not disclose the identity of the sponsors. One of the authors (Kalish) is a consultant/speaker for a large distributor of nutritional supplements [16] and also a consultant/speaker/endorser of the laboratory used in this study [17]; these relationships are not disclosed in the article. According to the authors' interview [18] and press release [19] regarding their publication, they provide “training in functional medicine” and seminars related to the treatments used in this study.

6. Fecal microbiologic testing; antimicrobial treatments

The authors fail to detail the laboratory methodology for the microbiologic testing and to describe the relevance of such testing and the results. Per the footnote describing the mastic product, the authors do not clearly describe the identity nor the ingredients of this treatment.

While the functional medicine approach to healthcare is science-based, eclectic, and effective [20], research that uses the name “functional medicine” should accurately reflect its definitions and practice. Such research, as with all research, should employ reproducible laboratory methodology, should accurately describe all aspects of treatments, must properly discuss risks of treatments, should use standard testing methods to assess response to treatment as well as safety and disclose commercial interests.

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Alex Vasquez DC ND DO FACN is Director of the International College of Human Nutrition and Functional Medicine (ICHNFM.ORG) in the United States and Europe. Dr Vasquez lectures and consults internationally and has published more than 100 professional articles and letters and more than 12 books, most recently including *Inflammation Mastery Fourth Edition*. Dr Vasquez has served as a consultant researcher and lecturer for Biotics Research Corporation.

Alex Vasquez, DC ND DO FACN
Carrer del Bisbe Laguarda 5, 08001, Barcelona, Spain
E-mail address: avasquez@ichnfm.org

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