Assessment of and Treatment Applied to Food Addiction to Encourage Self-Management of Obesity in a Rural Healthy Behaviors Clinic

NCT03431831

31 Mar 2017

Study Protocol and Statistical Analysis Plan

Summary

The purpose of this pilot study is to assess obese clients for two phenotypes, those testing positive and those testing negative for Food Addiction (FA) (Yale Food Addiction Scale, YFAS) and determining the efficacy of four treatments: usual care (IC, dietary and physical activity instruction), individual motivational interviewing alone (MI), individual MI with pharmacotherapy (MI+P) for improving outcome measures within each phenotype, and pharmacological therapy (P).

Background/significance

The ongoing epidemic of obesity is of great concern, especially among rural Americans, where the rate of obesity is greater than that of Americans living in urban areas. The costs related to obesity and its comorbidities continues to rise and includes the psychological implications of obesity. Scotts Bluff has an overweight/obesity rate of 71% according to the 2014 Scotts Bluff County Health Dept Community Health Assessment. Recently it has been suggested that addiction-like tendencies toward foods, (especially highly processed foods that are high in fat and sugars) (HPFS) is contributing to the epidemic (Schulte 2015, Flint 2014, Iozzo, 2012; Pursey, 2014). In order to assess addictive-like eating behavior, the Yale Food Addiction Scale (YFAS) has been developed in relation to DSM V Substance-Related and Addictive Disorders (SRAD) symptom criterion or clinical impairment/distress. The YFAS has been tested to be psychometrically sound. One study using the YFAS found that nearly 20% of obese persons tested positive for food addiction (FA), yet few if any interventions to address obesity have specifically targeted individuals who test positive for FA.

Empirical evidence is growing for the idea that food addiction may be a contributor to obesity and eating-related problems (Gearhardt, Corbin, & Brownell, 2009a,b). This hypothesis proposes that highly processed foods, high in fat and sugar (HPFS) (e.g., pizza, chocolate, chips), may be capable of triggering an addictive response in individuals with vulnerable characteristics (e.g., impulsivity). Early evidence in animal and human studies suggests that HPFS foods may activate reward related neural circuitry in a similar manner as drugs of abuse. Additionally, behavioral indicators of substance-use disorders, such as loss of control and use despite negative consequences, have been observed in response to HPFS foods. Shared mechanisms (e.g., reward dysfunction, emotion regulation difficulties) and genetic profiles also appear to contribute to both food addiction and substance-use disorders. Thus, existing evidence demonstrates biological and behavioral parallels between individuals with food addiction and substance-use disorders and suggests that HPFS foods may be most likely to have an addictive potential for some individuals.

The Yale Food Addiction Scale (YFAS) is currently the only validated measure to assess symptoms of food addiction. The current version is the YFAS 2.0 is a 35-item self-report questionnaire that applies the DSM-5 diagnostic criteria for substance-use disorders to consumption of HPFS foods. The YFAS 2.0 provides two scoring options: a symptom count (a sum of the eleven diagnostic criteria) and a diagnostic threshold that reflects the criteria for a substance dependence diagnosis (the presence of two or more symptoms plus clinically significant impairment or distress).

The YFAS has good internal consistency ranging from á = .76.92 and demonstrates convergent validity with measures of eating pathology (e.g., emotional eating, food craving) and incremental validity in predicting binge eating frequency above and beyond existing measures. The YFAS has been used to assess food addiction in both community and treatment-seeking samples. Reducing highly processed foods, especially those high in fat and sugar Highly processed foods that are high in fat and sugar (HPFS) are typically low-nutrient simple carbohydrates (LNSC). There is growing recognition that the nature of carbohydrates consumed is an important dietary consideration. A key to healthy eating is reducing consumption of LNSC(e.g., sugars and starches) in favor of complex carbohydrates [e.g., fruits, vegetables (except potatoes), legumes, and whole grains] and minimally processed proteins (nuts, fresh lean meats).

Low-nutrient simple carbohydrates: LNSC are composed of single chain carbon atoms and are rapidly digested and absorbed, resulting in rapid peaks in blood glucose and insulin, followed by a drop in blood glucose and increased perceptions of hunger. Commonly, these foods have little nutritional value and tend to be high in calories. They include processed and homemade foods made with white flour, sugar, and corn syrup such as white breads, tortillas, cold cereals, pastas, candies, pastries, and sugar-sweetened beverages (e.g. fruit drinks, soda, and sports/energy drinks), many of which are commonly consumed in American households. Particularly concerning is that these foods may have addictive properties, affecting dopamine levels. LNSC contribute to many chronic diseases, including type 2 diabetes, hypertension, cardiovascular disease, obesity, inflammation, and metabolic syndrome, and acute conditions such as hunger, satiety, mood, and glycemic load.

High dietary intake of LNSC is associated with lower HDL cholesterol concentrations, an important coronary risk factor. Obesity itself is also associated with low HDL cholesterol levels, as well as increased triglyceride levels, in both children and adults. Results from interventions limiting LNSC intake show promise, with individual studies showing decreases in one or more variables of energy intake, blood pressure, lipid levels, and weight and improved glucose tolerance and hyperinsulinemia in adults age 18 and older.

Complex carbohydrates and natural fats: There is growing evidence that deriving dietary carbohydrates primarily from complex (e.g., whole fruits and vegetables, legumes, whole grains) rather than simple carbohydrate sources may help reduce the risk of developing or aid in the treatment of cardiovascular disease, type II diabetes, and metabolic syndrome and may aid in weight loss. These benefits are thought to derive from the non-starch polysaccharide, dietary fiber, and possibly other components of these foods. Therefore, limiting HPFS foods and increasing CC and natural fat intake is an integral component of our intervention and is consistent with recommendations advocating intake of slowly absorbed complex carbohydrates rather than rapidly absorbed simple carbohydrates. Healthy fats such as nuts, fresh lean meats, avocados, olive oil are also absorbed slowly and have nutrients important in reducing risk of developing cardiovascular disease, type II diabetes and metabolic syndrome.

Motivational Interviewing to limit HPFS intake and increase CC and natural fat intake The framework for the proposed study was adapted from the Predicting and Changing Behavior Theory (PCBT), which proposes that an individuals' attitudes/beliefs (perceptions toward a behavior), perceived norms (including social pressures within a culture or family), and perceived behavioral control (self-efficacy or belief about the ease or difficulty of performing a behavior) are the primary determinants influencing intention to engage in a particular behavior. The PCBT has been used to predict behaviors such as weight

loss, physical activity, and self-efficacy for healthy eating in American populations. However, few, if any, studies have focused on using this approach to encourage obese Americans to reduce their HPFS intake and increase their CC and natural fat intake in an effort to move them toward self-management of obesity, nor have they assessed the impact of such interventions on their diet and/or biometrics. Our MI intervention with and without pharmacotherapy is designed to effect behavior change by sharing information on the benefits of limiting HPFS intake and increasing CC and natural fat intake (addressing attitudes/beliefs), and providing support to increase perceived behavioral control by decreasing participants ambivalence and barriers (addressing self-efficacy), which will support participants in limiting their HPFS intake and increasing their CC intake. MI is evidence-based, client-centered, and individualized, empowering individuals to establish their own realistic goals for behavior change by emphasizing personal choice and affirming client decisions.

Pharmacotherapy for Obesity/Addiction (naltrexone-bupropion)

Recent studies have assessed the efficacy of combination treatments of long-acting acting opioid antagonists (naltrexone) and antidepressant drugs (buproprion) in lowering the body weight of obese patients. Buproprion seems to have a complementary effect of decreasing hunger in combination with naltrexone, producing significant long-term decreases in weight. A multicenter phase III trial was conducted that randomly assigned 1,742 overweight individuals to receive an oral preparation of a sustained release pharmaceutical. The intervention continued for 56 weeks after which mean reduction in body weight was significantly higher in the pharmaceutical groups than placebo groups. Pharmaceutical groups were treated with naltrexone 16 mg plus buproprion and 32 mg naltrexone plus buproprion. In the proposed study, dosing protocols will be followed for treatment of obesity: 1 tablet (90mg/8mg) initially week 1; increase by 1 tablet/day each subsequent week until daily maintenance dose of 2 tablets twice daily (360 mg bupropion/32 mg naltrexone) is achieved at the start of week 4. Use will be discontinue used at month 4 if no clinical response is observed.

Contribution to Science

This study addresses a critical topic and will contribute to the science of treating obese patients, particularly those with FA as diagnosed by the YFAS. We hypothesize that using a team of interventionists delivering an addiction-adapted MI intervention to support obese patients in reducing their HPFS intake and increasing their CC and natural fat intake will enhance the success of our interventions, thereby helping reduce the incidence of addiction/overweight/obesity, improving biometric measures, and reducing the risk for comorbidities associated with obesity. Use of the YFAS and evaluating the interventions in both obesity phenotypes, is expected to help identify better targeted approaches for addressing self-management of obesity by clients in each phenotype. Though this study focuses on a rural population, investigators anticipate that this approach can be adapted to broader populations, including those in urban settings.

Statistical justification for the total number of subjects needed to complete the research to achieve the scientific objectives.

The prevalence of FA is estimated to be 25% in the population of urban adult women who have a BMI classification of overweight or obese. Using this prevalence along with a medium effect size, a statistical power analysis was performed for sample size estimation with G*Power 3.1. The design is a stratified four-group design with a pre and post measurement. Stratification by obesity phenotype (positive or negative for FA) will occur first, followed by random assignment to one of four treatment groups [Information Control (dietary and physical activity instruction), MI alone(diet and physical activity instruction supported by MI), MI((diet and physical activity instruction supported by MI+P(Contrave). Using an f = 0.25, an alpha = .05 and power = 0.95, the a priori F test, analysis of variance, omnibus, one-way model gives a projected sample size of 252. As a pilot study, this study is underpowered for statistical hypothesis testing, and analyses will focus on descriptive statistics, estimation of effect sizes, and hypothesis generation and a sample of 40 eligible patients will be enrolled (10 in each group). This meets the pilot study guideline of at least 10% of a fully powered trial and remains realistic in terms of time and cost (Hertzog, 2008) while allowing for 50% attrition. It is expected that 25% of the population will meet the criteria of FA and therefore will need to screen and consent a total of 160 participants to reach the 40 people positive for FA. No more than 160 subjects will be consented for the entire pilot study.

Proposed methods/approach

Investigators propose assessing obese clients with the YFAS as part of their intake once they are referred to the Healthy Behaviors Clinic by Regional West physicians/practitioners. A nurse researcher with expertise in MI and a nurse practitioner will perform intake assessments, obtain consent and randomly assign participants in each phenotype (positive or negative for FA) to one of three treatment groups (usual care, individual MI alone, and individual MI with pharmacotherapy). Interventions will occur over 6 months. A clinical psychologist with expertise in the YFAS (University of Michigan) will serve as a consultant on this project and a registered dietitian (University of Nebraska Lincoln) will serve as a co-investigator.

Investigators expect that MI and MI+P and P will be more effective in improving outcome measures than IC. We also expect that response to the treatments will differ between the two obesity phenotypes (those testing positive and those testing negative for FA).

To determine if MI alone or MI+P or P is effective in treating obese patients with and without FA (based on the YFAS) as determined by :

-Higher MI confidence, importance and readiness to change scores

-Reduced intake of foods that are highly processed and high in fat and sugar (HPFS) and increased intake of complex carbohydrate foods(fresh fruits, vegetables, whole grains) and minimally processed proteins (nuts, fresh meats) (ASA24-2016® dietary recall)

-Improved biometric measures (BMI, body composition, waist circumference, and blood pressure)

-To determine whether the two obesity phenotypes (with and without FA) differ in their response to the four treatments.

Initial Screening for Eligibility (Suicidal Ideation, Pregnancy test (urine test), Lactation, Recruitment): Participants will be recruited from obese patients referred to the Healthy Behaviors Clinic by Regional West Physicians. Nurse researchers who work at the Healthy Behaviors Clinic will inform potential participants about the study and, if they agree to participate, will consent them.

Both treatment groups,Those who test positive for and those who test negative for FA (food addiction) will be assigned to one of four treatment arms, IC, MI, MI/P and P. All will receive dietary and exercise information. After consenting, each participant be administered the YFAS to determine their obesity phenotype (positive or negative for FA). Participants within each phenotype will be randomly assigned to one of the intervention (MI or MI+P, or P) or the IC information control (diet and physical activity instruction, which will be no less than current standard of care) treatment groups using a randomization schedule (assignments in numbered, sealed, opaque envelopes; one set for each phenotype) 1:1:1:1 ratio, provided by our statistician, Dr. Struwe. Phenotype assessment and treatment assignment will continue until the sample size (n=10) is met for each phenotype-treatment group category. Those in the control group will be seen at the same time periods as each treatment group to maintain their interaction time with the clinic. They will receive diet and exercise instruction at each time point.

Intervention Conditions (MI, MI+P): MI is theorized to decrease a patients ambivalence and increase his/her perceived behavioral control (self-efficacy) for limiting HPFS and increasing CC intake by emphasizing personal choice and control in decision-making and by affirming the patients self - management ability. Interventionist nurses will deliver MI sessions following data collection at baseline, 1, 2,3, and 4 weeks and 2, 3, 4, 5, and 6 months to promote sustained behavioral change.50 A written MI algorithm will be used to ensure uniform implementation of the intervention.

MI will be operationalized by the nurse asking the patient about his/her knowledge, limiting HPFS/increasing CC and natural fat intake, defining FA, and explaining why it is important to limit their HPFS/increase their CC and natural fat intake. The nurse will ask the patient to rate the importance of limiting HPFS/increasing CC and natural fat intake (scale of 1-10) and their confidence in their ability to do so (scale of 1-10). The nurse will focus on the lower score and ask the patient why they chose that score and what they thought it would take to increase the number. If the patient rates the importance of understanding of limiting HPFS/increasing CC and natural fat intake low, the nurse will provide information on the benefits of limiting HPFS/increasing CC and natural fat intake to reduce the their risk of obesity, diabetes, heart disease, and numerous other co-morbidities associated with overweight. If the patient rates their confidence in their ability to limit HPFS/increase CC and natural fat intake as low, the nurse will provide the patient with strategies to decrease barriers and increase confidence, such as a list of healthy snack food choices, stepped changes (3 sodas per day to 2 sodas and 1 water per day, etc.), and having the patient choose healthy foods at the store. The same questions will be asked at each time point.

Nurse responses will be tailored to the specific motivational issues of each individual patient at each time point. During each session, the nurse will document the patients responses to the MI algorithm (levels of confidence, importance, and readiness to change), their perceived barriers and concerns, and suggestions to address them/setting achievable goals. The MI documentation form will ensure that all nurses collect the same data and provides a record that the nurses can reference during their sessions to help them adjust each MI session to the patients' individual needs. If a patient reveals a new barrier that is not included in the training materials, the nurses will meet with team members to discuss the new barrier and strategies to address it will be shared with all interventionists.

In the group with pharmacotherapy added to the MI, the naltrexone-buproprion (Contrave) protocol will be added to the patients intervention. Dosing protocols will be followed for treatment of obesity: Orally, 1 tablet (90mg/8mg) initially week 1; increase by 1 tablet/dayeach subsequent week until daily maintenance dose of 2 tablets twice daily (360 mg bupropion/32 mg naltrexone) is achieved at the start of week 4. Use will be discontinued at month 4 if no clinical response is observed. This drug (Contrave) is to be taken with a high fat meal.

In the pharmacotherapy group alone, dosing protocols will be followed for treatment of obesity: Orally, 1 tablet (90mg/8mg) initially week 1; increase by 1 tablet/day each subsequent week until daily maintenance dose of 2 tablets twice daily (360 mg bupropion/32 mg naltrexone) is achieved at the start of week 4. Use will be discontinued at month 4 if no clinical response is observed. This drug (Contrave) is to be taken with a high fat meal.

The IC control group will receive diet and physical activity information to encourage them to adopt healthier eating (limit HPFS/increase CC intake) and physical activity behaviors. IC information sessions will occur at the same time points as the intervention sessions (baseline, 1, 2,3, and 4 weeks and 2, 3, 4, 5, and 6 months) and will be similar in length. The PI and co-PIs will develop information packets for each session, (self-management, avoiding highly processed LNSC foods, low intensity physical activity, avoiding highly processed fatty foods, medium intensity physical activity, avoiding LNSC beverages, importance of water as a beverage to hydrate and reduce cravings, avoiding high fat beverages, high intensity physical activity, importance of CC intake).

Data Collection

All research personnel will be CITI-trained. A nursing student will assist the nurse researchers with data collection. Each data collector will undergo fidelity checks (performed by the PI) for each measurement procedure before they will be allowed to collect data. They will also be trained in using the ASA24-2016® dietary recall, so they can assist the patients as needed.

The current version of the YFAS, the YFAS 2.0, will be used to assess participants obesity phenotype (positive or negative for FA). This measure adapts the eleven DSM-5 diagnostic criteria for substance-related and addictive disorders when the substance is HPFS foods. In order to meet the diagnostic threshold on the YFAS, individuals must report at least two of the eleven diagnostic indicators of FA plus clinically significant impairment or distress.

The Automated Self-Administered 24-hour Recall, version ASA24-2016® will be completed at each time point to assess changes in patients dietary intake. This web-based 24-hour dietary recall instrument has been used effectively by hundreds of researchers and has face validity and similar intake results to the AMP.10 A strength of the ASA24-2016® is that it includes most traditional American foods/ingredients.

Height: The patients height will be used in determining BMI and BIA measures. We will use the average of 2 heights (cm) measured with the Seca EC0123 stadiometer. During measurement, patients will be in socked feet with heels placed against the back of the platform and facing straight forward.

Body Composition: Bioelectrical impedance analysis (BIA) will be used to determine body composition. Estimated standard error for BIA is ± 3.5-5%. We will use a Tanita SC-250 body composition analyzer and follow a standardized protocol to measure percent body fat, body fat mass, fat free mass, percent body water, muscle mass, bone mass, BMI, and visceral fat. The software also classifies patients as underfat, healthy, overfat, or obese based on percent body fat, age and gender.

Waist circumference: We will use the average of 2 measurements (cm) performed with the patient standing erect with their arms at their sides. Waist circumference will be measured at the uppermost lateral border of the right ilium at the end of normal expiration using an inelastic tape measure positioned around the trunk parallel to the floor. This measure is included because it is a better indicator of body fat and, therefore, health risk than

BMI: In addition, results of a recent study in this population demonstrated that waist circumference has potential as a means of identifying patients with or at risk for obesity and hypertension.

Blood Pressure: We will use the average of 2 blood pressure measurements performed using an Omron HEM- 907 automatic blood pressure monitor. The measurements will be performed while the patient is quiet and still using the appropriate sized cuff placed snugly around the upper arm approximately 2 to 3 cm above the antecubital fossa with the mark on the cuff aligned with the artery.

Determinants of Change Measures: MI Algorithm Questions: These reflect the PCBT determinants of behavior change (the patients perceptions toward limiting HPFS/increasing CC intake). They assess patient attitudes/beliefs (importance score), perceived norms (perceived barriers), and perceived behavioral control/self-efficacy (confidence score). These measures will be recorded by the interventionist nurses during each MI session for their assigned patients.

If a subject experiences success in managing their weight while participating in the study,(which will be determined by a 5% decrease in BMI or body fat or total body mass over 4 months) the subject may continue with the weight management plan after completing all study related visits. All participants may continue with clinic visits following the study and may have available to them, usual care, MI, Contrave (unless they have taken it in the study and it was not effective), and bariatric surgery options. All subjects taking Contrave will be screened at each visit for suicidal ideation. In addition, they will be asked to call Dr. Bowman immediately if they have any such feelings or symptoms of suicidal ideation. If they present with suicidal ideation, Dr. Bowman will interview them using the Suicide Screening Algorithm (see documents) to determine the severity of the symptoms and make additional medical referrals as necessary. If the case is emergent, they will be immediately escorted to the ER or asked to come into the ER, if it is a phone visit. . If the case is urgent, they will be referred to psychiatric personnel in the office where Dr. Bowman practices as a Psychiatric NP. They will be withdrawn from the study at this time and

Dr. Aguirre will be notified. Dr. Bowman will follow up with these patients. At the six month visit a PHQ-9 and the YFAS (from the WALI) will be readministered. An appt for a 12 month sustainability measure will be set up.

Statistical Methods to Analyze Data

Missing data will be evaluated. For summated scales on which fewer than 20% of an individuals responses are missing, the individuals mean on the remaining items may be substituted, as appropriate. For analyses requiring complete data, imputation of missing values using the EM algorithm or multiple imputations will be considered, as appropriate. Scoring algorithms for each instrument will be used per the published use manual. Each statistical test will be conducted at p=.05 level. Data will be analyzed using descriptives (means, medians, standard deviations of scores), independent t-tests, correlation coefficients and analysis of variance. In Aim 1, ANOVA will be used to assess differences between the three treatment groups on the YFAS to determined changes in MI confidence, importance and readiness to change scores as well as ASA24-2016® dietary recall and biometric measures. Correlational analysis will be used to explore the relationships between ASA24-2016® dietary recall and biometric measures. In Aim 2 independent t-test will be used to determine if the positive and negative YFAS groups differ across treatment responses.