BMJ Open

Comparing dietary patterns of depressed patients versus healthy people in a case control protocol

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ABSTRACT

Introduction: Major depressive disorder is the leading cause of disability around the world. Because of the high rate of medication discontinuation by patients and the risk of recurrence, factors such as nutrition could be useful for the prevention or treatment of depression. The relationship between depression and dietary patterns has been reported in a few studies but with controversial results. Therefore, we have decided to study the possible effects of cultural, social, racial, geographic and environmental conditions on this relationship in an Iranian population.

Methods and analysis: In our case control protocol, 110 cases and 220 controls will be individually matched based on age, sex and area of residence. New cases of depression, based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV), will be recruited from two psychiatric clinics in Tehran. Interviewers will then go to each patient's home and invite qualified individuals to participate in the study as controls. Food intakes of all participants will be obtained by semiquantitative food frequency questionnaires covering the past year; these will be transformed into actual food intake (g/day). Dietary patterns will be determined by the principal components method. Conditional logistic regression, as a multivariate analysis, will be used for assessing the relationship between dietary patterns and depression, taking into consideration the potential role of different variables. The results may help to identify differences in dietary patterns between depressed and healthy people.

Ethics and dissemination: The study protocol has been approved by ethics committee of Tehran University of Medical Sciences. At the beginning of the study, a written informed consent form will be signed and dated by subjects and investigators. The results will be published in due time.

INTRODUCTION

Depressive disorder is a leading cause of disability around the world, affecting approximately 121 million people.[1] According to the WHO, depression is the fourth most common global burden of disease, and could be the second most common global burden by the year 2020.[2 3]

In order to diagnose a patient with major depression, five of the following symptoms should be present for at least 2 weeks: feeling depressed, sad or blue; absence of interest or enjoyment; increased or decreased sleeping; increased or decreased appetite together with weight change; feeling agitated, feeling unsettled or slowness; feeling of worthlessness or guilt; low energy; difficulty in concentration; and feeling that life is worthless or suicidal actions.[4]

Risk factors for depression include gender, socioeconomic status, lack of social support, family history of affective disorders, loss of a parent before the age of 10 years, drug abuse, history of physical or sexual abuse in childhood, use of oral contraceptives in women, using gonadotrophin stimulation for the treatment of infertility in women, stress, genetic backgrounds, medical illnesses such as cancer and diabetes, vascular brain changes and malnutrition.[4 5]

Drug therapy for depression has been successful in 60–80% of patients. However, <25% of all depressed patients receive treatment.[1] Furthermore, depression is a chronic or recurrent condition. Because of poor medication compliance in patients with depression and a high rate of recurrence, it is important to consider other factors, such as nutrition related factors, in the prevention and treatment of unipolar depression.[2]

To date there have been many reports on the relationship between depression and deficient nutrient intake.[2] For example, tryptophan, as a dietary amino acid, is the precursor of brain serotonin. People with decreased brain serotonin are considered to be vulnerable to affective disorders. Synthesis of serotonin is limited by the inaccessibility of tryptophan.[6]

Moreover, consumption of specific fatty acids is shown to have a possible beneficial

effect on some mental disorders,[7] such as depression in middle aged women.[8] Omega 3 long chain polyunsaturated fatty acids produce anti-inflammatory eicosanoids that reduce levels of proinflammatory cytokines in depressed patients. These polyunsaturated fatty acids have antidepressant protective actions. This is characterised by the relationship between lower levels of fish consumption and increased incidence of depression.[9] There are known biological mechanisms which link dietary omega 3 deficiencies to psychiatric illnesses, including a decrease in serotonin and dopamine levels by 50% in animal models; damaged neuronal transport, connectivity, updated apoptosis and dendritic arborisation; and disturbance of the hypothalamic pituitary adrenal axis.[10]

Traditional analyses in nutritional epidemiology mainly investigate the association between diseases and lack or presence of single or multiple nutrients or foods. Although this type of analysis is relatively valuable, it has several conceptual and methodological limitations. First, people do not consume individual nutrients. Food consists of various combinations of nutrients which may have alleviating or exacerbating effects. Second, the effect of a single nutrient may be very low and hard to measure, while the collective effects of some nutrients in a dietary pattern are easily detectable. Third, as nutrient intake is generally associated with certain dietary patterns, single nutrient analysis may be altered by the effects of dietary pattern. For example, low dietary fat is accompanied by higher intakes of vegetables, fruits, fibre, folate and whole grains. Intakes of these as a dietary pattern may be related to a decreased risk of coronary heart disease independently. These dietary components are potential confounders in the relationship between fat intake and coronary disease.[11] In addition, adjustment for these factors in multivariable analyses may not eliminate all of the confounding effects as these dietary components may interact with each other.[12]

The aim of this protocol is to investigate the relationship between depression and dietary patterns in subjects, rather than the effects one or more specific nutrients. A few studies in different countries with diverse dietary patterns have shown an association of these patterns with an increased risk of depression.[13–15] Therefore, more studies are needed investigating other dietary patterns that are related to depression.

Aim of the protocol (hypothesis)
To discover the relationship between dietary patterns and types, and depression morbidity.

METHODS AND DESIGN
Study design
An individually matched case control observational design will be used in this study.

Objectives
▶ Comparing mean birth rank, education level and family size between depressed and healthy subjects (depression is considered as the primary outcome).
▶ Comparing mean cigarette smoking or use of pipe or hookah per week between the two groups.
▶ Comparing mean anxiety and depression scores, weight, height, body mass index and physical activity score between the two groups.
▶ Comparing the frequency of unemployment history, occupational status, marital status, life history of traumatic events, childhood history of traumatic events and family history of alcoholism between the two groups.
▶ Comparing mean daily intake of energy, macronutrients and micronutrients between the two groups.
▶ Comparing mean daily intake of energy, macronutrients and micronutrients, based on dietary pattern, between the two groups.
▶ Comparing depression OR values among tertiles of dietary pattern scores.
▶ Comparing depression OR values among tertiles of dietary pattern scores after adjusting for other independent variables.

Group selection
Case group
Patients will be diagnosed by a psychiatrist as having major depressive disorder or unipolar depression, using the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV). With no history of depression in the past year, patients should meet the inclusion and exclusion criteria outlined below. No symptoms should have appeared more than 3 months before the diagnosis. Patients will be recruited from two psychiatric clinics in Tehran (Imam Hossein and Baharloo psychiatric clinics).

Control group
The control group will include individuals with no major depression, based on the Beck Depression Inventory (BDI-II), and no history of depression in the past year. Interviewers will go to each patient's home and invite qualified individuals to participate in the study.

Ratio of cases to controls
In this study, the ratio of cases to controls will be 1:2.

Matching patients with controls
Matching will be done individually, based on age, sex and residential area. Age categories for matching will be 18–30, 31–40, 41–50 and 51–65 years.

Inclusion criteria
▶ Major depressive disorder diagnosed by a psychiatrist using DSM-V criteria into one of three categories (mild, moderate or severe, based on BDI-II).

- Lack of major depressive disorder in the control group at the time of the study, based on BDI-II.
- Maximum period of 3 month intervals from onset of five symptoms of depression to the beginning of the study.
- Age 18–65 years.
- Residing in Tehran, the place of the study.

Exclusion criteria

- Suffering from cognitive impairment or other psychotic illnesses diagnosed by a psychiatrist.
- Severe depression, lacking ability to cooperate and answer the questions.
- Suffering from hormonal disorders, including Addison's, Cushing's disease, hyperthyroidism or hypothyroidism, and hyperparathyroidism, according to a physician diagnosis or medication intake.
- Suffering from chronic diseases, including cancer, heart disease, diabetes, stroke, fibromyalgia, kidney or liver failure, multiple sclerosis and Parkinson disease, according to a physician diagnosis or medication intake.
- History of trauma, bruises, cuts, fractures, bleeding, burns, accidents and other similar events in the past 3 months, resulting in unconsciousness and hospitalisation.
- Suffering from chronic and infectious diseases, including HIV, mononucleosis, tuberculosis, viral hepatitis and pneumonia in the past 2 weeks.
- Alcohol and drug addiction at the time of the study or in the past 3 months, based on patient confession to the psychiatrist.
- Body mass index ≥ 40 kg/m^2.
- Pregnancy and lactation at the time of the study or in the past year.
- Using any type of special diet in the past 2 months.
- Using any type of special diet for more than 2 months in the past year.

Sample size

Sample size calculations were performed using the software open Epi, with two sided confidence, power=80, ratio of controls to cases=2, per cent of controls exposed=25,[16] per cent of cases with exposure=40 and OR=2.[17] Sample size was calculated as 110 depressed subjects and 220 control subjects. We will include at least 10% more samples to cover incomplete dietary questionnaires that may reduce the final number of participants available for analysis.

Data collection
General information

General information, medication use and some confounders will be obtained using a general questionnaire.

Anthropometric and blood pressure measurements

Anthropometric measurements, including height, weight and waist circumference, will be performed for all participants. Height will be measured in the standing position without shoes using a height gauge, and weight will be measured using weighing scales with minimal wear. Waist circumference will be measured in the standing position, intermediate between the lower margin of the ribs and the iliac crest, while breathing normally without clothes. Blood pressure will be measured after 15 min of rest in a sitting position.

Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria

These criteria have been designed by the American Psychological Association[18] and have been standardised in Iran.[19] The criteria will be used to diagnose depression in patients admitted to the psychiatric clinics of Imam Hossein and Baharloo in Tehran.

Beck Depression Inventory

This questionnaire will be used for quantitative rating of depression in depressed subjects and for screening of depression in the control group. These criteria have been standardised in Iran.[20]

Beck Anxiety Inventory

This scale has been standardised in Iran[21] and will be used for a quantitative measure of anxiety in the depressed and control groups as a confounder. This scale has 21 items and the total score is 0–63. A score of ≤ 15 is considered normal. Scores of 16–31, 32–47 and 48–63 are considered to indicate mild, moderate and severe anxiety, respectively. Anxiety is measured to adjust as a confounding variable.

Physical activity questionnaire

As physical activity can be related to depression, it is necessary to estimate physical activity as another confounder. A classified physical activity questionnaire, based on the metabolic equivalent (MET), will be used, which consists of nine levels of activity, from rest and sleep (MET=0.9) to vigorous activity (MET ≥ 6). The questionnaire has been prepared in previous studies in Europe and was validated with the daily physical activity questionnaire and the CSA Accelerometry (Model 7164 Ambulatory Monitor).[22] Reliability and validity of the questionnaire have been confirmed in the study of Kelishadi et al in Iran.[23] This questionnaire has high reliability and is significantly associated with the results of the International Physical Activity Questionnaire and 7 day records of Iranian youth physical activity. Physical activity is calculated based on metabolic equivalent hours per day (MET-h/day).

Dietary analysis

A semiquantitative food frequency questionnaire will be used to determine food intake in the previous 12 months. Data from the semiquantitative food frequency questionnaire will be transformed into actual food intake (g/day). The food frequency questionnaire

was designed in the Tehran Lipid and Glucose Study in the fourth phase of the nutrition cohort; it contains 168 items, and its reliability and validity have been confirmed in district 13 of Tehran.[24] As the reliability and validity of the questionnaire for the population in the present study have not been evaluated, a pilot study was done to make any necessary changes to the questionnaire.

Statistical analysis

Dietary patterns will be determined by exploratory factor analysis. We will enter extracted food groups into the factor analysis and will use a principal components method to determine the number of factors or dietary patterns. We will use varimax rotation to identify major dietary patterns, based on the number of food groups. As each participant will receive a factor score for each explored dietary pattern, we will categorise participants into tertiles of dietary pattern scores.

To examine the relationship between depression and the characteristics of individuals, such as the scores of the tertiles of their dietary patterns, we will use the χ^2 test, McNemar's χ^2, the paired t test and Pearson's correlation coefficient. Multivariate analyses will be conducted using a conditional logistic regression model to assess the potential importance of different variables. In this method, the response variable (primary outcome) is depression (yes, no). Conditional logistic regression is used because of individual matched cases and controls. In addition, the following method will be used for investigating the association of the measured values in the two groups:

$$\text{Logit}(y=1)=\alpha_i+\beta_i X_i (i=1-n)$$

where α_i is the random intercept in the equation of conditional logistic regression and β_i is the coefficient of the independent variable in the regression model, including dietary patterns and other control variables in moderating the relation of dietary patterns.

Ethical issues and informed consent process

The study protocol has been approved by the ethics committee of Tehran University of Medical Sciences (91-03-161-19374). The investigators will provide subjects with all related information in the preferred language of the subject and at a level of complexity that is understandable to subjects. Prior to the subject's participation in the study, a written informed consent form will be signed and dated by the subject and investigator.

Limitations

A case control study cannot determine the temporal relationship between dietary patterns and depression. It can generate results that describe differences in identified dietary patterns in depressed and healthy people.

DISCUSSION

Instead of studying the effect of one or a few nutrients, evaluating patterns of food consumption represents the real effects of nutrients, and also the interactions between nutrients. In addition to understanding the biological mechanisms, this evaluation reflects the complex interactions and relationships among people, cultures and societies, and will help us to study social and psychological mechanisms.[17] According to evidence based reports of the relationship between food and emotion, it seems that understanding the relationship between depression and dietary patterns is more promising than studying its relationship with one or a few nutrients.

The association between depression and dietary patterns has been discussed in a few studies, with controversial results.[14–25] For example, in the study of Sanchez-Villegas there was a significant inverse relationship between depression and adherence to a Mediterranean diet, including lower red meat consumption.[15] However, according to Jacka et al,[14] subjects on a traditional diet, including red meat, had lower odds of major depression and anxiety compared with those on a western diet. It is important to carry out these types of investigations in various countries, with the aim of studying the effects of cultural, social, racial, geographic and environmental conditions on the relationship between dietary pattern and depression.[26] Moreover, advising people to adhere to a special dietary pattern is more practical than to a particular nutrient, such as cobalamin or folic acid. We hope that the results of the current protocol can provide a new approach in the field of nutritional interventions in depressed patients.

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