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Original article

The effects of dietary inositol on dimensional obsessive compulsive scale score

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Abstract. *Objective:* The aim of the study was to explain the relationship between obsessive and compulsive disorder scores of university students, inositol levels in their diet and Mediterranean diet compatibility and to use nutrients as a protective method for disease formation. *Material and Methods:* 168 volunteers from Tekirdağ Namık Kemal University School of Health, School of Health and Faculty of Medicine were subjected to a 'nutritional habits form' consisting of 13 questions, a 'Mediterranean diet compliance scale' consisting of 14 questions, a 'nutrient consumption frequency questionnaire' containing inositol-rich foods and a dimensional Obsessive Compulsive Disorder scale consisting of 20 questions in the 2019-2020 academic year. *Results:* Of the participants, 83.3% had a DOCS score below 40 while 16.7% had a score of 40 and above. Daily inositol intake was 1000 mg and more in the 63.1% of the participants and was below 1000 mg in 36.9%. A statistically significant relationship was found between the concerns about "germs and contamination," "concerns about being responsible for harm, injury, or bad luck," "concerns about symmetry, completeness, and the need for things to be 'just right'" categories of the DOCS and the amount of daily inositol intake ($p<0.05$). It was also found that there was a significant relationship between the amount of daily inositol intake (>1000 mg or <1000 mg) and the differences in the DOCS score. The DOCS score increased when the amount of daily inositol amount was below 1000 mg and the score decreased when the amount of daily inositol amount was above 1000 mg; thus, they were negatively correlated ($p<0.05$; $r=-0.203$). Of the participants, 93.5% were in the incompatible category of the Mediterranean Diet Compatibility Scale, and no significant relationship was found between the scale score and the amount of daily inositol intake and the DOCS score ($p>0.05$). *Conclusion:* It is considered that adding nutrition richer than inositol to the diet based on the energy need of the individuals might be preventative for Obsessive and Compulsive Disorder (OCD).

Keywords: Inositol, Obsessive Compulsive Disorder, Mediterranean Diet, Serotoni Receptor, Secondary messenger

Introduction

Inositol is a simple polyol precursor with important effects in the brain messenger system. Inositol, which can be also synthesized by various organs in the body, is a glucose isomer as well as is used by the noradrenergic, cholinergic and serotonergic receptors and acts as the main mediator of the phosphatidylinositol (IP) cycle in the secondary messenger system in the brain (1). IP 6 has several essential functions for human health such as enhancing the immunity system, preventing kidney stone formation by inhibiting pathologic calcification, providing a cardiovascular benefit by reducing high serum cholesterol level and reducing pathologic thrombotic activity. Field researches on depression, schizophrenia, bipolar disorder, lack of attention and

hyperactivity disorder, panic attack and OCD (Obsessive Compulsive Disorder) have been conducted in the field of psychology (2).

A large body of evidence shows the complexity lying under the neurotransmitter network of the cortical-striatal-thalamo-cortical (CSTC) circuit, dopamine (DA), serotonin (5HT), glutamate (Glu), and OCD neuropathology. Glu and gamma amino butyric acid (GABA) dysfunction was considered as a disease (3). The studies supported that oral inositol administration induces a 20% increase in the brain inositol concentration; the absolute inositol levels in the brain do not remain constant throughout life, and the inositol levels in the brain reduce with advancing age and when required, oral inositol is needed to protect the cell integrity (4-6).

When the relationship between OCD and inositol is examined, three important mechanisms are encountered. These are dopamine receptors, nigrostriatal dopamine pathways, serotonin receptor regulation. A hypothesis that has not been proven yet is that elevated levels of glucuronic acid as a result of the intake of a large amount of inositol increase the excretion of P450 hydroxylated xenotoxic or ototoxic metabolites as glucuronides (4).

It was suggested that the upregulation of D2 receptor may play an important role in the behavioral effects of inositol since long-term inositol administration causes a significant increase in the absence of serotonin receptors (3). Several studies revealed that selective serotonin reuptake inhibitors (SSRI) are effective in OCD, and inositol reverses desensitization of serotonin receptors (5, 6). Inositol seems to have a similar effect as antidepressant drugs, especially SSRIs. The key 5-HY receptor sub-types bind to the phosphatidylinositol second messenger system, forming the therapeutic profile of inositol in OCD treatment (6). However, because the putative site of action of inositol is intracellular, inositol is also notable for its ability to represent an important and novel therapeutic agent, other than SSRIs, for the treatment of psychiatric disorders (6, 7).

Myoinositol administration at a dose of 12-18 gram/day has been the subject of several studies on various neuropsychological disorders and diseases. These include a wide range of diseases including autism, Alzheimer, depression, hyperactivity and attention disorder, schizophrenia, bipolar disorder, panic attack and OCD. In placebo-controlled studies, it showed activity in OCD, depression and panic disorder after 3 weeks. The side effects are limited with a mild gastrointestinal disorder in more than 100 individuals (8).

Since inositol is a natural compound with a few known side effects, it can be appealing for patients who are unsure about taking medication. Also, due to the high availability of inositol in nature, people can intake it with their daily diets, which makes it appealing for patients who are unsure about taking psychiatric medication (8).

Although it was found that adult individuals intake 1 g inositol in different forms per day, there is no certain consumption amount recommended by RDA (9). However, several studies showed that the recommended inositol amount varies by the energy amount in the individual's diet, but it is 1500 mg for a 2500 kcal diet (10). When this amount was increased to 4-6 grams for the treatment in the presence of various diseases such as PKOS, diabetes, insulin resistance, positive results were achieved. Much higher inositol is needed in the treatment of various psychiatric diseases.

The clinical study data revealed a few critical points regarding myoinositol treatment. It was found that the administration of myoinositol at a dose of 12 g/day and higher causes gastrointestinal symptoms such as nausea, gas, loose stools, diarrhea, while these symptoms increased to serious levels if it is administered at a dose of higher than 30/day. It was tested that the dosage of 4 g/day of inositol that is commonly used in clinics is completely free of side effects (11)

A diet containing inositol includes foods that are natural, easily accessible and more affordance compared with drugs. A study found 487 foods of whose inositol amount was determined by gas-liquid chromatography (10). The study results showed that whole grain foods such as cereals, oats and bran, etc. contain a higher amount of inositol than refined foods; starchy vegetables contain highly variable amounts of inositol. Among them, beans and peas contain the highest amount of inositol, while corn and carrots contain relatively small amounts of inositol. Little inositol was

found to be present in the meat and fat exchanges, commercially-prepared beverages or most of miscellaneous foods (10). Thus, seeds such as oilseeds, beans and cereals should keep an important place in a diet rich in inositol. Depending on the energy requirement, the individual should consume at least one serving of almonds, walnuts, cashews or peanuts during the day; whole-grain breads and cereal foods with meals; high amount of legumes such as dry beans, beans, peas, artichokes, okra in the desired form such as salad, bean salad, appetizer, meal; fruits of the season such as prunes, orange, tangerine, cherry, melon in intermediate meals (10). Thus, foods may be used as some kind of protector against diseases. Accordingly, the study aims to explain the correlation between the DOCD (Dimensional Obsessive-Compulsive Disorder) Scale scores, the inositol intake levels and the Mediterranean Diet adherence of university students.

Material and methods

Study design and participants

168 voluntary students who have continued in education in Tekirdağ Namık Kemal University in the 2019-2020 academic year were administered the 'Dietary Habits Form' consisting of 13 questions, the 'Mediterranean Diet Adherence Scale' consisting of 14 questions, the 'Food Consumption Frequency Questionnaire' containing items on inositol-rich foods and the 'DOCD' scale containing 20 questions. This study was approved by the Tekirdağ Namık Kemal University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee with the ethics committee decision with protocol number 2020.26.01.26 and dated 04.02.2020.

General characteristics and dietary habits

In this part, the general characteristics and dietary habits of the university students who were volunteer to participate in the study were examined with 13 questions. The general characteristics questions were about their sex, age, health status and department where they study; while the dietary habits questions were about their personal opinions about dietary habits, dietary supplements that they use, and their tea and coffee consumption status. Also, a questionnaire about the frequency of consuming inositol-rich foods was administered. This questionnaire is calculated in the amount of 1 gram inositol, Turkey 'is used which can be consumed foods containing inositol (10). The consumption frequency of foods is divided into daily, every other day and weekly. Then, the consumption amounts of these foods were recorded by the volunteers who participated in the survey. The amount of inositol in each food was first calculated as g/week and then converted to mg/day according to the amount of consumption separately for all volunteers.

Mediterranean diet adherence scale

In this part, the Mediterranean Diet Adherence Scale was fulfilled to describe the affinity of individuals to healthy nutrition (12, 13). The scale consists of 14 questions, and each question is scored as 1 or 0 depending on the consumption amount. A total score of 7 and higher shows that the individual has an acceptable adherence to the Mediterranean Diet, while a total score of 9 and higher shows that the individual has a strict adherence to the Mediterranean Diet (12).

Dimensional obsessive-compulsive disorder scale

In this part, the DOCD scale consisting of 20 questions, each rated on a 0–4 scale, was administered. The total score from the scale represents the OCD score of the patient. It contains 5 items for each of the most consistent 4 OCD symptom dimensions which were determined in statistical analyses. These dimensions are I) contamination, II) responsibility for causing damage and making mistake, III) symmetry and ordering, IV) unacceptable thoughts (14). The total maximum score from the scale is 80, and those with the DOCD score of 40 and higher and those with the DOCD score of less than 40 were examined in terms of daily inositol intake (mg).

Statistical analysis

The data were analyzed with IBM SPSS Statistics 22.0 (IBM Corporation, Armonk, NY, USA) program.

The Shapiro-Wilk test was used to examine whether the distribution of continuous numeric variables was normal. The descriptive statistics were expressed as mean±standard deviation or median (minimum-maximum) for continuous numeric variables, while the categorical variables were expressed as the number of cases and percentages (%). The independent t-test was performed to evaluate the correlation under the study. Correlation analysis was performed to determine the direction of correlation between daily inositol intake and DOCD score. The confidence interval was found as 95% and the results with $p<0.05$ were considered statistically significant.

Table 2. Examination of the Mediterranean Diet Adherence Scale score, DOCD score and Daily Inositol Intake of the Participants

Variables		Number (n)	Percentage (%)
Mediterranean Diet Adherence Scale Score	Non-adherent	157	93.5
	Adherent	11	6.5
DOCD scale score	<40	140	83.3
	≥40	28	16.7
Daily Inositol Intake Amount (mg)	<1.000	62	36.9
	≥1000	106	63.1

Percentage Frequency Analysis

Results

According to Table 1, 72% of the participants were women, 28% were men and 96% were single and 4% were married.

According to Table 2, 93.5% of the participants were not adherent to the Mediterranean Diet and 6.5% were adherent to the Mediterranean Diet. 83.3% of the participants had a DOCD score of less than 40, and 16.7% had a DOCD score of 40 and higher. In terms of daily inositol intake, 36.9% of the participants consumed inositol less than 1000 mg, while 63.1% consumed inositol more than 1000 mg.

When Table 3 was examined, no significant difference was found between the Mediterranean Diet Adherence Scale score and the daily inositol intake ($p>0.05$). No statistically significant difference was found between the DOCD score and the Mediterranean Diet Adherence Scale score of the participants ($p>0.05$).

According to Table 4, there was a statistically significant difference between the daily inositol intake amount and the DOCD score of the participants ($p<0.05$). There was a statistically significant difference between the daily inositol intake and the "concerns about germs and contamination" sub-dimension score ($p<0.05$). There was a statistically significant difference between the daily inositol intake and the "concerns about being responsible for harm, injury or misfortune" sub-dimension score ($p<0.05$). No statistically significant difference was found between the daily inositol intake and the "unacceptable thoughts, examples" sub-dimension score ($p>0.05$). There was a statistically significant difference between the daily inositol intake and the "concerns about symmetry, completeness, and the need for things to be 'just right'" sub-dimension score ($p<0.05$).

According to Table 5, there was a statistical correlation between the daily inositol intake amount and the DOCD score of the participants ($p<0.05$). A negative correlation was found between the daily inositol intake and the DOCD score ($r<0$). As the daily inositol intake increases, the DOCD score decreases and vice versa.

Table 1. Distribution of the Participants by their Demographic Characteristics

		Number (n)	Percentage (%)
Sex	Women	121	72.0
	Men	47	28.0
Marital Status	Single	161	96
	Married	7	4
Studied department	Nutrition and Dietetics	65	38.7
	Medicine	61	36.3
	Nursing	26	15.5
	Other	16	9.6
Total		168	100

Table 3. Examination of the Mediterranean Diet Adherence Scale score, the DOCD score and the daily inositol intake amount of the participants

Variables	Mediterranean Diet Adherence Scale Score	N	Mean ±SD	p
DOCD scale score	Non-adherent	157	27±11.3	0,211
	Adherent	11	31.5±13.2	
Daily Inositol Intake (mg)	Non-adherent	157	1536.2 ±1119.8	0,216
	Adherent	11	1108.6 ±811.9	

Independent Samples T-Test

Table 4. Correlation between the DOCD, DOCD categorical score and the daily inositol intake of the participants

Variables	Daily Inositol Intake (mg)	N	Mean ±SD	p
DOCD score	<1.000	62	30.3 ±14.23	**0,019**
	≥1000	106	25.5 ±9.1	
Concerns about germs and contamination	<1.000	62	9.60 ±3.76	**0,011**
	≥1000	106	8.20 ±3.18	
Concerns about being responsible for harm, injury or misfortune	<1.000	62	6.68 ±5.18	**0,045**
	≥1000	106	5.20 ±3.14	
Unacceptable thoughts, examples	<1.000	62	7.34 ±4.32	0.56
	≥1000	106	6.97 ±3.64	
Concerns about symmetry, completeness, and the need for things to be 'just right'	<1.000	62	6.63 ±4.48	**0,015**
	≥1000	106	4.84 ±3.83	

Independent Samples T Test

Table 5. Examination of the Direction of Correlation between the Daily İnositol Intake Amount and the DOCD score of the participants

Variable	N	r	p
DOCD score	168	1	**0,008**
Daily Inositol Intake Amount	168	-0,203	

Correlation Analysis

Discussion

The relationship of various dietary habits and nutrients in the world with several diseases has been studied and explained. Such studies may provide important information on the role and activity of nutrients (13). Considering the toxic effects of drugs used in the treatment of psychiatric diseases, treatments which are less toxic and more tolerable in the long term gain more importance (8).

Mediterranean diet is an eating pattern that is rich in olive oil and poor in saturated fat and involves abundant consumption of fruits and vegetables, cereals, legumes, nuts, high consumption of pulp, moderate consumption of fish and chicken (2-4 times/week), low consumption of meat (1-2 times/month), low intake of red wine (1 glass/day for women, 2 glass/day for men) (12). Whole grains, legumes, some fresh vegetables and fruits, and oilseeds contain a high amount of inositol (10). They are mostly in the

same food groups; they show similar characteristics. In this study, it was found that 93.5% of the participants were not adherent to the Mediterranean Diet and 6.5% were adherent to the Mediterranean Diet, while 83.3% had a DOCD scale score of less than 40, and 16.7% had a DOCD scale score of 40 and higher. In terms of daily inositol intake, 36.9% of the participants consumed inositol less than 1000 mg, while 63.1% consumed inositol more than 1000 mg. No significant difference was found between the Mediterranean Diet Adherence Scale score and the daily inositol intake. Besides, studies showed that a diet containing high amount of processed foods increases the risk for developing psychiatric symptoms such as depression and anxiety; however, the Mediterranean Diet protects against developing a mental disorder (15). Retrospective studies provided evidence suggesting that there is a positive correlation between Mediterranean Diet and slower cognitive decline, mild cognitive impairment (MCI), reduced risk for progression of Alzheimer disease (AD), lower AD risk and reduced crude mortality in AD patients (16). In a study, 224 depression cases were followed up and an inverse association was found with depression for participants assigned to a Mediterranean diet supplemented with nuts compared with participants assigned to the control group; however, this was not significant (17). In another study with 334 participants, the cognitive tests were followed. According to the results, in an older population, a Mediterranean diet supplemented with olive oil or nuts was associated with improved composite measures of cognitive function (18). In a study examining the association between OCD and Mediterranean Diet, the Mediterranean Diet was administered to 9 men with Obsessive-Compulsive Tic Disorder to promote a balanced diet through non-specific Mediterranean dietary advices. After one month, the OCD scale score was reduced significantly. It was concluded that healthier dietary patterns may be associated with the recovery of tics and obsessive-compulsive traits in boys who are diagnosed with the same conditions (19). In this study, no statistically significant difference was found between the DOCD score and the Mediterranean Diet Adherence Scale score of the participants. Based on these results, it can be said that the Mediterranean Diet and the diet containing inositol may contain similar foods but they cannot substitute for one another; however, the Mediterranean Diet has an impact on some cognitive disorders and neuropsychological diseases, but it has not so much impact on DOCD score as the diet containing inositol.

Several studies revealed that selective serotonin reuptake inhibitors (SSRI) is effective in OCD, and inositol reverses desensitization of serotonin receptors (5, 6). Inositol seems to have a similar effect as antidepressant drugs, especially SSRIs (6). However, because the putative site of action of inositol is intracellular, inositol is also notable for its ability to represent an important and novel therapeutic agent, other than SSRIs, for the treatment of psychiatric disorders (6, 7). In the light of this information, 18 g inositol was administered to 13 patients with OCD for 6 weeks to understand the effect of inositol on OCD. When the inositol group and the placebo group were compared, it was found that OCD symptoms were significantly reduced in the inositol group. A 10-week study was performed with 38 individuals to determine the efficacy and tolerability of inositol in adults with trichotillomania. The study results showed that 42.1% of patients were much or very much improved compared with the placebo group (35.3%) (20). In another study, a trial of 12 g daily of inositol in 28 depressed patients for 4 weeks was performed, it provided a significant improvement on depression compared with placebo, however, no changes were noted in hematology, kidney or liver function. Then, the discontinuation of inositol treatment caused a rapid relapse in a significant number of patients (1, 8). Another study compared the effect of inositol and fluvoxamine in panic disorder. 18 g/day inositol and 150 mg/day fluvoxamine were administered to twenty patients for one month. The results showed that inositol administration reduced the frequency of panic attacks, while nausea and tiredness were less common compared with fluvoxamine (8). This study found that there was a statistical correlation between the daily inositol intake amount and the DOCD score of the participants. There was a statistically significant difference between the daily inositol intake amount and the 'germs and contamination', 'concerns about being responsible for harm, injury or misfortune' and 'concerns about symmetry, completeness, and the need for things to be 'just right" sub-dimensions' scores. No statistically

significant difference was found between the daily inositol intake and the "unacceptable thoughts, examples" sub-dimension score. These results also supported similar studies (1, 8, 20). It also revealed that inositol has therapeutic activity by including OCD in the range of SSRI-responsive diseases including depression, panic attacks (8, 21). Besides, it is advantageous because it has minimal side effects compared to drugs used in psychiatry and did not cause any damage to the organs in long-term use (8, 11).

A study evaluating the therapeutic activity of inositol reported that the inositol concentrations were significantly lower in cerebrospinal fluid (CSF) of both unipolar and bipolar depressive patients compared with healthy control subjects. It was reported that oral administration of a high dose of inositol (6 g/day) could increase the inositol concentration in CSF by up to 70% after approximately 15 years (1). In another study, to evaluate neurochemistry of the frontal cortex in adolescents with symptoms of sleep and depression, MR spectra were acquired from the anterior cingulate cortex (ACC), the dorsolateral prefrontal cortex, and frontal white matter, and the concentrations of N-acetyl aspartate, creatine, choline-containing compounds, glutamine + glutamate and inositol were evaluated and correlated with sleep and clinical measures in the sample of 19 individuals. Sleep was evaluated with self-report questionnaires and ambulatory polysomnography recordings. The concentrations of inositol were found lower in both frontal regions and the cortical region in depressive adolescents compared with the controls. Inositol concentrations in the frontal cortex correlated negatively with depression severity, subjective daytime sleepiness, insomnia symptoms and the level of anxiety. It correlated positively with total sleep time and overall psychosocial functioning (22). This study found a negative correlation between the daily inositol intake and the DOCD score. As the daily inositol intake increases, the DOCD score decreases and vice versa. When similar studies were compared with this study, it was seen that the effect of dietary inositol on DOCS was not limited to a single category and total scale score, but affected almost all categories. It was shown that when comparing with other inositol used as a drug, dietary inositol could also affect the OCD scale score. Several studies supported that inositol has a high availability in nature so people can easily intake it including by their daily diets, it has minimum side effects even no side effect until a certain dose, which all make it appealing for patients who are unsure about taking psychiatric medication (8, 11). Accordingly, since treatment processes take long (≥6 weeks) and foods rich in inositol form the basis for a healthy diet, the diet should be arranged with foods which the individual consume or would consume so that it contains ≤12 g inositol considering the side effects caused by high intake of inositol and the energy requirement and diseases of the individual to make the diet applicable for a long time. In other studies, inositol was administered with drugs or in synthetic form, while in this study, inositol was administered with diet and in natural form. Also, it was administered as a precaution against the disease in the pre-disease stage not to treat the disease. Since it is a patient group being in interaction with drugs, every drug group to be added to daily life will be demanding and costly. Besides, a large number of drugs may wear the patient down, and negatively affect treatment continuity. However, nutrition is essential for the continuity of vital activities, and every individual needs a certain level of energy. If the study results are compatible with other studies, the addition of inositol in a diet with appropriate modifications and methods after testing in patient groups will be less costly and convenient method to enhance the progress of treatment and ensure the continuity of treatment. Consequently, a significant correlation was found between the daily inositol intake and the 'concerns about germs and contamination', 'concerns about being responsible for harm, injury, or bad luck', 'concerns about symmetry, completeness, and the need for things to be "just right' dimensions' scores of the participants. A negative correlation was found between the inositol amount in diet and the DOCD score. The DOCD score was higher in participants with the daily inositol intake of below 1000 mg, while it was lower in participants with the daily inositol intake of 1000 mg and above. No statistically significant correlation was found between the Mediterranean Diet Adherence Scale and the inositol intake amount and the DOCD score. However, further studies are needed on this subject.

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