Polyunsaturated Fatty Acid Intake and Symptom Severity of Patients with Schizophrenia in Ernaldi Bahar Hospital, South Sumatra, Indonesia

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Abstract

Background/Aims: The treatment of schizophrenia is commonly viewed from a pharmacological and social perspective, but issues of nutrient intake are seldom examined. However, the various study reported that polyunsaturated fatty acids (PUFAs) concentration is reduced in the plasma of schizophrenic. Therefore PUFAs intake may have a correlation with symptom severity of schizophrenic. This study aimed to assess the PUFAs intake of schizophrenic and its correlation with symptom severity of of schizophrenic.

Method: This cross-sectional study was conducted on 63 schizophrenia hospitalized patients in Ernaldi Bahar Hospital, South Sumatra, Indonesia. The symptom severity of of schizophrenic were determined using the validated Indonesian version of PANSS. Dietary intake was assessed using a 3-day food weighing. Correlation between variables was determined using the Spearman Correlation Coefficient.

Results: The result showed a significant negative correlation between omega-3 fatty acids and Positive scale, Negative Scale, General psychopathology and risk of aggression with r=-0.345, r= -0.408, r= -0.483, and r= -0.406 respectively ($p<0.01$). The omega-6 fatty acids intake were negatively correlated with Positive scale, Negative Scale, General psychopathology and risk of aggression with r= -0.390, r= -0.496, r=-0.525, and r=-0.389 respectively ($p<0.01$). A statistically significant correlation was seen between ratio of omega-6/ omega-3 and Positive scale, Negative Scale, General psychopathology and risk of aggression with r=0.249, r= 0.256, r= 0.356, r=0.343 respectively ($p<0.01$).

Conclusion: These findings suggest that increasing PUFAs intake might have a positive health outcome in of schizophrenic.

Keywords: *Omega-3, omega-6, ratio of omega-6/omega-3, schizophrenia.*

Introduction

Schizophrenia represent an important public health problem due to their prevalence and associated incapacity. Schizophrenia is a neurodevelopmental and neurodegenerative disorder displaying disturbance in multiple neurotransmission that presents as psychosis, often with paranoia and delusion[(1)]. Symptoms of schizophrenia are classified into positive symptoms, negative symptoms and cognitive symptoms. Positive symptoms include auditory hallucinations, which often criticize or abuse them. These auditory hallucinations can lead to the development of strange beliefs or delusions[(2)]. Negative symptoms are reduced motivation, impoverished speech, blunted affect and social withdrawal[(3)]. Cognitive symptoms have shown as poor executive functioning and working memory. This condition could lead to a suicide attempt in schizophrenic. Suicide mortality rate in schizophrenic is

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higher in this group than in the general population. The lifetime suicide rate among schizophrenic is estimated to be 4% to 10% [4]

Due to the limitations of antipsychotic drugs to achieve adequate rates of clinical remission and functional recovery in schizophrenic have promoted the search for complementary approaches. Recently, the potential of diet and nutrients to improve the mental health of the population and for the treatment of psychiatric disorders being discussed. Previous research suggests that abnormalities myelination and dopamine system have been implicated in schizophrenia, yet the mechanism underlying these abnormalities are not fully [5,6]. Hence PUFAs are essential for neurodevelopment, disturbances of PUFAs metabolism may be involved in the etiology and pathology of neurodevelopmental disorders like schizophrenia. PUFAs are The major constituents of all cell membrane phospholipids and have important role in numerous biological processes including receptor binding, neurotransmission, signal transduction and the synthesis of active metabolites (i.e. eicosanoids) [5,7,8]. Furthermore, previous evidence suggests that PUFA also play a role in myelination[5,9].

The PUFAs have the most functional and are divided into two main types: omega-6 and the omega-3. Arachidonic acid (AA) and docosahexaenoic acid (DHA) are the most abundant fatty acids in the central nervous system. AA, dihomogamma-linolenic acid and eicosapentaenoic acid (EPA) are also important as cell-signaling and enzyme-regulating molecules and as precursors of eicosanoids (prostaglandins, thromboxanes, and leukotrienes). Meanwhile, EPA and DHA showed potential beneficial effects on neuropsychiatric diseases[10,11]. Moreover, The AA/DHA (omega-6/ omega-3) ratio is important in the maintenance of an appropriate level of biological membrane fluidity, which is in turn, essential for ion channel function, membrane receptor activity and the release of neurohormones. Dysfunctional of numerous neurotransmission pathways have been found to be in schizophrenia, which raises the probability that membrane phospholipids that modulate the activity of both receptors and are involved in signal transduction may be implicated of schizophrenia[7]. Since the late 1980s, it has been revealed that PUFA metabolism disturbances in schizophrenic. It has been revealed that deficiencies of PUFA described in red blood cell (RBC) membrane [6,8].

Although, it has been proposed the potential of diet and nutrients to improve the mental health of the population and for the treatment of psychiatric disorders, issues of the nutrient intake of schizophrenic and its correlation psychiatric symptoms in schizophrenia are seldom examined (especially in Indonesia). Therefore, we conducted a study aimed to assess the PUFAs intake of schizophrenic and its correlation with symptom severity of schizophrenic.

Methodology

Study Design and Participants: This cross-sectional study was conducted on 63 schizophrenia hospitalized patients in Ernaldi Bahar Hospital, South Sumatra, Indonesia. Participants with a nasogastric tube and not following all data collection sequences were excluded from the study.

Weighed Food Records: Total daily dietary intake data were collected using a combination of a 3-day record and weighing-back method. Food consumption was then registered by keeping records of amounts served and weighing waste after the meal.

Dietary data were converted into PUFAs intake using the Indonesia fatty acid composition table, Singapore Food Nutrition Composition (Singapore Health Promotion Agency) and Nutrisurvey software.

Symptom Severity of Schizophrenic: Symptomseverity of patients were assessed using Indonesian version of Positive and Negative Syndrome Scale. The assesment was conducted by certified nurse. PANSS consists of 33 items including 7 positive scale items, 7 negative scale items, 16 general psychopathology items, and contains 3 additional points to meet the risk of aggression. PANS is approved by clinicians who are approved and approved on a scale of 1-7 with 1 (none), 2 (minimum), 3 (mild), 4 (moderate), 5 (mild), 6 (severe), 7 (very heavy) with a range of positive and negative scales from 7-49 and range the scale of general psychopathology from 16 to 112.

Statistic Analysis: Only data from subjects completing the study were analyzed. Before analysis, the normality test beforehand on all variables used the Kolmogorov-Smirnov test. Correlation between PUFAs intake (Omega-3; Omega-6; Ratio of Omega-6/ Omega-3) and Psychiatric symptoms (Positive scale; Negative Scale; General psychopathology; Risk of aggression) were tested using the Spearman Correlation Coefficient.

Result

Respondent Characteristics: Characteristics data showed in this study showed that 43 respondents (68.3%) are male and 20 respondents (31.7%) are female. Mean age of the respondent was 36.5 years old with 20 years old for the youngest and 59 years old for the oldest.

PUFAs Intake: This study found that the majority of respondents had an average intake of omega-3 fatty acids that were sufficient and exceeded the recommended adequacy of omega-3 fatty acids with minimum intake 0.5 g and maximum 3.5, meanwhile mostly respondent have omega-6 intake was below the recommended adequacy rate with minimum intake 3.5 g and maximum 16.4 g.

Table 1: PUFAs Intake

PUFA	Median (min-max)
Omega-3 (g/day)	1.20 (0.5-3.5)
Omega-6 (g/day)	6.20 (3.5-16.4)
Ratio of Omega-6/Omega-3	5.00:1 (1.4:1 - 7.6: 1)

The ratio of omega-6 / omega-3 ratio data were obtained from the comparison of omega-6 and omega-3 fatty acid intake of respondents. The distribution of ratio of omega-6 / omega-3 respondents can be seen in the Table 1. A lower n-6 to n-3 PUFAs ratio (ideal ratio around 2:1) consumption has been recommended in order to reduce the formation of pro-inflammatory eicosanoids from omega-6 and to increase the production of anti-inflammatory mediators from omega-3[13].

Psychiatric Symptoms: Several previous studies suggest that the negative symptoms of schizophrenia, including social withdrawal, lack of motivation; decreased affective responsiveness, impoverished speech, and movement, contribute more to poor quality of life and functional outcomes for individuals with schizophrenia than do positive symptoms [15,17]. The result of psychiatric symptoms assessment using PANSS showed in table 2.

Table 2: Psychiatric symptoms

Symptom Severity of schizophrenic	Median (min-max)
Positive scale	14 (7-48)
Negative Scale	13 (7-31)
General psychopathology	33 (18-59)
Risk of aggression	6 (3-15)

Correlation between PUFAs intake with PANSS score: EPA and DHA, play important roles in the development and maintenance of normal central nervous system (CNS) structure and function. Evidence has emerged over the last three decades which suggests that the fatty acid composition of the habitual diet may be relevant to the pathophysiology and potentially etiology of neuropsychiatric disorders including schizophrenia[12,19,20].

Table 3: Correlation between PUFAs intake andsymptom severity of schizophrenic

PUFA	Positive scale	Negative Scale	Generalpsychopathology	Risk of aggresion
Omega-3 (g/day)	-0.345*	-0.408*	-0.483*	-0.406*
Omega-6 (g/day)	-0.390*	-0.496*	-0.525*	-0.389*
Ratio of Omega-6/Omega-3	0.249*	0.256*	0.356*	0.343*

* Significant with *p value*<0 .01

Therefore, we conducted a correlation test between PUFAs intake and symptom severity of schizophrenic (presented in PANSS score). The result showed a significant negative correlation between omega-3 fatty acids and Positive scale, Negative Scale, General psychopathology and risk of aggression. The omega-6 fatty acids intake were negatively correlated with Positive scale, Negative Scale, General psychopathology and risk of aggression. A statistically significant correlation was seen between ratio of omega-6/omega-3 and Positive scale, Negative Scale, General psychopathology and risk of(Table 3).

Discussion

PUFA's dietary deficiency and its metabolism abnormalities have beenlong implicated in the pathophysiology and etiology of recurrent mood disorders including schizophrenia. Previously researchs have provided converging evidence implicating PUFAs insufficiency, and increases omega-6/omega-3 ratio, in

the pathophysiology of mood disorders[19]. Low level of membrane and erythrocite PUFAs have been observed in schizophrenic[1,21]. Meanwhile, Omega-3 fatty acids EPA and DHA are derived from ALA and are dietary essential fatty acids[22]. Hence improve omega-3 intake may reduce psychiatric symptoms in schizophrenicby speeding up the response to treatment and the tolerability of commonly used antipsychotic drugs due to changes in neurotransmission[23,24].

Previous studies also showed that omega-3 and omega-6 fatty acids in the erythrocyte membranes correlated significantly with improvement in PANSS sub-scale scores [25]. Recent studies discussed the possibility that omega-3 fatty acid and dopamine system represent different aspects of the same etiology and pathology of schizophrenia[6,12].

The dopamine system consists of 4 dopaminergic pathways. The nigrostriatal dopamine pathway projects from dopaminergic cell bodies and ends in the caudate nucleus. Low dopamine levels within this pathway are thought to affect the motor organs. The mesolimbic pathway, extending from the ventral tegmental area of the brainstem to axon terminals in limbic areas, plays an important role in the positive symptoms of schizophrenia in the presence of excess dopamine. The mesocortical pathway extends from the ventral tegmental area of the brain stem to the frontal cortex. Low mesocortical dopamine levels cause negative symptoms and cognitive deficits in schizophrenia. The tuberoinfundibular pathway extends from the hypothalamus to the pituitary gland. Normally, the prefrontal dopamine system suppressively controls the limbic dopamine system[6,12,15,26]. Previous research predicts that decrease dietary omega-3 fatty acids cause changes in the double layer of cell membrane phospholip. This changes may decrease dopamine concentration in the frontal lobe[6,12]. This mechanism might explain the relevance of omega-3 fatty acids intake and psychiatric symptoms schizophrenia.

Another PUFAs beside omega-3 also have a critical role in brain development and maintenance of brain structure and function such as omega-6. Previous studies showed that sufficient levels of omega-6 (especially AA) are required to improve neurological health[9]. Meanwhile, AA concentration is found reduced in peripheral blood measures of schizophrenic[5,21]. This condition suggests that increase AA intake may have a positive impact on psychiatric symptoms in schizophrenic. The beneficial effects of omega-3 fatty acids in psychiatric disorders are well publicized, but the omega-6 fatty acids role are seldom discussed. However, these fatty acids (omega-3 and omega-6) are proven involved in the production of eicosanoids and affect the membrane fluidity, by their incorporation into membrane phospholipids[13].

Hence the same enzymes are involved in the generation of long chain n3-PUFAs and long chain n6-PUFAs, ALA and LA and their respective metabolites compete for the same enzymatic machinery. In consequence, high levels of LA may inhibit the conversion of ALA to long chain n3-PUFAs and vice-versa. Consequently, there are strong indications that an increased ratio of omega-6 to omega-3 may reduce the availability of omega-3, which triggers oxidative stress that involved in the pathogenesis of depression[9,20].

Previous study showed that increase omega-6 to omega-3 ratio may be induce of a pro-inflammatory response. Therefore a stronger inflammatory response may increase the production of free radicals and reduce PUFA levels. Reduced anti-inflammatory activity may be involved in negative symptoms and cognitive impairment observed during the acute stages of schizophrenia episodes[27]. Consistent with previous research, the result of our study also showed that the ratio of omega-6 to omega-3 intake has a significant positive correlation and PANSS score.

Conclusion

Nutritional intervention through adequate and balanced intake ofPUFAs might decrease thesymptom severity of schizophrenic which can be seen based on PANSS score, but the improvement inPANSS score is also inseparable from pharmacological and psychological intervention.

Competing Interest: There is no competing interest in conducting this research.

Ethical Clearance: Ethical Approval from Ethics committee of Universitas Esa Unggul was taken (No. 0337-18.327/PKE-KEP/FINAL-EA/UEU/VIII/2018).

Source of Funding: This research was self-funded

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