Comparison of folic acid levels in schizophrenic patients and control groups

C C Arthy1*, M M Amin1 and E Effendy1

1Department of Psychiatry, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia
*Corresponding author: ccarthy15@gmail.com

Abstract. Folic acid deficiency is a risk factor for schizophrenia through epidemiology, biochemistry and gene-related studies. Compared with healthy people, schizophrenic patients may have high homocysteine plasma values and homocysteine or low levels of folic acid, which seems to correlate with extrapyramidal motor symptoms caused by neuroleptic therapy and with symptoms of schizophrenia. In this present study, we focus on the difference of folic acid level between schizophrenic patient and control group. The study sample consisted of schizophrenic patients and 14 people in the control group and performed blood sampling to obtain the results of folic acid levels. The folic acid level in both groups was within normal range, but the schizophrenic patient group had lower mean folic acid values of 5.00 ng/ml (sb 1.66), compared with the control group with mean folic acid values of 10.75 ng/ml (sb 4.33). there was the group of the control group had a higher value of folic acid than the schizophrenic group.

1. Introduction
Schizophrenia is a debilitating condition, affecting 1% of the population worldwide. Symptoms of schizophrenia are positive and negative symptoms; including hallucinations, paranoia, delusion, dull affects, and social withdrawal.[1]

Vitamin therapy may be useful for schizophrenic patients by preventing or reversing symptoms of vitamin deficiency disease or by normalizing regular brain metabolism when administered in higher doses than is needed to prevent deficiency.[2]

The first study of the incidence of folic acid deficiency in psychiatric patients, proposed by Carney, measuring folate serum levels in 423 patients admitted to the mental hospital ward. The author says that the high incidence of folate deficiency occurs in patients with depression (29-30%), organic psychosis (24%) and schizophrenia (20%).

Folic acid metabolism is a major mechanism in a carbon metabolism that interacts with the methionine cycle and the transmatalation reaction. Studies measuring folic acid serum levels in schizophrenic patients consistently found significantly lower rates in those with the disorder than those of control group.[1]

Folic acid deficiency can have various effects on schizophrenic neurochemistry, as a single carbon donor in the synthesis of glycine and serine. Folate is converted to 5-methyltetrahydrofolate (5-MTHF) by methylenetetrahydrofolatereductase (MTHFR); 5-MTHF is an active form that serves as a methyl (carbon single) donor for various pathways. 5-MTHF is combined with B12 to form the chemical structure required for the synthesis of methionine from homocysteine. Methionine in turn is
necessary for the synthesis of S adenosylmethionine (SAM) which is a methyl donor for various biochemical reactions that affect brain development and function, including DNA and RNA synthesis, DNA methylation (which regulates access to transcriptional evidence) and synthesis of amino acids and monoamines, including neurotransmitters involved in negative and positive symptoms in schizophrenia.[3,4]

2. Method

2.1. Study design & Patients characteristics
This study was analytic numerical unpaired using cross-sectional with 28 subjects of research divided into two groups, consisting of 14 people who are schizophrenic patients who went to the Outpatient Installation of Mental Hospital Prof. M. Ildrem, Medan and 14 people who are the control group. The sample in this study was by consecutive sampling.

In all subjects, approval needs their participation in the study (informed consent). For samples from schizophrenic patients in this study should meet inclusion criteria: Male and female patients aged 18-55 years who were with schizophrenia based on PPDGJI-III criteria had received antipsychotic treatment for six weeks, a total score of 60 or more in Positive and Negative Syndrome Scale (PANSS). Exclusion Criteria: Patients taking folate or vitamin supplements during the last three months have a history of neurological disorders and other medical conditions, patients being pregnant or breastfeeding. As for the control group, inclusion criteria: male and female subjects with age group 18-55 years who were not diagnosed with schizophrenia based on PPDGJI-III criteria and exclusion criteria: subjects were taking folate or vitamin supplements during the last three months has a history of neurological disorders and other general medical conditions, has a history of substance use and/or substance abuse, the patient is pregnant or lactating.

2.2. Blood sample
Way to take blood: a blood sample is taken once, which is around 8-10 am. Blood was taken through median cyst vein of cubiti as much as threecc. Blood is immediately deposited then centrifugation is done and measured levels of folic acid.

3. Results and Discussion
From table 1, the sample is dominated by age group 31-45 years old with 8 subjects (57.1%), while in the control group as many as 14 subjects (100%) were 18-30 years old. For the sex characteristics of schizophrenic patients, the same number was between male and female (50%; 50%), whereas in the control group, female sex was the most subject, ten subjects (71.4%).

Table 1. Categorical demographic.

| Categorical Demographic | Schizophrenic Patients | Control Group |
|-------------------------|------------------------|---------------|
|                         | (n=14) | % | (n=14) | % |
| Age                     |        |   |        |   |
| 18 - 30 yr              | 3      | 21.4 | 14      | 100.0 |
| 31 – 45 yr              | 8      | 57.1 | 0       | 0 |
| 46 - 55 yr              | 3      | 21.4 | 0       | 0 |
| Gender                  |        |   |        |   |
| Male                    | 7      | 50.0 | 4       | 28.6 |
| Female                  | 7      | 50.0 | 10      | 71.4 |

Table 2. Mean difference of folic acid content.

| Folic Acid | Average | Average Difference (IK95%) |
|------------|---------|---------------------------|
| Control Group (n=14) | 10.750 (4.33) | 5.74 (3.19 – 8.29) |
| Schizophrenic Patients (n=14) | 5.007 (1.66) |                      |
The difference in folic acid yield between schizophrenic patients and the control group was between 3.19 and 8.29.

4. Conclusion
This study is a study comparing folic acid levels between schizophrenic patients and the control group. The mean value of folic acid levels in the group of schizophrenic patients and control group are in table 2. Folic acid levels in both groups were within normal range, but the schizophrenic patient group had lower mean folic acid values of 5.00ng/mL, compared with the control group with mean folic acid values of 10.75ng/mL. The differences in the results of folic acid among schizophrenic patients and the control group were between 3.12 and 8.36.

In this study, there is the group of the control group had a higher value of folic acid than the schizophrenic group. The results of this study have similarities with previous studies by Koren et al, Studies of 70 psychiatric patients in Canada, reported that psychiatric patients, both male and female, both tend to have lower serum folate levels than the population generally.[5] Kim & Moon from Korea reported, most groups of schizophrenic patients had low levels of folate, whereas the normal control group had high or normal folate levels.[6]

Compared with healthy people, schizophrenic patients may have high homocysteine plasma values and homocysteine or low levels of folic acid, which seems to correlate with extrapyramidal motor symptoms caused by neuroleptic therapy and with symptoms of schizophrenia.[3]

In this study, there was a significant difference in the results of folic acid levels between schizophrenic patients and the control group. Schizophrenic patients who have low levels of folic acid may be given folic acid therapy to improve the extent of the adequacy of folic acid. This study is expected to be a preliminary feature for further research and can be developed to assess the effect of folic acid on whether it is associated with positive and negative symptoms in schizophrenic patients.

References

[1] Arrol M, Wilder L and Neil J 2014 Nutritional interventions for the adjunctive treatment of schizophrenia: a brief review *Nutr. J.* **13** 1-9
[2] Hoffer L 2008 Vitamin therapy in schizophrenia *Isr. Psychiatry Relat. Sci.* **45** 3-10
[3] Stanger O, Fowler B, Pietrzik K, Huemer M, Haschke-Becher E, Semmler A, Lorenzl S and Linnebank M 2009 Homocysteine, folate and vitamin B12 in neuropsychiatric diseases: review and treatment recommendations *Expert Rev. Neurother.* **9** 1393-412
[4] Borba C, Fekadu A, Teferra S, Bekele D, Shibre T, Oppenheim C, Biresaw S, Mulugeta A, Schoenfeld D and Henderson D 2014 A placebo-controlled trial of folate with B12 in patients with schizophrenia with residual symptoms in Ethiopia using a sequential parallel comparison design *Br. J. Med. Med. Res.* **4** 4090-104
[5] Koren G, Cohn T, Chitayat D, Kapur B, Remington G, Reid D and Zipursky R 2002 Use of atypical antipsychotic during pregnancy and the risk of neural tube defects in infants *Am. J. Psych.* **159** 136-7
[6] Kim T and Moon S 2011 Serum homocysteine and folate levels in korean schizophrenic patients *Psychiatry Investig.* **8** 134-40