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Research Article

Analysis Factor Contributed BDNF Level Serum in Schizophrenia Patients During Antipsychotic Treatment at Reksodiwiryo Army Hospital and Siti Rahmah Islamic Hospital Padang Indonesia

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ABSTRACT

Schizophrenia is a debilitating and long-lasting psychiatric condition characterized by its severity. The main causes of this disorder are still complex and not fully understood. Schizophrenia is a serious and lifelong psychiatric condition, is estimated to affect around 1% of the population throughout their lifetime. This study aims to determine the contribution of serum Brain-derived neurotrophic (BDNF) levels in schizophrenia patients during antipsychotic treatment at Reksodiwiryo Army Hospital and Siti Rahmah Islamic Hospital, Padang, Indonesia. Duration of antipsychotic treament range 1 year to 10 years. The method used in this research was a random perspective approach and consecutive sampling for patients undergoing outpatient treatment at the Reksodiwiryo Army Hospital and Siti Rahmah Islamic Hospital, Padang City, Indonesia. The sample consisted of 43 patients diagnosed with schizophrenia through structured clinical interviews (mini ICD 10). The results obtained in this study were that of the 43 total patients observed, sociodemographics were found with women (51.2%) being more numerous than men (48.8%), the age of most patients encountered was in the age range of 36-25 years (28%) and duration of illness <5 years (34.9%) is smaller than >5 years (65%), for various treatments ranging from FGAs, SGAs and combination of FGAs and SGAs where the highest results were found in patients with SGAs treatment (37.2%). From the statistical analysis, the correlation between serum BDNF levels was insignificant with negative and positive symptoms.

Keywords: Brain-derived neurtopic factor, negative symptoms, positive symptoms, schizophrenia.

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INTRODUCTION

Schizophrenia is a debilitating and long-lasting psychiatric condition characterized by its severity. The main causes of this disorder are still complex and not fully understood. Schizophrenia is a serious and lifelong psychiatric condition, is estimated to affect around 1% of the population throughout their lifetime.[1] It has identified patterns for key circuits, particularly the frontal, temporal, and mesothelial brain regions, in the development of positive, negative, and cognitive symptoms.[2] Generally identified in the early stages of adulthood, this condition is associated with a reduced life expectancy of approximately 15 years.[3] Pharmacotherapy, as the main therapeutic method, and psychosocial therapy, as its complement, effectively target several symptom dimensions, while most symptoms persist regardless of the treatment modality.[4-6]

The diagnosis of schizophrenia is determined by evaluating a series of clinical criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders-V and the International Classification of Diseases-10. This diagnostic process does not involve objective laboratory testing.[7] The absence of standardized, unbiased instruments has prompted an increased focus on investigating potential biomarkers to diagnose and manage schizophrenia. There is a wealth of information explaining the involvement of brain-derived neurotrophic factor (BDNF) in many processes, such as neural development, regeneration, survival, and maintenance in the brain. Furthermore, this evidence suggests a potential link between BDNF and the pathophysiology of schizophrenia.[8, 9] Most existing literature on this subject extensively examines the biological implications of brain-derived neurotrophic factors in schizophrenia.[10]

BDNF plays important roles in various aspects of neuronal function in the adult brain, including neuronal plasticity, apoptosis, neurotransmitter regulation, and survival of dopaminergic, cholinergic, and serotonergic neurons. These neural populations have been implicated in the processes underlying memory and cognitive changes observed in individuals with schizophrenia, as previous research has shown.[11, 12] Brain-derived neurotrophic factor (BDNF) has been found to facilitate many cellular and molecular processes associated with neurotransmitter release.[7] Brain-derived neurotrophic factor (BDNF) is a neurotrophin that has been extensively investigated and is known for its widespread presence in both the peripheral and central nervous systems. Brain development includes various aspects such as neurogenesis, neural differentiation, maturation, and survival.[13, 14] Abnormal BDNF activity can result in changes in nerve cell growth, viability, adaptability, and synaptic connections. There is a proposition indicating that changes in plasticity and neurotransmission have an important role in the impairment of higher cognitive processes observed in individuals with schizophrenia.[15]

BDNF has been suggested as a potential biomarker for schizophrenia and cognitive recovery.[16] It is widely recognized for its significant involvement

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in the development and maintenance of the central nervous system.[16] According to Bathina and Das (2015), it appears that this particular factor plays a role in the processes of neural differentiation, maturation, and survival.[17] Furthermore, it is known that this factor exhibits neuroprotective impacts in challenging circumstances, such as glutamatergic stimulation, cerebral ischemia, hypoglycemia, and neurotoxicity. The involvement of BDNF in learning and memory processes has been demonstrated in previous research.[18] BDNF influences neural plasticity by activating intracellular signaling cascades via the TrkB receptor.[19] Recent neuroimaging studies suggest that there may be a link between changes in brain-derived neurotrophic factor levels in individuals with schizophrenia and changes in the structural connectivity required for cognitive processes. Specifically, increased concentrations of BDNF have been observed in brain regions experiencing tissue damage.[18] This suggests that dysregulated BDNF levels in schizophrenia may reflect impaired compensatory mechanisms to repair damage, which in turn inhibits the ability to induce neuronal plasticity and dendritic growth. This dysfunction is thought to be related to the typical dysfunctional signaling pathways observed in individuals with schizophrenia.[20, 21]

Therefore, several studies have addressed the possible role of BDNF in neuropsychiatric disorders, including schizophrenia spectrum disorders (SCZ). The latter is a severe neuropsychiatric disorder associated with gradual impairment in multiple domains of functioning.[22] Its neurodevelopmental component appears prominent, and although the first episode of psychosis is generally observed in late adolescence or early adulthood, it is often preceded by prodromal symptoms that include nonspecific changes in mood and behavior[23], social withdrawal, and cognitive symptoms.[24] Neuroinflammation may be a key player in the pathophysiology of SCZ. Indeed, one mechanistic hypothesis involves the interaction of dysregulated cytokine levels and BDNF modulation.[25] Increased pro-inflammatory cytokines have been associated with decreased BDNF gene expression, which may impact cognitive decline in patients with SCZ.[26] The potential relationship between serum BDNF levels and SCZ has been examined in a variety of studies, and a large number of studies found reduced BDNF levels in these patients.[27-29] This is the background for the author to conduct research regarding serum BDNF levels in schizophrenia patients during antipsychotic treatment at the Reksodiwiryo Army Hospital and the Siti Rahmah Islamic Hospital, Padang, Indonesia.

MATERIALS AND METHODS

This study used consecutive sampling of patients undergoing outpatient treatment at Mental Health Clinic of Reksodiwiryo Army Hospital and Siti Rahmah Islamic Hospital, Padang City, Indonesia. This research has received ethical clearance from the Research and Health Ethics Commission of the Faculty of Medicine, Universitas Baiturrahmah (ethic number: No: 040/ETIK-FKUNBRAH/03/02/2023). The sample consisted of 43 patients were diagnosed with schizophrenia through structured clinical interviews using mini ICD 10 regarding their age, length of treatment, and medications recommended by health workers at the hospital. Patients used in this study must meet the criteria of inclusion. 1) Schizophrenia patients in the outpatient clinic at Padang City Hospital Psychiatric Clinic, namely Reksodiwiryo Army Hospital and Siti Rahmah Islamic Hospital; 2) The patient has received antipsychotic therapy for more than three months. Antipsychotis were used to treat patient are divided into two classes, the first generation antipsychotics (FGA). FGA were haloperidol and trifluoperazine. Second Genertaion Antipsychotis (SGA) were clozapine, olanzapine and risperidone; 3) The patient is willing to voluntarily serve as a research subject by signing an informed consent. For exclusion criteria: The patient was possessing an unstable mental state, experiencing other mental health issues, suffering from neurological conditions, and having a history of alcohol and other drug use aside from tobacco use.

At first, patients were screened using inclusion and exclusion criteria. Patients who met the inclusion and exclusion criteria were asked if they could participate in the study to get informed consent. Then, the subject's demographic information was completed, and the PANSS score evaluation of the study topic was carried out. Next, BNDF levels in serum were assessed using the ELISA KIT, which was carried out at the Biomedical Laboratory, Faculty of Medicine, Baiturrahmah University. Blood samples were collected 3 mL from the Median cubital vein for serum BDNF analysis using the ELISA Method (Merck, Saint Louis, USA) and used as manufacturer protocol. BDNF was calculated based on a standard curve and the ELISA assay performed duplicated with a minimum detectable dose of Human BDNF was determined to be 80 pg/ml, inter-assay: CV< 10% and intraassay: CV<12%.

Statistical analysis

The research uses the method of cross-sectional analysis statistic software SPSS. It is analyzed using descriptive and analytic analyses including frequencies, mean and standard deviations with percentage (for qualitative data), Paired t Test, Pearson Correlation Test (r), One Way ANOVA Test (F).

RESULT AND DISCUSSION

The participation of 43 SCZ patients regarding the interview results related to the patient's sociodemographic and clinical profile can be seen in the table.

Sociodemographic and clinical data from the sample are in Table 1. The highest number of SCZ patients found were women (51.2%), for the highest average age, namely in the age range 26-35 years (28), with general patients having been diagnosed later, from 5 years. For self-treatment, patients varied from First-generation antipsychotics (FGAs), and Second-generation antipsychotics (SGAs) to a combination, for patients with the most treatment using SGAs, namely (37.2%). Based on the mechanism of action, antipsychotics are divided into two groups, namely dopamine receptor antagonists (DRA) or generation I antipsychotics (APG-1) and serotonin-dopamine antagonists (SDA)

Table 1: The demographic characteristics of the research subject.

Characteristics	f	%
Gender		
Woman	22	51.2
Man	21	48.8
Age		
17-25 years old	6	14
26-35 years old	10	23.2
36-45 years old	12	28
46-55 years old	11	25.6
1-65 years old	3	7
>65 years old	1	2.2
Long time sick		
<5 years	15	34.9
>5 years	28	65.1
Treatment		
FGAs	2	4.7
SCAs	16	37.2
FGAs combination	1	2.3
SGAscombination	11	25.6
Combination of FGA and SGA	13	30.2

Table 2: Serum BDNF levels.

Variable	Mean
BDNF Serum	8.18
Negative Symptoms	21.33
Positive Symptoms	10.67
Onset of Illness	29

Table 3: The Correlation between BDNF and PANSS.

Score	Coefficient Correlation (r)	p
BDNF with negative symptoms	0.3	0.09
BDNF with positive symptoms	0.1	0.37
BDNF with onset of illness	0.03	-

or generation II antipsychotics (APG-II). Generation I antipsychotic drugs are also called conventional or typical antipsychotics, while generation II antipsychotics are called new or atypical antipsychotics.[30]

The analysis of data presented in Table 3 reveals the absence of a statistically significant connection between serum BDNF levels in individuals diagnosed with schizophrenia (SCZ) and the presence of negative or positive symptoms.[1, 31, 32] Previous studies reported no significant association between peripheral BDNF levels and PANSS scores.[33, 34] According to another study, it was shown that there was a significant decrease in PANSS scores among psychotic patients following six weeks of antipsychotic medication. Nevertheless, Pirildar et al. (2004) found no significant correlation between PANSS scores and peripheral BDNF levels.[35] The findings presented in this study provide further support for the conclusions drawn in a recent meta-analysis conducted by Fernandes et al. (2015)[36], which found no significant correlation between levels of serum and plasma BDNF and PANSS scores. However, earlier research has indicated a notable correlation between PANSS scores and BDNF levels, as demonstrated by Pillai et al. (2010).[37]

Rizos et al. (2008) discovered a noteworthy inverse relationship between serum brain-derived neurotrophic factor (BDNF) levels and scores on the positive and negative subscales of the Positive and Negative Symptoms Scale (PANSS) in a cohort of drug-naïve individuals experiencing their first episode of schizophrenia (SCZ).[38] On the other hand, a separate study conducted by Cui et al. (2012) reported elevated BDNF levels in individuals with greater positive PANSS scores.[39] The observed disparities in the outcomes of prior investigations can be ascribed to the clinical diversity inherent in the participant cohorts employed in these studies. Furthermore, various factors, including the treatment status of patients, the duration of the disease, the clinical subtype of schizophrenia (SCZ)[40, 41], and the medium used for measuring brain-derived neurotrophic factor (BDNF) levels (serum or plasma), may potentially impact the assessment of the association between the severity of psychopathological symptoms and BDNF levels.[22, 42]

Zhang et al. (2010) have suggested that the augmentation of brain-derived neurotrophic factor (BDNF) levels can potentially mitigate the neurodegenerative mechanisms associated with schizophrenia.[43] This proposition is based on the understanding that deficiencies in BDNF can contribute to alterations in both the structural and functional aspects of the brain, which are implicated in the manifestation of schizophrenia's psychopathology.[44, 45] The etiology of schizophrenia has been associated with neurodevelopmental defects and dysregulation of the dopamine system. Hence, it may be inferred that BDNF has the potential to serve as an indicator of atypical neurodevelopment and neurotransmission in individuals with schizophrenia, as shown by Huangf et al. (2008).[46-48] The measurement of serum BDNF levels is commonly conducted in many psychiatric diseases, and the utilization of BDNF is implicated in therapeutic interventions for numerous psychiatric disorders.[49, 50] Various factors have been found to influence BDNF, including but not limited to gender, smoking behaviors, and body mass index (BMI). The participants included in this investigation were male patients, as other studies have indicated that gender impacts serum BDNF levels. Estrogen plays a multitude of roles throughout the central nervous system. The survey conducted by Pluchino et al. (2013) demonstrated that estrogen can modulate the expression of brain-derived neurotrophic factor (BDNF) by interacting with the estrogen response element located within the BDNF gene.[51-54] In a separate study, Sen et al. (2008) showed that the effects of testosterone on neuronal survival facilitated BDNF.[55]

There is a lack of evidence to suggest that the observed increases in BDNF levels were influenced by a sense of "stress". Both the enjoyment ratings and observations made by laboratory personnel did not indicate that the cognitive training, which resembles a game, was perceived as more stressful compared to the commercial computer games. It remains uncertain whether there would be an observed rise in BDNF in other cognitive remediation methods or as a potential reaction to effective behavioral or pharmacological cognitive interventions.[49]

CONCLUSION

Schizophrenia patients undergoing antipsychotic treatment were seen from the serum BDNF levels. There was no correlation between positive symptoms and BDNF level serum. Likewise, there was no correlation between negative symptoms and BDNF level serum. Limitation of this study is the small number of research samples. The sample was administered medications for a period of time that was relatively broad—more than 3 months to 10 years. In the future, further research needs to be carried out on observing serum BDNF levels in schizophrenia patients from the start of treatment to several weeks of observation so that it can be seen whether there is a decrease or increase in serum BDNF levels.

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