REDUCTION OF DRD2 MRNA EXPRESSION IN SCHIZOPHRENIA PATIENTS AFTER THE TECHNICAL INTERVENTION OF SPIRITUAL QUR'ANIC EMOTION FREEDOM

Lilin Rosyanti¹, Indriono Hadi¹, Jayalangkara Tanra², Mochammad Hatta³, Muhammad Nasrum Massi³, Andi Asadul Islam⁴
¹Department of Nursing, Poltekkes Kemenkes Kendari, Indonesia
²Department of Psychiatry, Hasanuddin University, Makassar, Indonesia
³Department of Medical Microbiology, Hasanuddin University, Makassar, Indonesia
⁴Department of Medical Neurosurgery Hasanuddin University, Makassar, Indonesia
¹lilin6rosyanti@gmail.com

ABSTRACT

To determine the effect of SQEFT therapy on decreasing DRD2 mRNA gene expression in schizophrenic patients. A quasi-experimental study was conducted at the Mental Hospital of Southeast Sulawesi Province, Indonesia. The research begins from March to August 2018, consisting of schizophrenic patients divided into two experimental and control groups with the same A and B, and one healthy control group C, composed of ordinary healthy people. Schizophrenic patients in group A were given therapeutic intervention SQEFT. No intervention was conducted in control groups B and C. Data were analyzed using SPSS 20. After SQEFT intervention group A, there was a decrease in the expression of DRD2 mRNA gene (P <0.005) Mean score (2.63 ± 1.74). There was a difference in group A and group B after the intervention (p = 0.000), the expression level of DRD2 mRNA gene was lower in group A. There was no difference between group A and group C (p-value = 0.334), the level of expression of the DRD2 mRNA gene in the group. An after SQEFT therapy was the same as in healthy control group C, it became normal. SQEFT intervention can reduce the expression level of DRD2 mRNA in schizophrenic patients and is well-tolerated, suitable for chronic psychiatric inpatients.

Keywords: SQEFT, Schizophrenia, Gene Expression, DRD2

I. INTRODUCTION

Schizophrenia is a severe chronic mental illness associated with brain and behavioral disorders, impact perception, cognition, and social function [1]. In Indonesia, cases of schizophrenia mental disorder reach 400,000 people or 1.7/1,000 population [2]. The etiology and pathophysiology of schizophrenia remain unclear. Diagnosis is based on problematic clinical symptoms. The application of easily detectable peripheral molecular indicators can substantially help diagnose mental disorders [3]. A hypothetical model was developed between schizophrenia and the dysregulation of the dopamine receptor pathway. Dopamine (DA) is a neurotransmitter that modulates central nervous system functions, such as movement, appreciation, cognitive function, motivation, learning, and goal-oriented behavior [4].

Dopamine serves as an essential neuromodulator in synaptic plasticity processes that affect dopaminergic (tonic and fascia) signals to different nervous systems, such as the basal ganglia, prefrontal cortex [5]. Some dopaminergic neurotransmission components can cause excess dopaminergic activity, such as synthesis, release, increased DA affinity receptors, and effector main segment mechanisms. Positive symptoms of schizophrenia are associated with hyperdopaminergic neurotransmission in the mesolimbic dopamine pathway. In contrast, negative symptoms and cognitive deficits are caused by hypodopaminergic activity in the Dopamine D2 receptor isocortex pathway (DRD2) [6].

It is needed a different therapy approach that helps reduce dopamine hyperactivity to the patient with schizophrenia, and one of the approaches is spiritual therapy. Spiritual therapy is part of nursing intervention. The holistic nursing perspective makes nurses view each patient as a biopsychosocial and spiritual creature who should implement
spirituality in research, treatment, and nursing [7]. SQEFT (Spiritual Qur'anic Emotional Freedom Technique) combines spiritual intervention that combines Quranic therapy and EFT. This combination intervention is expected to be an intervention for mental health practitioners (doctor, nurse, psychologist), the patient's family, and society. The instrument test has been conducted as an additional therapy for the patient with schizophrenia [8].

Al-Qur ‘an therapy is the healing and treatment of Muslims’ physical, spiritual, and social diseases [9]. Reading and listening to the Koran naturally creates a calming effect, promotes relaxation; eliminate negative physical and mental disorders; stimulates the release of endorphins in the brain, which have a positive impact on mood and thoughts; increase concentration; reduce stress, anxiety, depression; and become a nonpharmacological treatment to complement existing therapies [10]. EFT is a set of methods oriented towards the body's energy systems for releasing emotional and physical stress. EFT intervention stimulates neurotransmitters. The presence of tapping on meridian points stimulates the body to release endorphins and monoamines, which control pain, promote relaxation, and provide kinesthetic energy. Furthermore, there are suggestions of sentences that make individuals surrender, accept, and give thanks to Allah for the conditions they are experiencing [11].

### II. METHODS

Research of The SQEFT therapy was conducted in March-August 2018 for 30 days. Criteria Study subjects were those diagnosed with schizophrenia based on IV diagnostic statistics (DSM-IV); undergoing treatment in a mental hospital, examining the initial value of the BPRS ≤ 60; supporting criteria, good communication, calm, cooperative, and willing to be respondents. Approval was obtained from the medical ethics committee at Hasanuddin University, Makassar, Indonesia. Subject; The 20 schizophrenic patients were divided into two groups; group A: who received SQEFT therapy (n = 10), and group B: Control who did not receive SQEFT therapy (n = 10), and group C: healthy control subjects (n = 10). For group A schizophrenia, before and after the SQEFT intervention, the expression level of DRD2 mRNA was assessed, and after 30 days of SQEFT therapy, the DRD2 mRNA level was measured again. Then the results were compared between groups B and C.

Furthermore, the demographic and clinical characteristics of the subject were shown in Table 1.

<table>
<thead>
<tr>
<th>Characteristic (Mean ± SD)</th>
<th>Schizophrenia of SQEFT (n=10)</th>
<th>Schizophrenia of Non-SQEFT (n=10)</th>
<th>Healthy control (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>1.60±0.51</td>
<td>1.50±0.52</td>
<td>1.50±0.52</td>
</tr>
<tr>
<td>Age (year)</td>
<td>2.00±0.81</td>
<td>2.40±1.72</td>
<td>1.80±0.78</td>
</tr>
<tr>
<td>Education</td>
<td>3.00±0.94</td>
<td>2.90±0.73</td>
<td>1.30±0.48</td>
</tr>
<tr>
<td>Occupation</td>
<td>1.80±0.42</td>
<td>1.90±0.31</td>
<td>1.30±0.48</td>
</tr>
<tr>
<td>Ethnic</td>
<td>2.80±1.68</td>
<td>3.90±2.02</td>
<td>3.10±1.37</td>
</tr>
<tr>
<td>Marital Status</td>
<td>1.50±0.52</td>
<td>1.60±5.16</td>
<td>1.30±0.48</td>
</tr>
<tr>
<td>Long time in illness</td>
<td>1.50±0.70</td>
<td>1.70±0.82</td>
<td></td>
</tr>
<tr>
<td>Relapse</td>
<td>2.30±1.15</td>
<td>2.50±1.08</td>
<td></td>
</tr>
<tr>
<td>BPRS pre-SQEFT</td>
<td>51.70±2.49</td>
<td>59±1.33</td>
<td></td>
</tr>
<tr>
<td>BPRS post SQEFT</td>
<td>22.70±0.82</td>
<td>56.4±1.42</td>
<td></td>
</tr>
</tbody>
</table>

BPRS grading was conducted twice, before and after therapy of SQEFT.

**SQEFT Program Protocol.**

<table>
<thead>
<tr>
<th>Week</th>
<th>Program Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beginning</td>
<td>- Introduction,</td>
</tr>
<tr>
<td></td>
<td>- Grading BPRS, informed consent</td>
</tr>
<tr>
<td></td>
<td>- Explaining SQEFT intervention</td>
</tr>
<tr>
<td>First week (50 minutes)</td>
<td>- SQEFT therapy (therapist: researchers and nurses)</td>
</tr>
<tr>
<td></td>
<td>- Religious Advice and Counseling</td>
</tr>
<tr>
<td></td>
<td>- Doing ablution</td>
</tr>
<tr>
<td></td>
<td>- Doing shalat for two rak'ahs</td>
</tr>
<tr>
<td></td>
<td>- Wishing for healing</td>
</tr>
</tbody>
</table>
- Praying to ask to heal
- Deep breathing while zikr (Subhanallah, Alhamdulillah, Allahu akbar)
- Beginning to do Qur'anic therapy by stating surah Al-Fatiha, Throne Verse, Al-Iklash, Al-Falaq, and An-Nas: each surah that was read was blown on the hand and touched to all over the body.
- Listening to surah Ar-Rahman
- Beginning EFT procedures: The Set-Up, The Tun In, dan The tapping
- Deep breathing technique while zikr
- Doing prostration of gratitude
- Evaluation
- Distributing SQEFT procedure sheet to be learned

<table>
<thead>
<tr>
<th>Week</th>
<th>Details</th>
</tr>
</thead>
</table>
| Second Week (50 minutes) | - Observing the program in the first week  
- The intervention was similar to the first week |
| Third Week (80 minutes) | - Observing the program in the first and second week  
- The intervention was similar to the second week  
- 30 minutes. SQEFT intervention was done independently |
| Fourth Week (80 minutes) | - Observing the program in the first week until the third week  
- The intervention was similar to the third week, Evaluation |

Doing nucleic acid extraction and working real-time PCR was for determining the profile of target gene mRNA expression. PCR Program was done by using a Real-Time PCR machine (CFX Connect system, Biorad Laboratories, Real-Time PCR 96 well 0.1 ml, USA)

Table 3. The primary sequence of dopamine receptor of D₂R [5]

<table>
<thead>
<tr>
<th>GEN</th>
<th>Primary sequence</th>
<th>Location</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRD2</td>
<td>For: 5’-AGACCATGAGCCGTAGGAAG-3’.</td>
<td>Exon 7</td>
<td>96 bp</td>
</tr>
<tr>
<td></td>
<td>Rev.: 5’-GCAGCCACGAGATGATA-3’</td>
<td>Exon 8</td>
<td></td>
</tr>
</tbody>
</table>

### III. RESULT

Change of mRNA DRD2 level for the patient with schizophrenia after SQEFT intervention

Table 4. Level of mRNA DRD2 Expression in Treatment Group of SQEFT Intervention

<table>
<thead>
<tr>
<th>Variable</th>
<th>Expression of mRNA DRD2 for the Patient with Schizophrenia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Pair 1</td>
<td>Pre-post SQEFT</td>
</tr>
</tbody>
</table>

Paired sample T-test

Table 5. Statistic Test of the Level of mRNA DRD2 Expression in Three Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>mRNA DRD2 Expression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Group A – Group B</td>
<td>2.60</td>
</tr>
<tr>
<td>Group A – Group C</td>
<td>0.44</td>
</tr>
<tr>
<td>Group B – Group C</td>
<td>3.04</td>
</tr>
</tbody>
</table>

one way ANOVA Multiple Comparison
The clinical symptom of schizophrenia is indicated by positive signs (hallucination, delusion), negative symptoms, and cognitive disorders. A positive symptom of schizophrenia is correlated with hyperdopaminergic neurotransmission in the brain, particularly in the mesolimbic dopamine pathway. Meanwhile, negative symptoms and a cognitive deficit of schizophrenia are caused by hyperdopaminergic activity in the mesocortical way [12]. Dopamine is a dominant catecholamine neurotransmitter in the central nervous system involved in controlling motoric function, cognition, appreciation, cognitive behavior, autonomous movement, and neuroendocrine secretion. Dopaminergic transmission manages axonal plasticity and modulates adult neurogenesis. Dopamine receptor is a protein that will bind dopamine so that chemical information will be transmitted to postsynaptic neurons. The bond between the neurotransmitter and its receptor will stimulate an enzymatic reaction. First, its receptor will stimulate or hinder G Protein in the nerve cell membrane that then will activate adenylyl cyclase. Next, it will stimulate the form of Camp until it has occurred phosphorylation in the cell needed for the neuron activity [13]. D2 receptor influences the Prefrontal cortex (PFC) for a patient with schizophrenia. PFC is central against function and motivation. In primates, dopamine neurons from the ventral tegmental region and subside nigra pars compacta deliver afferent signals to PFC and modulate PFC functions through several receptor subtypes, including the receptor of Dopamin D2 [14].

The hypothesis in schizophrenia is "dopaminergic hyperactivity." This hypothesis is supported by nearly all antipsychotic drugs that patients take to block or reduce DRD2-mediated signaling. Antipsychotic drugs taken by patients can bind to the DRD2 receptor, clinically reducing positive symptoms (hallucinations and delusions) but causing serious side effects, exacerbating negative symptoms, affective and cognitive deficits [15]. Several studies have shown an increase in DRD2 through positron-emission-tomography examination; in mice, DRD2 overexpression occurs in the striatum [16]. increased postsynaptic DRD2 in the postmortem schizophrenic brain tissue [17].

Behavior change-based therapy, education cannot overcome all of the symptoms of schizophrenia. Meanwhile, antipsychotic medicine is effective for treating psychotic symptoms, but cognitive deficit, effective, and psychomotor [18]. Thus, the importance of an additional intervention is to help treat and improve the symptoms of schizophrenia. Furthermore, SQEFT therapy emphasizes self-cleansing, spiritual from all of the diseases and shirk, praying and zikr, reading Al-Quran, listening to Al – Qur’an while doing EFT, releasing negative emotional energy by stating affirmation sentence to increase sincerity, submission, and asking for healing only to Allah SWT. In the trial of the SQEFT instrument in inpatient schizophrenia, there was a decrease in the value of the BPRS [9]. Spiritual intervention for Muslim patients has positive results on the health status and minimizes the symptoms of the disease [19].

Several types of research regarding the effect of Qur’anic therapy, the Qur’anic therapy can overcome the mental disorder [20], overcome magic disease [21], treatment for depression [22], treatment for a psychological disorder. Besides, a patient who regularly attends Qur’anic therapy sessions is successful in being healed, 81.8% [23]. Moreover, repetition in reading and listening to Al-Qur’an for medical and psychiatry patients has decreased depression and anxiety [24]. Besides, it also influences to reduce major depression of chronic medical patients [25], reduce stress [26] overcome mental disorder [27], brain and heart work [28], increase the memory and
cognition [29], cognitive therapy [30], increase the alpha frequency EEG power spectrum during reading Al-Qur'an [31]. Psychological health after the earthquake [32], the use of spirituality in psychotherapy [33].

Moreover, there is research about EFT therapy, reducing psychological symptoms, anxiety including phobia, headche tension, depression, and insomnia [34], addiction, emotional [35], an emotional problem that is faced by the patient with chronic disease, and the management of physical symptom. The improvement of post-trauma stress disorder (PTSD) consists of anxiety, depression, obsessive-compulsive behavior, anxiety, phobia, hostility, interpersonal sensitivity, paranoia, psychosis, somatization, and insomnia [36], influencing cortisol level, the immune system [37].

It is necessary to develop behaviors that can improve healing, train concentrations, increase motivation, appreciation, hope, surrender, clean heart and soul, and pray, dhikr, and listen to the Koran. For example, saying positive sentences as a suggestion takes advantage of meridian points that stimulate brain function to balance DRD2 levels in the mesolimbic, mesocortical, and nigrostriatal pathways [38]. In addition, during daily therapy sessions, learning habits form so that dopamine neurons project into the striatal area, and information is transferred to the PFC; as a result, dopamine cells do not respond to negative thoughts and stimuli, resulting in new and appropriate adjustment behavior [39].

V. CONCLUSION

After the SQEFT intervention group A, there was a decrease in the mean DRD2 mRNA gene expression score. There were differences in group A and group B after the intervention, the level of gene expression DRD2 mRNA was lower in group A. There was no difference between group A and group C, the level of DRD2 mRNA gene expression in group. An n after SQEFT therapy is the same as in healthy control group C, it became normal. SQEFT therapy intervention can decrease DRD2 mRNA expression level in schizophrenic patients who are well tolerated and suitable for psychiatric inpatients.

REFERENCES