



Article

Effect of Music Therapy on The Improvement of Clinical Symptoms and Cognitive Functions of Schizophrenia Patients Receiving Risperidone Therapy

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Abstracts

Introductions: A variety of therapeutic approaches has been widely studied in various countries to treat schizophrenia. Music therapy as non-pharmacotherapy management has not been widely used. Data about effectiveness, the ideal number of sessions, and methods of music therapy have not been widely studied. To determine the effect of music therapy on the improvement of clinical symptoms and cognitive function of schizophrenic patients that are receiving risperidone therapy. **Methods:** This study was a comparative analysis study. Sampling with consecutive sampling on the population of patients who were hospitalized in the Regional Special Hospital of South Sulawesi Province. The treatment group received risperidone therapy and music therapy (active and receptive) in 6-8 sessions with a duration of 45 minutes/session, and the control group only received risperidone 2-4 mg/day. The instruments used were the PANSS and the MoCA-Ina scale, examined in the second and fourth weeks, and also using the ESRS scale to evaluate the side effects of treatment. **Results:** There was a significant difference between two group in decreasing of PANSS score for negative symptoms ($p=0.000$), general psychopathology (4th week $p=0.011$), and cognitive function (4th week $p=0.000$) especially on visuospatial components ($p=0.001$), attention ($p=0.009$) and abstraction ($p=0.011$). There was no significant difference in decreasing of PANSS score for positive symptoms ($p=0.109$). **Conclusions:** Music therapy can be a non-pharmacological therapy of choice to support the improvement of negative symptoms, cognitive function, and general psychopathology in the stabilization phase of schizophrenic patients.

Introductions

Schizophrenia is a severe and chronic mental disorder characterized by a range of symptoms including delusions, hallucinations, disorganized speech or behavior, and impaired cognitive and affective abilities. Patients with this disorder experience a decline in function in various aspects of life and ultimately have implications for social and economic life [1, 2]. Data from the World Health Organization (WHO) in 2018 stated that around 23 million people worldwide suffer from schizophrenia and according to data from the Basic Health Research (Riskesdas) in 2018, the prevalence of schizophrenia in Indonesia is 6.7 per 1000 households ladder. This data is an increase from the data in 2013 which recorded the prevalence of people with schizophrenia at 1.3 per 1000 households [3, 4].

Various therapeutic approaches have been widely studied in various countries including Indonesia to treat schizophrenia, both pharmacotherapy and non-pharmacotherapy approaches (psychotherapy and psychosocial interventions). Pharmacotherapy approaches have been shown to reduce positive and negative symptoms of schizophrenia while non-pharmacological approaches focused on improving cognitive function, perceptual function, and social cognition as well as improving the quality of life of people with schizophrenia [1,2,5].

Recent studies have focused on the use of pharmacotherapy in the form of atypical antipsychotics (Second Generation Antipsychotic / SGA) to treat patients after the acute condition of schizophrenia has been managed. Selection of SGAs such as Risperidone is based on the ability of these drugs to improve cognitive function, positive symptoms, negative symptoms, and lower neuroleptic side effects compared to First Generation Antipsychotic (FGA) drugs [5-7]. Comprehensive treatment for

people with schizophrenia in the form of combining pharmacological and non-pharmacological therapies has shown more optimal results when compared to using only a single approach [1, 7].

Non-pharmacological approaches are usually used after the patient has passed the acute phase, namely in the stabilization phase and the maintenance phase (stable) such as supportive therapy, family psychoeducation, and psychosocial interventions [1, 7, 8]. Several psychosocial intervention techniques in schizophrenic patients have been studied with different therapeutic effects such as social skills training, family-oriented therapy, assertive community treatment, group therapy, cognitive behavior therapy, art therapy, music therapy, individual therapy, and mindfulness therapy (Mindfulness-Based Stress Reduction and Mindfulness-Based Cognitive Therapy) [7, 8].

Music therapy has been studied in several countries regarding its effectiveness in improving positive and negative symptoms, and social cognition function of schizophrenic patients [9, 10]. Music therapy has also been linked to its effects on physiological responses and activities of the nervous system, endocrine system, and cardiovascular system leading to mental and body stabilization, emotional enhancement, cognitive function, and positive behavior [11-13]. In addition, music therapy is also effective for increasing emotional relaxation, cognitive processing abilities, and positive behavioral changes in chronic schizophrenic patients [10, 14]. Most previous studies have ignored the standard type of pharmacotherapy given to patients and some studies have focused on only one approach to music therapy (active or receptive) [9, 13, 14]. One study has combined active music therapy (playing music or singing) and receptive (listening to music) but given to chronic schizophrenic patients [10].

Research on music therapy in schizophrenic patients in Indonesia is still limited so it is rarely applied in clinical practice in mental hospital treatment rooms, including in South Sulawesi. This study aims to explore the effect of music therapy (active and receptive) on the improvement of clinical symptoms and cognitive function in schizophrenic patients receiving Risperidone therapy.

Methods

Research Design

The type of research used was experimental research with a comparative analysis approach

Time and Place

This research was carried out in April-May 2021 in Regional Special Hospital of South Sulawesi Province.

Sample

Sampling was done by consecutive sampling. The sample size formula was determined using the formula:

$$\begin{aligned}
 n1=n2 &= Y \left[2 \left(\frac{Z\alpha + Z\beta}{X1-X2} \right) SD \right]^2 \\
 &= 0.540 \left[2 \left(\frac{(1.96+0.84)10}{8} \right)^2 \right] \\
 &= 10.37
 \end{aligned}$$

n1=n2: Total samples; Zα: Type error 1 [15]; Zβ: Type 2 error [15]; Y: Correction factor due to repeated measurements; SD: Standard deviation; X1-X2: The difference that is considered significant [15]; n1=n2 = 10 minimum samples for each group

Selection Criteria

Inclusion criteria: (a) Patients diagnosed with schizophrenia according to DSM V and PPDGJ 3 for less than 5 years; (b) Patients aged 20-45 years; (c) The patient has passed the acute phase (PANSS-EC < 15); (d) Able and willing to take part in music therapy sessions; (e) Getting Risperidone therapy 2-4 mg/day; (f) Receive sedative therapy (Clozapine 25 mg night or Chlorpromazine 100 mg night)

Exclusion criteria: (a) Have organic comorbidities; (b) Have a history of drug

consumption before entering the hospital; (c) Not willing to take part in music therapy sessions.

Drop Out Criteria: (a) Not regularly following the session of music therapy, (b) Not regularly consuming Risperidone

Instruments

Positive and Negative Syndrome Scale (PANSS) consists of 33 items, among others: 7 items of positive scale, 7 items of negative scale, 16 items of general psychopathology, and there are 3 additional items to assess the risk of aggression. PANSS was assessed by a trained clinician and was rated on a scale of 1-7. Scores of 1 (none), 2 (minimum), 3 (mild), 4 (moderate), 5 (somewhat severe), 6 (severe), and 7 (very heavy) so that the positive and negative scale ranges from 7-49 and the general psychopathology scale ranges from 16 to 112. The MoCA-Ina scale consists of 30 points that are tested by assessing several cognitive domains: (1) Executive function: assessed by trail making B (one point), phonemic fluency test (one point), and two-item verbal abstraction (one point); (2) Visuospatial: assessed by clock drawing test (three points) and drawing a three-dimensional cube (one point); (3) Language: mention three animals (lion, camel, rhino; three points), repeat two sentences (two points), language fluency (one point); (4) Delayed recall: mention five words (5 points), recall after five minutes (5 minutes); (5) Attention: assessing alertness (1 point), reducing sequentially (3 points), digits forward and backward (1 point each); (6) Abstraction: assessing the similarity of an object (2 points); (7) Orientation: mention the date, month, year, day, place and city (1 point each). All points are then summed and interpreted: a score of 26-30 points is considered normal cognitive function, a score <26 indicates cognitive impairment.

Subject Allocation

In this study, subjects were divided into 2 groups:

1. Treatment Group: Schizophrenic patients who received Risperidone 2-4 mg/day and music therapy (active and receptive) for 6-8 sessions (4 weeks)

2. Control Group: Schizophrenic patients who received Risperidone therapy 2-4 mg/day without music therapy

Intervention

The treatment group was given music therapy with the following conditions:

- a. Duration of each session was 45 minutes
- b. The first and last ten minutes were used for receptive music therapy and the remaining 25 minutes were used for active music therapy.
- c. For active music therapy: singing songs, improvising songs, playing simple musical instruments. The song used in this case was chosen by the patient himself.
- d. Passive/Receptive music therapy: listening to classical music in turn and the task of rewriting songs.

Measured PANSS and MoCA-Ina scores in the second week (end of session-4) and fourth week (end of session-8) after being given a music therapy session.

Statistical Analysis

Statistical analysis using SPSS 24.0. To see the significance of the effect of active and receptive music therapy in the treatment group using the General Linear Model and Mann Whitney with a p-value of <0.05 is considered significant.

Ethics

This research has received approval from the Biomedical Research Ethics Commis-

sion on Humans, Faculty of Medicine, Hasanuddin University, and received approval from participants and their families

Results

In this study, a sample of 20 subjects was taken which was divided into 2 groups, namely the treatment group and the control group, each of which 10 subjects met the inclusion criteria. To provide descriptive data related to the frequency distribution of research subjects, a statistical descriptive analysis was carried out and the data obtained is shown in Table 1.

The median value of PANSS for positive symptoms in the treatment group week 0 was 18.5, the second week was 14, and the fourth week was 11.5, while for the control group, week 0 was 19, the second week was 16, and the fourth week was 12. The median PANSS value for negative symptoms in the treatment group week 0 was 24, the second week was 16.5, and the fourth week was 11, while for the control group, week 0 was 21, the second week was 17, and the fourth week was 15. Values the median PANSS for general psychopathology in the treatment group week 0 was 43.5, the second week was 32.5 and the fourth week was 27, while for the control group, week 0 was 45.5, the second week was 36, and the fourth week was 30. The median value of the Moca-Ina scale in the control group week 0 was 17.5, the second week was 22.5 and the fourth week was 26.5, while for the control group, week 0 was 21, the second week was 22, the fourth week was 24.5 (**Table 1**)

Table 1 Demographic Characteristics of Subjects and Research Variables

Characteristics of		Treatment n=10 (%)	Control n=10 (%)	p-value
Gender	Male	4 (40%)	5 (50%)	*0.548
	Female	6 (60%)	5 (50%)	
Age	26-30	2 (20%)	0 (0%)	*0.069
	31-35	2 (20%)	1 (10%)	
	36-40	3 (30%)	6 (60%)	
	41-45	3 (30%)	3 (30%)	
Education	Elementary School Equivalent	0 (0%)	2 (20%)	*0.168
	Junior High School /Equivalent	3 (30%)	2 (20%)	
	High School/Equivalent	6 (60%)	6 (60%)	
	S1	1 (10%)	0 (0%)	

Characteristics of		Treatment n=10 (%)	Control n=10 (%)	p-value
Job	Not Working	1 (10%)	2 (20%)	*0.307
	Labor	1 (10%)	1 (10%)	
	Farmer	3 (30%)	1 (10%)	
	Self-employed	3 (30%)	3 (30%)	
	Household	2 (20%)	3 (30%)	
Marital Status	Not Married	2 (20%)	0 (0%)	*0.464
	Married	5 (50%)	7 (70%)	
	Widow/Widower	3 (30%)	3 (30%)	
PANSS (Positive Symptoms) Mean (sb)	Week 0	18.6 (1.50)	19.1 (1.85)	
	Week 2	14.1 (1.73)	16.1 (1.73)	
	Week 4	11 (1.86)	12 (2.11)	
PANSS (Negative Symptoms) Mean (sb)	Week 0	23.3 (2.45)	20.4 (2.46)	
	Week 2	16.2 (2.78)	17.4 (2.5)	
	Week 4	11.1 (1.5)	14.9 (1.9)	
PANSS (General Psychopathology) Median (min-max)	Week 0	43.5 (42-56)	45.5 (35-48)	
	Week 2	32.5 (30-45)	36.0 (33-40)	
	Week 4	27.0 (24-30)	30.0 (27-35)	
Moca-Ina Median (min-max)	Week 0	17.5 (15-21)	21.0 (18-22)	
	Week 2	22.5 (19-26)	22.0 (19-24)	
	Week 4	26.5 (24-29)	24.5 (23-27)	

One-way ANOVA: Homogeneity of variance test (*p>0.05)

Comparative Analysis of Changes in PANSS Scale Score and MoCA-Ina Treatment Group and Control Group

Comparative analysis of changes in the value scale PANSS Positive Symptom and Negative Symptoms before and after therapy (at 2 and 4 weeks) between groups was carried out using the Generalized Linear Model Test / repeated ANOVA (Numerical comparative test of two unpaired groups with more than one measurement with data distribution “normal”).

In Table 2, the p-value in the comparison of PANSS scores (positive symptoms) in the two groups at week 0 was 0.516 (p>0.05), week 2 was 0.019 (p< 0.05) and the 4th week was 0.109 (p>0.05), which means that there was a statistically significant difference in changes in the PANSS Score (Positive Symptoms) between groups at week 2, and there was no difference in changes in PANSS Score (Positive Symptoms) between groups at week 0 (before therapy) and week 4 (after therapy).

Table 2. Comparative Analysis of Positive Symptom PANSS Scores in the Treatment Group and Control Group

PANSS (Positive)	Treatment (n=10)	Control (n=10)	p-value
	Average(sb)	Average (sb)	
Week 0	18.6 (1.50)	19.1 (1.85)	0.516
Week 2	14.1 (1.73)	16.1 (1.73)	*0.019
Week 4	11 (1.86)	12 (2.11)	0.109

Repeated ANOVA test (*p<0.05)

In Table 3, the p-value in the comparison of PANSS scores (Negative Symptoms) in the two groups at week 0 was 0.017 (p<0.05), week 2 was 0.324 (p>0.05) and week 4 was 0.000 (p<0.05), which means that there was a statistically significant difference in Table 3. Analysis Comparison of PANSS Scores Negative Symptoms in the Treatment Group and Control Group

changes in the PANSS (Negative Symptoms) Score between the groups at week 0 (before therapy) and week 4 (after therapy), and there was no difference in changes in the PANSS Score (Negative Symptoms) between groups at weeks 2.

PANSS (Negative)	Treatment (n=10)	Control (n=10)	p-value
	Average (sb)	Average (sb)	
Week 0	23.3 (2.45)	20.4 (2.46)	*0.017
Week 2	16.2 (2.78)	17.4 (2.5)	0.324
Week 4	11.1 (1.5)	14.9 (1.9)	*0.000

Repeated ANOVA test (*p<0.05)

Comparative analysis of changes in the values of the MoCA-Ina scale before and after therapy (2nd and 4th weeks) between groups was carried out using the Repeated Mann-Whitney Test (Numerical comparative test of two unpaired groups of more than one measurement with “abnormal” data distribution).

In Table 4, the p-value on the com-

parison of changes in MoCA-Ina scores between groups at week 0-2 was 0.000 ($p < 0.05$), week 2 was 0.165 ($p > 0.05$) and week 4 was 0.000 ($p < 0.05$), which means that there was a statistically significant difference in changes in MoCA-Ina scores between groups at week 0 (before therapy) and week 4 (after therapy), and there is no difference in changes in MoCA-Ina scores between groups at week 2.

Table 4 Comparative Analysis of MoCA-Ina Scores in the Treatment Group and Control Group

	Group (n)	Median	p-value
		(Minimum-Maximum)	
Moca-Ina Change Week 0-2	Treatment (n=10)	4.5 (2-6)	*0.000
	Control (n=10)	1.5 (0-3)	
Week Moca-Ina Change 2-4	Treatment (n=10)	4 (2-6)	0.165
	Control (n=10)	2.5 (1-5)	
Moca-Ina Change Week 0-4	Treatment (n=10)	8.5 (6-11)	*0.000
	Control (n=10)	4.5 (2-6)	

*Mann-Whitney test (*p < 0.05)*

In Table 5, the p-value in the comparison of changes in the seven Cognitive Components on the MoCA-Ina Scale between groups at weeks 0-4 were: Visuospatial/Executive Functions 0.001 ($p < 0.05$), Naming Functions 0.280 ($p > 0.05$), Attention Functions 0.009 ($p < 0.05$), Language Function 0.684 ($p > 0.05$), Abstraction Function 0.011 ($p < 0.05$), Memory Function 0.631 ($p > 0.05$), Orientation Function 0.853

($p > 0.05$), which means that there were differences in changes in Visuospatial Function/Executives, Attention Functions, and Intergroup Abstraction Functions that were statistically significant at week 4 (after therapy), and there was no difference in changes in Naming Function, Language Function, Memory Function, and Orientation Function between groups at week 4 (after therapy).

Table 5. Comparative Analysis of MoCA-Ina Score Components in the Treatment Group and Control Group

MoCA-Ina Component	Group (n)	Median	p-value
		(Minimum-Maximum)	
Visuospatial Change / Executive	Treatment (n =10)	2 (1-3)	*0.001
	Control (n=10)	1 (0-1)	
Change of Name	Treatment(n=10)	0 (0-1)	0.280
	Control (n=10)	0 (0-1)	
Change Attention	Treatment (n=10)	2 (0-3)	*0.009
	Control (n=10)	1 (0-2)	
Change Language	Treatment (n=10)	1 (0-2)	0.684
	Control (n=10)	1 (0 -1)	
Change in Abstraction	Treatment(n=10)	1 (0-2)	*0.011
	Control (n=10)	0 (0-1)	

MoCA-Ina Component	Group (n)	Median	p-value
		(Minimum-Maximum)	
Change in Memory	Treatment(n=10)	1.5 (0-2)	0.631
	Control (n=10)	1 (0-3)	
Change of Orientation	Treatment(n=10)	1 (0-2)	0.853
	Control (n=10)	1 (0-2)	

*Mann-Whitney test (*p<0.05)*

Discussions

The combination of active and passive music therapy as adjuvant therapy for schizophrenic patients receiving risperidone therapy has not been studied before, especially regarding how effective it is in improving the clinical symptoms and cognitive function of schizophrenic patients. This study used the PANSS and MoCA-Ina scales to determine how much improvement in clinical symptoms and cognitive function of schizophrenic patients after being given music therapy. Theoretically, risperidone therapy has been shown to improve clinical symptoms and cognitive function in schizophrenic patients, mainly because of its binding to dopamine and serotonin receptors [1, 15, 16]. The same thing was found in this study where all samples studied, both the treatment group and the control group, experienced a significant decrease in the PANSS scale scores (positive symptoms, negative symptoms, and general psychopathology) and significant MoCA-Ina (Table 1).

The treatment group in this study was given active and receptive music therapy for 6-8 sessions and then assessed the extent of the difference in clinical symptom improvement with the control group who only received risperidone therapy. The results of this study found that although a decrease in the PANSS scale scores (all domains) and MoCA-Ina occurred in both groups, there was a significant difference in the score reduction that occurred in the treatment group, especially for negative symptom improvement, general psychopathology, and cognitive function. This is in accordance with previous studies which

stated that the addition of music therapy was considered an important intervention to improve cognitive function in schizophrenic patients [10]. The same thing was also expressed in a meta-analysis study which stated that music therapy with the intervention of ‘singing, improvisation and music learning’ (active method) was effective in providing improvement in symptoms of depression, negative symptoms, and global functioning of schizophrenic patients [9]. The biological explanation stating that listening to music can stimulate the dopaminergic neurons in the prefrontal cortex is mainly responsible for the negative symptoms and cognitive function can be a solid foundation for the improvement of symptoms experienced by the sample treatment groups in this study [17, 18]. The improvement in positive symptoms shown in Table 2,3 in this study did not show significant results. This result was in line with what has been stated in a systematic review that the short-term effect of music therapy on positive symptoms of schizophrenia was not significant [14]. Another study revealed different results where it found that music therapy in addition to having a good effect on cognitive function, was also effective in improving positive and negative symptoms in patients with schizophrenia [9]. The literature revealed that if schizophrenic patients can pay attention, learn, and remember as a result of improved cognitive function, they can cope better with positive sequelae [16,19]. The researcher assumed that the insignificant improvement in positive symptoms in this study might be due to the short duration of the study.

Several previous studies revealed that

small size for the results achieved after the administration of 3-10 sessions of music therapy, and a large effect after the administration of 16-52 sessions of music therapy [9, 14]. However, in this study, by giving active and receptive music therapy simultaneously in each session, there was a significant improvement in negative symptoms, general psychopathology, and cognitive function even though the number of sessions given was shorter, namely 6-8 sessions (4 weeks), with duration of 45 minutes for each session. This was supported by previous research which stated that the effectiveness of music therapy not only depend on the number of sessions available but also on the therapy process, the type of background music chosen, and the qualifications of the therapist [9].

Almost all domains of cognitive function such as executive function, learning, memory, attention/attention, verbal fluency, and abstraction abilities in schizophrenic patients experience deficits [20, 21]. This study specifically showed significant results in several domains of cognitive function, such as executive function, attention, and abstraction ability (table 5). These results were in line with previous studies which revealed that with the administration of music therapy, there was a significant increase in attention and calculation, and language and construction [10]. Research has consistently shown that dopamine is the primary neurotransmitter involved in neuroplasticity, and dopaminergic neurons in the brain's reward network, including the ventral tegmental area (VTA) and nucleus accumbens (NA), have been implicated in reward-related cortical remodeling, learning, and long-term potentiation of the hippocampus (strengthening of synapses due to increased long-lasting signal transmission between two neurons). The increased transmission of dopaminergic neurons stimulated during music therapy will encourage the strengthening of synaptic plasticity in the brain and thus the patient's cognitive function will improve

[17, 18].

The number of samples taken in this study was still small so even though the results showed a significant improvement, the distribution of sample backgrounds such as the culture of origin, presence or absence of musical talent in the family, and other factors might not be representative in general. In addition, the trend of positive results in this study required a more in-depth analysis of the biochemical factors that trigger changes in neurotransmitter patterns in the brain so that music therapy can have an impact on cognitive function and negative symptoms in schizophrenic patients. We see an opportunity for this music therapy to be a non-pharmacological therapy option that is quite effective because it takes a relatively short time but has a good impact on improving cognitive function.

Conclusions

Music therapy (a combination of active and receptive methods) can be a non-pharmacological therapy of choice to improve the negative symptoms, cognitive function, and general psychopathology in the treatment of the stabilization phase of schizophrenic patients receiving risperidone.

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Not declaration

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