



EVALUATION OF ANTIPSYCHOTIC DRUG USE IN PARANOID SCHIZOPHRENIA PATIENTS

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ABSTRACT

One of schizophrenia's treatment is pharmacological therapy using antipsychotic. This study aims to determine the demographic description (age, gender and length of stay), determine the pattern of antipsychotic drug use, determine the level of appropriateness of antipsychotic drug therapy based on the right patient, the right indication, the right drug, the right dose, and the right interval of administration based on the Rational Drug Use Module and Drug Information Handbook 27th Edition and determine the reduction in the final symptoms of schizophrenia patients after receiving antipsychotic drug therapy at the Inpatient Installation of dr. Soeharto Heerdjan Mental Hospital Jakarta for the period January - June 2023. The research method used is descriptive, with cross sectional design. Data collected retrospectively and using purposive sampling techniques. The study analyzed 95 prescription samples, showing that schizophrenia is more experience in in the range of 26-35 years old (44,21%) and in men (67.37%). The most common antipsychotic use was the atypical combination antipsychotic with the percentage of 37.5%. The single atypical antipsychotic most commonly prescribed is atypical antipsychotic with the percentage of 57.15%. The results showed that the appropriateness of the use of antipsychotics in correct patient is in 100%, correct indication is in 100%, correct drug is in 100%, correct dose is in 97.89% and the exact dosing interval of drug is in 92.63%. There was a decrease in schizophrenia symptoms in patients after undergoing hospitalization as seen from the decrease in Positive and Negative Syndrome Scale-Excited Component (PANSS-EC) scores with an average percentage decrease of 48%. This difference is clinically effective because the decrease exceeds 19– 28 %.

Keywords: antipsychotic; evaluation; PANSS-EC; paranoid schizophrenia

How to cite (in APA style)

Azizah, H. (2025). Evaluation of Antipsychotic Drug Use in Paranoid Schizophrenia Patients. Indonesian Journal of Global Health Research, 7(2), 133-142. <https://doi.org/10.37287/ijghr.v7i2.5178>.

INTRODUCTION

Mental health remains an under-addressed issue in Indonesia. Currently, the country has approximately 236 million people with mental health disorders, with 6% of the population suffering from mild mental disorders. Among them, 0.17% experience severe mental disorders, and 14.3% are affected by psychotic disorders (Syarif, Nursiah & Idris, 2020). The management of schizophrenia therapy involves a relatively long treatment period, often lifelong. According to the 2018's Indonesian Basic Health Research results, 7% of individuals with schizophrenia do not receive regular treatment due to an inability to tolerate the side effects. A study by Yulianty et al. (2020) indicated that the combination of first and second-generation antipsychotics leads to extrapyramidal side effects in 98.3% of cases. More severe side effects may arise from irrational medication use. Rational drug use, including proper indication, dosage, medication choice, and patient selection, is often compromised in daily practice, whether in community health centers, hospitals, or private institutions. Inaccurate indications, inappropriate drug selection, incorrect dosage, or mismatched patients can lead to treatment failure in schizophrenia. Correct use of antipsychotics is crucial for maintaining effective therapy and influencing patients' willingness to continue pharmacological treatment. Inappropriate antipsychotic use can impair patients' functioning, ultimately leading to non-compliance with medication and increased relapse rates (Dania et al., 2019). A study

conducted by Faqih et al. (2021) on the evaluation of antipsychotic treatment in schizophrenia patients at Sambang Lihum Mental Hospital in South Kalimantan reported that 117 patients (96.7%) received the correct medication, 118 patients (97.5%) received the appropriate dosage, and 74 patients (61.2%) received treatment at the correct frequency. Based on the above findings, further research on the evaluation of antipsychotic medication usage—including appropriate medication, patient, dosage, and frequency needs to be conducted in other hospitals to ensure effective therapy. One such hospital is dr. Soeharto Heerdjan Mental Hospital in Jakarta, which is a specialized mental health institution and a national referral center for patients with mental disorders.

METHOD

This research used a descriptive method with a cross-sectional design. Data were collected retrospectively from the prescription records of paranoid schizophrenia patients inpatient during the period of January to June 2023. The population in this study were all inpatient paranoid schizophrenia patients at the Inpatient Installation of dr. Soeharto Heerdjan Mental Hospital Jakarta during the period of January to June 2023 and administratively recorded in medical record. The sample used was all the prescription of the paranoid schizophrenia patients who received antipsychotic therapy and met the inclusion and exclusion criteria of the study. The sampling technique used was purposive sampling, which involves selecting samples based on specific criteria that align with the characteristics of the research population. Only prescriptions that met the inclusion criteria were included as samples. The inclusion criteria used were medical record data of paranoid schizophrenia patients receiving antipsychotic therapy, medical record data of paranoid schizophrenia patients without comorbidities, underwent hospitalization at the Inpatient Installation of dr. Soeharto Heerdjan Mental Hospital Jakarta for the period January - June 2023, complete and legible medical record data of paranoid schizophrenia patients. Using Slovin's formula for calculation, 95 prescriptions were selected as the research sample.

RESULT

Patient Characteristics

As shown in Table 1, the sample of 95 prescriptions who were eligible for the study had paranoid schizophrenia inpatients who were majorly the age range from 26-35 years was 44,21%. Based on gender, paranoid schizophrenia inpatients were majorly male (67,37)

Table 1.

Frequency Distribution of Paranoid Schizophrenia Patients Based on Patient Characteristics

No.	Patient Characteristics	f	%
Age Range (Years Old)			
1	17-25	20	21,05
2	26-35	42	44,21
3	36-45	15	15,79
4	46-55	11	11,58
5	56-65	5	5,26
6	> 65	2	2,11
Gender			
1	Male	64	67,37
2	Female	31	32,63

Overview of antipsychotic use patterns

As shown in Table 2, based on antipsychotic prescription, combination drugs of antipsychotics were the most antipsychotics prescribed (36,84%).

Table 2.
Frequency Distribution of Paranoid Schizophrenia Patients Based on Type of Antipsychotic Prescription for Paranoid Schizophrenia Patients

Single Typical Antipsychotic	f	%
Trifluoperazine	1	100
Total	1	100

As shown in Table 3, 1 patient was administered typical antipsychotic single drug with Trifluoperazine, constituting 100% of the sample. Table 3. Frequency distribution of paranoid schizophrenia patients based on single drug typical antipsychotic usage groups at the inpatient installation of dr. Soeharto Heerdjan Mental Hospital Jakarta in the period January – June 2023. As shown in Table 4 the most commonly prescribed single atypical antipsychotic was risperidone with a percentage of 57.15%.

Table 4.
Frequency distribution of paranoid schizophrenia patients based on single drug atypical antipsychotic usage groups

Single Atypical Antipsychotic	f	%
Risperidone	20	57,15
Aripiprazole	8	22,85
Olanzapine	4	11,42
Quetiapine	1	2,86
Clozapine	1	2,86
Total	34	100

Table 5 showed most commonly used atypical combination therapy was the combination of Risperidon and Clozapine with a percentage of 37.5%.

Table 5.
Frequency distribution of paranoid schizophrenia patients based on combination of atypical antipsychotic usage groups

Combination of Atypical Antipsychotic	f	%
Olanzapin + Risperidone	4	12,5
Risperidone + Clozapin	12	37,5
Olanzapin + Quetiapin	3	9,38
Risperidone + Clozapin + Quetiapin + Aripiprazole	1	3,12
Olanzapin + Quetiapine + Aripiprazole	1	3,12
Olanzapin + Quetiapine + Clozapin	1	3,12
Risperidone + Quetiapine	2	6,25
Aripiprazole + Quetiapine	2	6,25
Risperidone + Clozapin + Aripiprazole	2	6,25
Risperidone + Aripiprazole	3	9,39
Aripiprazole + Olanzapine Injection	1	3,23
Total	32	100

Table 6 showed the most frequently used typical atypical antipsychotic combination therapy is the combination of Risperidone + Clozapin + Trifluoperazine and the combination of Risperidone + Trifluoperazine with 25% each.

Table 6.

Frequency distribution of paranoid schizophrenia patients based on combination of typical and atypical antipsychotic usage groups

Combination of typical and atypical antipsychotic	f	%
Olanzapin + TFP + Risperidone	1	3,57
Olanzapin + Trifluoperazine	1	3,57
Haloperidol + Clozapin + Quetiapin	1	3,57
Risperidone + Clozapin + TFP	7	25
Aripiprazole + Quetiapin + Clozapin + Haloperidol Inj.	1	3,57
Risperidone + Quetiapin + TFP	1	3,57
Aripiprazole + Haloperidol Injection	1	3,57
Haloperidol + Clozapin + TFP	1	3,57
Risperidone + Clozapin + Fluphenazin Injection	2	7,16
Risperidone + TFP	7	25
Risperidone + TFP + Olanzapin + Fluphenazin Injection	1	3,57
Risperidone + Haloperidol Injection	1	3,57
Trifluoperazine + Haloperidol Injection	1	3,57
Risperidone + TFP + Fluphenazin Injection	1	3,57
Risperidone + TFP + Clozapin + Fluphenazin Injection	1	3,57

Table 7.

Evaluation of the appropriateness of antipsychotic administration in paranoid schizophrenia patients

Evaluation	Appropriate / Inappropriate	f	%
Patient Appropriate	Appropriate	95	100
	Inappropriate	0	0
Appropriate Indication	Appropriate	95	100
	Inappropriate	0	0
Appropriate Medicine	Appropriate	95	100
	Inappropriate	0	0
Correct Dosage	Appropriate	93	97,89
	Inappropriate	2	2,11
Precise Frequency	Appropriate	88	92,63
	Inappropriate	7	7,37

Table 8.

Frequency distribution of paranoid schizophrenia patients based on length of stay

Length of Stay (Days)	f	%
1 – 10	8	8,42
11 – 20	84	88,42
21 – 30	3	3,16
Total	95	100

Table 8 showed the highest length of hospitalisation was 11 - 20 days with a total percentage of 88.42%.

Table 9 showed the results of the study on the final symptoms of patients after inpatient care at the Inpatient Installation of dr. Soeharto Heerdjan Mental Hospital Jakarta for the period of January to June 2023 showed a decrease compared to the PANSS-EC scores of patients upon admission. Table 9. Frequency distribution of paranoid schizophrenia patients based on PANSS-EC Score at the inpatient installation of dr. Soeharto Heerdjan Mental Hospital Jakarta in the period January – June 2023

DISCUSSION

Based on the results of research that has been conducted on inpatient paranoid schizophrenia patients at dr. Soeharto Heerdjan Mental Hospital Jakarta during the period of January - June 2023 as follows:

Patient Characteristics

In this study, the highest prevalence of paranoid schizophrenia at dr. Soeharto Heerdjan Mental Hospital Jakarta during the period of January - June 2023, occurred in the age group of 26–35 years with 42 patient (44.21%). The age group of 17–25 years had 20 patients (21.05%). The age group of 36–45 years had 15 patients (15.79%). The 56–65 years age group had 11 patients (11.58%). The lowest percentage in the age group above 65 years, with 2 patients (2.11%). The findings of this study are consistent with the results of the *Kajian Epidemiologis Skizofrenia Journal*, which states that the onset of schizophrenia typically occurs in late adolescence or early adulthood. Onset in males usually occurs between the ages of 15 and 25, while in females, it tends to occur between 25 and 35 years (Zahnia & Sumekar, 2016). The peak incidence during adolescence and early adulthood poses a high-risk period due to the stressors associated with this stage of life, often characterized by paranoid personality disorders or excessive suspicion, where individuals perceive everyone as an enemy. This condition is frequently not recognized by family members or the surrounding environment, as it is often mistaken for a normal part of the adjustment process. Early identification and intervention, particularly with medication are crucial, as untreated conditions lead to more frequent relapses and increased resistance to therapeutic efforts (Syarif et al., 2020).

In this study, the majority of patients with paranoid schizophrenia at the inpatient unit of dr. Soeharto Heerdjan Psychiatric Hospital, Jakarta, during the period of January–June 2023 were male with 64 patients, (67.37%). Female patients numbered 31 (32.63%). *Kajian Epidemiologis Skizofrenia Journal* indicates that schizophrenia is more prevalent in men than in women. The data obtained from this study align with findings that suggest men are at a higher risk of developing schizophrenia compared to women. Men are more vulnerable to mental health disorders due to the pressures of being primary breadwinners, whereas women generally face a lower risk of psychiatric disorders as they are better able to adapt to life situations. The lower number of female patients with paranoid schizophrenia can also be attributed to the antidopaminergic effects of estrogen. Estrogen influences dopamine activity in the nucleus accumbens by inhibiting dopamine release. An increase in dopamine receptors in the caudate nucleus, accumbens, and putamen is considered an etiological factor in the development of schizophrenia. Furthermore, the prognosis of schizophrenia tends to be worse in males than in females (Zahnia & Sumekar, 2016)

Overview of antipsychotic use patterns

The pattern of antipsychotic drug use in paranoid schizophrenia patients consists of the use of typical antipsychotic drugs and atypical antipsychotics which can be single use or a combination of both. Data was collected from the patient's medical record. The results of the study indicate that the most widely used pattern of antipsychotic drug use in paranoid schizophrenia patients is the type of combined antipsychotic therapy with a percentage of 63.16%. While the single antipsychotic therapy type shows a percentage of 36.84%. The data obtained suggests that the most frequent use of antipsychotics is with combined use. The use of a combination of antipsychotics results in a varied and larger receptor target that can enhance antipsychotic efficacy by increasing dopaminergic D2 receptor antagonists additively and is expected to reduce side effects related to the dose of each drug. (Paramitha et al., 2018) Referring to the study *Comparison of the Effectiveness of Antipsychotic Therapy Regimens for Schizophrenia Patients at dr. Ernaldi Bahar Palembang Mental Hospital* conducted by Saharuddin et al. (2020) the most commonly prescribed typical antipsychotic is Haloperidol.

However, the pattern of antipsychotic drug use in paranoid schizophrenia patients is not the same. This discrepancy may occur due to the selection of antipsychotics in patients determined by patient experience such as symptomatic response to the antipsychotic, side effect profile, and the comfort of the patient with the drug.

Trifluoperazine is an antipsychotic medication that has been in use since the 1950s for the treatment of schizophrenia. It is classified as a typical antipsychotic, proven effective in treating positive symptoms in schizophrenia patients, such as auditory hallucinations, visual disturbances, and delusional beliefs. Trifluoperazine works by blocking dopaminergic receptors, thereby reducing positive symptoms. (Meilina et al., 2022) The results of our study on the pattern of antipsychotic drug use in schizophrenia patients found that the most commonly prescribed single atypical antipsychotic was risperidone with a percentage of 57.15%. Risperidone is a type of atypical antipsychotic that has high affinity for serotonin 5-HT₂ receptors and intermediate activity against dopamine D₂ receptors. Beside blocking dopaminergic 2 receptors, risperidone can reduce positive symptoms and stabilise affective symptoms, and also works by blocking serotonin 2A receptors—causing increased dopamine release in certain brain regions and thus, reducing motor side effects. Risperidone is preferable for addressing negative symptoms in schizophrenia, lowering the relapse rate of psychosis and improving cognitive function. The medicine is effective for treatment in children, adolescents, adults, and the elderly. In several studies, Risperidone is more likely to improve scores on the Positive and Negative Syndrome Scale (PANSS). (Salwan et al., 2013) The researchers revealed that the most widely used typical atypical combination therapy was the combination of Risperidone and Clozapine with a percentage of 37.5%. Based on research conducted by Purwandityo et al. (2018) on inpatient schizophrenia patients at Prof. Soerojo Magelang Mental Hospital, the use of combined antipsychotics from risperidone and clozapine was the highest at 20.62%. The second generation antipsychotic combination can improve the positive and negative symptoms of schizophrenia and more effectively treat resistant patients, hence, the combination antipsychotic therapy is recommended for the treatment of schizophrenia in case of therapeutic failure in single drug prescribing. (Maylani et al., 2018)

Furthermore, aside from blocking dopaminergic 2 receptors, Risperidone also relieves positive symptoms and stabilises affective symptoms and also works by blocking serotonin 2A receptors, leading to increased dopamine release in certain brain regions thereby reducing motor side effects. The dopamine serotonin-antagonist effect leaves the output of dopamine unchanged thereby reducing extrapyramidal symptoms. (Rissa et al., 2020) Clozapine is a second-generation antipsychotic that belongs to the dibenzodiazepine class. It works by occupying D₂ receptors by only around 38% to 47%. The combination of clozapine and risperidone is effective as risperidone occupies D₂ receptors (63% to 89%), hence, the addition of risperidone is expected to increase the response to clozapine. (Maylani et al., 2018)

The prescription of combination therapy depends on the severity of schizophrenia symptoms. The high-use of combination therapy in the treatment of schizophrenia is due to the fact that the various types and classes of agents share different affinities, meaning that they are expected to complement each other for different receptors and play a better role in psychosis than monotherapy. The use of antipsychotic combinations will result in a greater variety of receptor targets, leading to increased antipsychotic efficacy. The results of research at dr. Soeharto Heerdjan Mental Hospital Jakarta, the most frequently used typical atypical antipsychotic combination therapy is the combination of Risperidone + Clozapine + Trifluoperazine and the combination of Risperidone + Trifluoperazine with 25% each. The research conducted by Musdalifah et al. (2019) in Sungai Bangkong Pontianak Mental

Hospital provides the same results. The most widely used combination is the combination of Risperidone, Clozapin, and Trifluoperazine. This is due to new antipsychotic drugs including clozapine, risperidone, and olanzapine displaying superiority compared to classic antipsychotics such as haloperidol in terms of overall response. The fact that schizophrenia is not treated successfully with typical single therapy resulted in the introduction of combination antipsychotics. In combination therapy, typical antipsychotics are considered as they have a rapid reduction in positive symptoms such as hallucinations and delusions, but also lead to relapse after discontinuation of typical antipsychotics.

Evaluation of the Appropriateness of Antipsychotic Use

Evaluation of the appropriateness of antipsychotic use in paranoid schizophrenia patients was conducted to identify compliance with the Drug Information Handbook 27th Edition and the National Guidelines for Mental Medicine Services. In this study, the evaluation of appropriateness was carried out following five indications, i.e., the patient appropriate, the appropriate indication, the appropriate medicine, the correct dosage, and the appropriate frequency. The appropriate patient is the accuracy of using drugs tailored to the patient's condition in accordance with the presence or absence of contraindications to the drug with the patient's condition. If there are contraindications to one of the drugs used by the patient, it is considered that it does not fulfil the criteria for the right patient. Of all patients with paranoid schizophrenia diagnoses who were given antipsychotics were in accordance with the patient's condition—signalling there were no contraindications.

Appropriate indication refers to the patient receiving medication with the correct indication according to the doctor's indication. In the case of antipsychotics given by doctors, it is according to the indication, that is, for the treatment of schizophrenia. The research findings suggested that all patients with paranoid schizophrenia received antipsychotic therapy. The data were evaluated using the standard Drug Information Handbook 27th edition and the National Guidelines for Mental Medicine Services and compared with the diagnoses listed in the patient's medical record showing a percentage of 100% accurate indications. Appropriate medication is the selection of a drug that certainly has a therapeutic effect that considers the effectiveness, safety, and compatibility of the drug with the patient. The selected drug must have a therapeutic effect according to the spectrum of the disease. The antipsychotic type given to the patient depends on the patient's response to the drug. For instance, a good response from the patient by experiencing symptomatic improvement with the administration of a particular antipsychotic means that the drug is effective for the patient. Otherwise, if the response of the patient is not good, the drug needs to be replaced with another antipsychotic. Drug selection for the patient is based on the history of the patient's condition. (Balqis et al., 2020).

Dosing accuracy determines the success of therapy. Excessive dosing, particularly for drugs with a narrow therapeutic range, carries the risk of side effects. In the opposite case, too small a dose does not guarantee the achievement of the expected therapeutic levels. (Balqis et al., 2020) The result of this study demonstrates that the accuracy of the dose of drugs administered to schizophrenia patients is 97.89%. While two patients with a percentage of 2.11% were given incorrect doses of drugs. The evaluation of the correct dosage of the medicine reveals that the Aripiprazole received by both patients was less than the regular dose. This occurs due to the need to adjust the dose if the patient runs the risk of hyponatremia or syndrome of inappropriate antidiuretic hormone (SIADH). Prescribing a dose less than the established therapeutic range may lead to suboptimal drug therapy. This happens because the drug level is below the minimum level of the drug to induce a therapeutic effect. (Apriliya et al., 2023)

Medication frequency should be practical and as simple as possible to facilitate patient compliance. The precise frequency of administration is the predetermined usage per day. The higher the frequency of drug administration, the greater the potential for patient non-adherence in consuming the drug. The precise frequency of drug administration is declared inappropriate as certain usage rules exceed and some are less than the recommended interval of drug administration. Haloperidol Injection is normally given every 4-6 hours in a day. There were four patients who had less than the interval of administration of Haloperidol Injection. However, if we look at the National Guidelines for Mental Medicine Services, the use of Haloperidol Injection can be repeated every 30 minutes with a maximum dose of 20mg/day. The use of Haloperidol Injection as an injectable drug option to get a faster onset of action which can lead to rapid symptom relief. The lack of administration interval of Haloperidol Injection may be related to the patient's symptoms that have declined and do not require an injection with a faster onset of action.

The length of hospitalisation for paranoid schizophrenia patients

The length of hospitalisation for paranoid schizophrenia patients may depend on the severity of the patient. Our study is differentiated with an interval range of 10 days. The highest length of hospitalisation was 11 to 20 days with a total percentage of 88.42%. From the results of our study, it is found that patients with hospitalisation <21 days are the most dominant, mainly because if the patient fulfils the criteria for discharge during treatment, such as being calm, cooperative, independent, regular medication, and regular diet—then outpatient treatment is allowed. These results are in agreement with research carried out by Faqih et al. (2021) regarding the length of hospitalisation of patients at Sambang Lihum Mental Hospital, South Kalimantan. Total number of patients with a length of stay of less than 21 days were 82 patients (67.8%).

Final symptoms of paranoid schizophrenia

After hospitalisation, the final symptoms of paranoid schizophrenia can be seen by comparing the patient's pre and post PANSS-EC scores. PANSS-EC is used to identify psychotic symptoms related to treatment targets and predict accurately and validly related to the patient's response to the treatment administered. The final symptoms of the patients after hospitalisation all decreased compared to the patient's PANSS-EC score at the time of admission. The details of the data is depicted in the following table. The PANSS-EC total score identifies the severity of the patient's schizophrenia. The lower the score obtained, the fewer symptoms suffered by the patient. Of the results of the study, all patients experienced a decline in schizophrenia symptoms after hospitalisation which could be seen from the decrease in PANSS-EC scores at the time the patient was discharged from hospitalisation. At dr. Soeharto Heerdjan Mental Hospital, the criteria for hospitalised patients are patients whose PANSS-EC score is >10. As for patients who have been discharged with a PANSS-EC score > 10, there is a possibility that the patient has experienced a PANSS-EC score lowering compared to the initial PANSS-EC score when the patient was admitted to hospitalisation—indicating an improvement in the symptoms of schizophrenia experienced. Other than to describe the symptoms experienced by the patient, the percentage of PANSS-EC score reduction can also be used to describe the clinical effectiveness of treatment. The percentage of PANSS-EC score reduction is clinically important once the reduction is at least $\pm 19\%$ – 28% . Our results uncovered that the average percentage of PANSS-EC score reduction was 48%. The difference is clinically effective because the reduction exceeds 19% – 28% .

CONCLUSION

The patient with paranoid schizophrenia at the Inpatient Installation of dr. Soeharto Heerdjan

Mental Hospital Jakarta in the Period January–June 2023 mostly suffered with the age group of 26-35 years totalling 42 patients (44.21%) and male gender totalling 64 patients (67.37%). The most commonly used antipsychotic drug therapy pattern is the atypical combination drug class—risperidone and clozapine with a total of 12 patients (37.5%). Single drug antipsychotics that are most commonly prescribed are atypical antipsychotics, risperidone in total of 20 patients (57.15%). The antipsychotic drug use is almost completely rational. Patient appropriate is 100%, appropriate indication is 100%, appropriate medicine is 100%, correct dosage is 97.89%, and precise frequency is 92.63%. There is a significant decrease in schizophrenia symptoms in patients after undergoing hospitalisation at the Inpatient Installation of dr. Soeharto Heerdjan Mental Hospital Jakarta as reflected by a decrease in the Positive and Negative Syndrome Scale-Excited Component (PANSS-EC) score at discharge with an average percentage decrease of 48%. The difference is clinically effective because the reduction exceeds 19%–28%.

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