Analytical Study of Antipsychotic Use in Schizophrenia Patients

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Abstract.
Background: Schizophrenia is a chronic mental disorder that affects thought processes, emotions, perceptions, and behavior. Antipsychotics are divided into first-generation (FGA) and second-generation (SGA) as the main therapy. Objective: To analyze the profile of antipsychotic use in hospitalized schizophrenia patients, including type, dose, route, frequency, and combination patterns. Methods: A retrospective observational study at Menur Mental Hospital Surabaya from July to September 2023 on 66 hospitalized schizophrenia patients. Data were analyzed descriptively. Results: The use of SGAs was more dominant than FGAs. The most common SGAs were clozapine 25 mg and risperidone 3 mg oral. The most common FGAs were trifluoperazine 5 mg and chlorpromazine 100 mg oral. The most common combination pattern was risperidone + clozapine. Conclusion: The pattern of antipsychotic use was dominated by the combination of risperidone and clozapine, reflecting the complexity of schizophrenia management that requires an individual approach.
Keywords: *Schizophrenia, FGA, SGA and antipsychotic combination.*

I. INTRODUCTION

Schizophrenia is a severe mental disorder with a high global prevalence and a significant impact on the quality of life of patients and their families (Tandon et al., 2013). This disorder is characterized by positive symptoms such as delusions and hallucinations, negative symptoms such as apathy and anhedonia, and cognitive impairment that impacts social and occupational functioning (van Os & Kapur, 2009). The WHO estimates that approximately 20 million people worldwide live with schizophrenia, with onset typically occurring between the ages of 15 and 35 (World Health Organization, 2022).

Modern management of schizophrenia relies heavily on pharmacological therapy, particularly the use of antipsychotics. First-generation antipsychotics (FGAs), such as haloperidol and trifluoperazine, primarily act as dopamine D2 antagonists and are effective in reducing positive symptoms, but are often associated with the risk of extrapyramidal syndrome, tardive dyskinesia, and hyperprolactinemia (Miyamoto et al., 2012). In contrast, second-generation antipsychotics (SGAs), such as risperidone, olanzapine, and clozapine, have a higher spectrum of metabolic side effects but offer a better tolerability profile, particularly regarding negative and cognitive symptoms (Leucht et al., 2013; Citrome, 2017).

The effectiveness of antipsychotics is influenced by several factors, including dose, duration of therapy, drug combination, and patient compliance. Combinations of antipsychotics are often used in cases resistant to single therapy, but increase the risk of side effects and pharmacological interactions (Kane et al., 2013). Furthermore, monitoring EPS and metabolic parameters is an important aspect of therapy to minimize additional morbidity (Muench & Hamer, 2010).

In Indonesia, epidemiological data on schizophrenia remains limited, but psychiatric hospitals and mental health facilities have recorded an increase in hospitalizations for schizophrenia, with diverse treatment profiles (Suhartono et al., 2019). Retrospective studies of hospitalized patients provide important information on antipsychotic use patterns, therapeutic effectiveness, and the prevalence of side effects. Such research can inform the development of more adaptive therapy guidelines, personalized dosing, and long-term monitoring strategies (Nasrallah, 2017).

In addition to pharmacological effects, non-pharmacological interventions such as cognitive-behavioral therapy, social rehabilitation, and family education have also been shown to improve patients' quality of life and reduce relapse rates (Wykes et al., 2011). Therefore, a comprehensive understanding of antipsychotic use in schizophrenia is important not only for clinicians and healthcare professionals, but also for policymakers and healthcare systems.

This study was conducted to analyze the profile of antipsychotic use in schizophrenia inpatients at Menur Mental Hospital, including drug type, dosage, route of administration, frequency, combination of therapies, and identification of EPS events. The main objective of this study was to provide an empirical overview that can be used to improve treatment strategies, increase therapy adherence, and minimize the risk of potentially harmful side effects for patients (Leucht et al., 2013; Kane et al., 2013).

Considering the complexity of schizophrenia, it is crucial to develop adaptive, evidence-based, and integrated antipsychotic therapy strategies with a multidisciplinary approach. This retrospective study is expected to significantly contribute to the development of safer and more effective clinical practices in Indonesia.

II. METHOD

This study used a retrospective design, analyzing medical records of inpatients who met the inclusion criteria at Menur Mental Hospital, Surabaya. Data collected included antipsychotic use profiles, including drug type, dosage, route of administration, frequency, and combination of therapies. The study was conducted from July to September 2023, with data collected from the hospital's medical records department to ensure the accuracy and consistency of information regarding pharmacological therapy provided to patients.

III. RESEARCH RESULTS AND DISCUSSION

A retrospective observational study at Menur Mental Hospital in Surabaya, involving 66 inpatients with schizophrenia, revealed several important findings regarding antipsychotic use patterns. Conducted from July 1 to September 30, 2023, the study provides a comprehensive overview of how antipsychotics are used in daily clinical practice, including a comparison between first- and second-generation antipsychotics, the combination patterns used, and the clinical considerations underlying the choice of treatment regimen.

The results of the study showed that the use of second-generation antipsychotics or SGAs was overall more dominant than first-generation antipsychotics or FGAs. From a total of 179 frequencies of antipsychotic use, SGAs occupied a larger portion with varying types and amounts of use. In the FGA group, trifluoperazine was the most frequently used with a frequency of 37 times via the oral route. Chlorpromazine followed with 15 times of oral use. Haloperidol HCl was recorded as being used 3 times orally and 17 times via intramuscular injection. Meanwhile, haloperidol decanoate in the form of intramuscular injection was used 2 times, and fluphenazine decanoate via the intramuscular injection route was recorded as being used 10 times.

Among the SGAs, clozapine was the most frequently used, with 50 oral uses. Risperidone was the second-highest, with 28 oral uses. Olanzapine was used six times orally and nine times intramuscularly. Quetiapine fumarate had the lowest use, with only two oral uses.

Most Frequently Used Antipsychotics: Clozapine was the most frequently used SGA, with a frequency of 50, while trifluoperazine was the most frequently used FGA, with a frequency of 37. This high rate of clozapine use suggests that a significant proportion of patients in this study may have had refractory schizophrenia, or resistance to other antipsychotic treatments. This is consistent with clozapine's status as a last-line or gold standard therapy for the treatment of schizophrenia that has not responded adequately to at least two other antipsychotics.

Antipsychotic Combination Patterns This study found that antipsychotic combinations were widely used in hospitalized schizophrenic patients, with various combination patterns. SGA-to-SGA combinations included risperidone plus clozapine used in 9 patients (13.6%), and olanzapine plus risperidone in 4 patients (6.1%), bringing the total number of two-SGA combinations to approximately 19.7%. FGA-to-SGA combinations were the most varied, with trifluoperazine plus clozapine being the highest at 10 patients (15.2%). Furthermore, trifluoperazine plus chlorpromazine was recorded in 3 patients (4.5%), chlorpromazine and risperidone in 2 patients (3.0%), and trifluoperazine plus olanzapine in 1 patient (1.5%). Meanwhile, the combination of two FGAs, haloperidol HCl and chlorpromazine, was found in 1 patient (1.5%).

Triple Antipsychotic Combinations: This study also found several triple antipsychotic combinations, indicating the high complexity of management in patients with very severe conditions. In the FGA plus two SGA pattern, haloperidol decanoate combined with risperidone and clozapine was found in 2 patients (3.0%), while haloperidol decanoate combined with clozapine and olanzapine was recorded in 1 patient (1.5%). The triple SGA combination of olanzapine, clozapine, and risperidone was used in 3 patients (4.5%).

In the two FGA plus one SGA pattern, various variants were found. Haloperidol decanoate combined with clozapine and trifluoperazine was recorded in three patients (4.5%). Injectable olanzapine combined with trifluoperazine and chlorpromazine was found in one patient (1.5%). Fluphenazine decanoate combined with clozapine and trifluoperazine was also recorded in one patient (1.5%), as was trifluoperazine combined with clozapine and haloperidol in one patient (1.5%). In addition, a combination of three FGAs, trifluoperazine, risperidone, and chlorpromazine, was found in one patient (1.5%).

1. Table 1 Characteristics of schizophrenia patients at Menur Mental Hospital

Characteristics		**Number of Patients**	
		Amount	**% (n=66)**
Gender	Man	47	71
	Woman	19	29
Age	Mature	63	95
	Geriatrics	3	5
Patient's domicile	Surabaya	35	53
	Outside Surabaya	31	47
Caregiver	Social Services	18	27
	Family/Independent	48	73
Work	Work	0	0
	Doesn't work	66	100
Types of schizophrenia	Not detailed	38	58
	Hebephrenic	14	21
	Paranoid	13	20
	Catatonic	1	2
	Residual	0	0

Characteristics of schizophrenia patients at Menur Mental Hospital (continued)

Characteristics		Number of Patients	
		Amount	% (n=66)
Other comorbidities *	Skin disease	15	23
	Diarrhea, dyspepsia, nausea & vomiting	10	15
	Periodontal	9	14
	Respiratory disease	5	8
	Flu & fever	4	6
	Anemia	1	2
	Bradycardia	1	2
	Trichotillomania	1	2
	No other accompanying illnesses	27	41

Compliance with taking medication	Obedient Not obey	33 33	50 50
Patient status	BPJS Independent	65 1	98 2
Length of hospitalization	≤ 14 days >More than 14 days	8 58	12 88

Table 2. Table of Types of FGA and SGA used by schizophrenia patients

Antipsychotic Class	The type used by the patient	Route of Administration	Number of Frequency of Use	Frequency of Use (%)
FGA (First Generation Antipsychotics)	Trifluoperazine	Oral	37	21
	Chlorpromazine	Oral	15	8
	Haloperidol HCl	Oral	3	2
		IM injection	17	9
	Haloperidol decanoate	IM injection	2	1
	Fluphenazine decanoate	IM injection	10	6
SGA (Second Generation Antipsychotics)	Clozapine	Oral	50	28
	Risperidone	Oral	28	16
	Olanzapine	Oral	6	3
		IM injection	9	5
	Quetiapine Fumarate	Oral	2	1
		Total	179	100

The dosage profile and route of administration of antipsychotics to schizophrenia patients are shown in Table II. Based on research results, SGAs and FGAs are used in all types of schizophrenia. Variations in the dosage of antipsychotics depend on the patient's condition.

Table 3. Dose profile and route of antipsychotics in schizophrenia patients

Types of Schizophrenia	Drug	Frequency of drug use*	Dosage & Frequency of Antipsychotic Administration	Description (During MRS)
Unspecified schizophrenia	Trifluoperazine	20	5 mg; 2 x ½ - 1 tablet	There are those who have switched to Olanzapine
Hebephrenic schizophrenia		7	5 mg; 2 x 1 tablet	No change in medication/dose
Paranoid schizophrenia		10	5 mg; 2 x 1 tablet	
Unspecified schizophrenia	Clozapine	28	25 mg 1-2 x ½ - 1 tablet	There is no change in dose/medication in undifferentiated schizophrenia.
Hebephrenic schizophrenia		10	25 mg 1-2 x 1 tablet	There was a change of medication to clozapine 100 mg (suspected resistance)
Paranoid schizophrenia		3	25 mg 1-2 x 1 tablet	No change in medication/dose
Catatonic schizophrenia		1	25 mg 1x1 tablet	No change of medication
Unspecified schizophrenia		3	100 mg; 2 x ½ tablet	No change of medication

Paranoid schizophrenia		3	100 mg; 1-2 x ½ - 1 tablet	No change of medication
Unspecified schizophrenia	Chlorpromazine	8	100 mg; 1 x 1 tablet	There was a change in medication
hebephrenic schizophrenia		3	100 mg 1x ½ -1 tablet	No change of medication
paranoid schizophrenia		4	100 mg; 1 x 1 tablet	There was a change in medication
Types of Schizophrenia	**Drug**	**Frequency of drug use***	**Dosage & Frequency of Antipsychotic Administration**	**Description (During MRS)**
Unspecified schizophrenia	Risperidone	7	3 mg; 2 x 1 tablet	No change of medication
Hebephrenic schizophrenia		4		
Paranoid schizophrenia		2		
Catatonic schizophrenia		1		
Unspecified schizophrenia		9	2 mg; 2 x 1 tablet	Risperidone dose changes in some patients (tapering up)
Hebephrenic schizophrenia		2		No change in dose
Paranoid schizophrenia		2		There was a change in medication
Paranoid schizophrenia	Haloperidol HCl	1	5 mg; 2 x 1 tablet	No change of medication
Unspecified schizophrenia		1		
Hebephrenic schizophrenia		1		
Unspecified schizophrenia		9	5 mg/ml IM injection	Given at the start of MRS
Hebephrenic schizophrenia		4		
Paranoid schizophrenia		4		
Unspecified schizophrenia	Haloperidol decanoate	2	50 mg/ml IM injection/3 weeks	Given when the patient is going to KRS
Paranoid schizophrenia	Fluphenazine decanoate	3	25mg/ml IM injection	Given when the patient is going to KRS
Unspecified schizophrenia		6		
Hebephrenic schizophrenia		1		
Types of Schizophrenia	**Drug**	**Frequency of drug use***	**Dosage & Frequency of Antipsychotic Administration**	**Description (During MRS)**

Unspecified schizophrenia	Olanzapine	7	10 mg/ml injection	Given at the beginning/end of MRS
Paranoid schizophrenia		2		
Unspecified schizophrenia		6	10 mg; 1-2 x ½ - 1 tablet	1 patient underwent a drug change to quetiapine fumarate/trifluoperazine
Paranoid schizophrenia	Quetiapine fumarate	1	400 mg; 1 x 1 tablet	No change of medication
Unspecified schizophrenia		1		

Combination antipsychotics are necessary in some cases of schizophrenia because this disease is difficult to improve. According to the Ministry of Health, the use of combination therapy shows better therapeutic outcomes than the use of a single antipsychotic. Research shows that combination antipsychotics are widely used by hospitalized schizophrenia patients. Table III: Dosage changes or antipsychotics due to the duration of treatmentthere are EPS side effects in patients.

TableIV. Use of Antipsychotic Combinations in Schizophrenia Patients.

Antipsychotic Class	**Generation**	**Types of antipsychotics**	**Number (N)**	**Percentage (%)**	**Analysis**
Single	FGA	Trifluoperazine	2	3.0	Paranoid schizophrenia patients
		Haloperidol decanoate	1	1.5	An unspecified schizophrenia patient was given haloperidol decanoate at the beginning of the MRS. During the MRS, trifluoperazine + chlorpromazine were given. At the end of the MRS, fluphenazine decanoate was given because auditory hallucinations persisted.
			1	1.5	Unspecified schizophrenia patient. Given haloperidol decanoate at the start of MRS. During MRS, given trifluoperazine + risperidone→clozapine + trifluoperazine
	SGA	Risperidone	2	3.0	Undetailed schizophrenia patients.
Combination of 2 antipsychotics	2 SGA	Risperidone + Clozapine	9	13.6	Patients with a primary diagnosis of undifferentiated and hebephrenic schizophrenia. In

Antipsychotic Class	Generation	Types of antipsychotics	Number (N)	Percentage (%)	Analysis
		Olanzapine + Risperidone	4	6.1	patients with hebephrenic schizophrenia, there was a change of medication from clozapine.→Risperidone due to EPS (diphenhydramine therapy was given). KRS medication was given a combination of Risperidone + THD + Clozapine. The risperidone + clozapine combination was continued with the addition of THD to prevent EPS. A patient with a primary diagnosis of paranoid schizophrenia and mixed schizoaffective disorder was given IM injection of olanzapine + risperidone (initial MRS). A medication switch was made to risperidone + trifluoperazine + THD. Unspecified schizophrenia patient. There was a change of medication from Risperidone + Olanzapine.→Clozapine. Patients with a history of non-compliance often throw away medication.
			2	3.0	
	FGA + SGA	Trifluoperazine + Clozapine	10	15.2	Patients with unspecified schizophrenia as the primary diagnosis and hebephrenic schizophrenia as a supporting diagnosis. Trifluoperazine was administered

Antipsychotic Class	Generation	Types of antipsychotics	Number (N)	Percentage (%)	Analysis
					concurrently with clozapine. Trifluoperazine and clozapine were alternated.→risperidone + clozapine (actual drug interaction in the form of hypotension)
			7	10.6	Unspecified schizophrenia patient. Trifluoperazine + clozapine drug change→risperidone + clozapine
			3	4.5	A patient with paranoid schizophrenia. Initially, the patient was given clozapine + trifluoperazine. During the initial follow-up, haloperidol decanoate was administered IM. At the end of the follow-up, fluphenazine decanoate was administered IM because the patient still occasionally experienced visual hallucinations.
		Chlorpromazine + Risperidone	2	3.0	Unspecified schizophrenia patients
Combination of 2 antipsychotics	FGA + SGA	Trifluoperazine + Olanzapine Trifluoperazine + chlorpromazine Trifluoperazine + chlorpromazine	1 3 3	1.5 4.5 4.5	An unspecified schizophrenia patient. Trifluoperazine was administered to MRS at the beginning (EPS occurred).→Olanzapine . Diphenhydramine HCL injection is given (for EPS therapy) Unspecified schizophrenia patient. Initially given trifluoperazine + chlorpromazine→trifluoperazine + clozapine

Antipsychotic Class	Generation	Types of antipsychotics	Number (N)	Percentage (%)	Analysis
					Unspecified schizophrenia patient. Initially given trifluoperazine + chlorpromazine→trifluoperazine + clozapine
	2 FGA	Haloperidol HCl + Chlorpromazine	1	1.5	Undetailed schizophrenia patients.
Antipsychotic Class	**Generation**	**Types of antipsychotics**	**Number (N)**	**Percentage (%)**	**Analysis**
Combination of 3 Antipsychotics	FGA + 2 SGA	Haloperidol decanoate + Risperidone + Clozapine	2	3.0	Unspecified schizophrenia patient. Haloperidol was given at the start of MRS, then risperidone + clozapine was given.→risperidone + clozapine
		Haloperidol decanoate + Clozapine + Olanzapine	1	1.5	Unspecified schizophrenia patient. Haloperidol decanoate was administered IM at the start of MRS, followed by clozapine + olanzapine.
	3 SGA	Olanzapine + Clozapine + Risperidone	3	4.5	Undetailed schizophrenia patients.
	2 FGA + SGA	Haloperidol decanoate + Clozapine + Trifluoperazine	3	4.5	The patient with schizophrenia was not identified. At the beginning of the MRS, the patient was given haloperidol decanoate injection.→clozapine + trifluoperazine
		olanzapine injection + trifluoperazine + chlorpromazine	1	1.5	An unspecified schizophrenia patient. Initially, MRS was given injectable olanzapine + trifluoperazine + chlorpromazine.→clozapine + trifluoperazine. There are EPS symptoms in the patient
		Fluphenazine decanoate + Clozapine + Trifluoperazine	1	1.5	Paranoid schizophrenia patient. At the end of the MRS, fluphenazine decanoate injection was given.→clozapine + trifluoperazine
		Trifluoperazine + Clozapine + haloperidol	1	1.5	Unspecified schizophrenia patient. Medication change from Trifluoperazine + Clozapine + Haloperidol→Risperidone→Sikzonoat
		Olanzapine + Clozapine + Risperidone	1	1.5	Unspecified schizophrenia patient. Drug changes: Olanzapine + Clozapine + Risperidone→Haloperidol→fluphenazine

Antipsychotic Class	Generation	Types of antipsychotics	Number (N)	Percentage (%)	Analysis
		Haloperidol decanoate + trifluoperazine + clozapine	3	4.5	Drug change Haloperidol + Trifluoperazine + Clozapine→Haloperidol
	3 FGA	Trifluoperazine + Risperidone + Chlorpromazine	1	1.5	Unspecified schizophrenia patient. Trifluoperazine + Risperidone + Chlorpromazine medication changes.→Clozapine

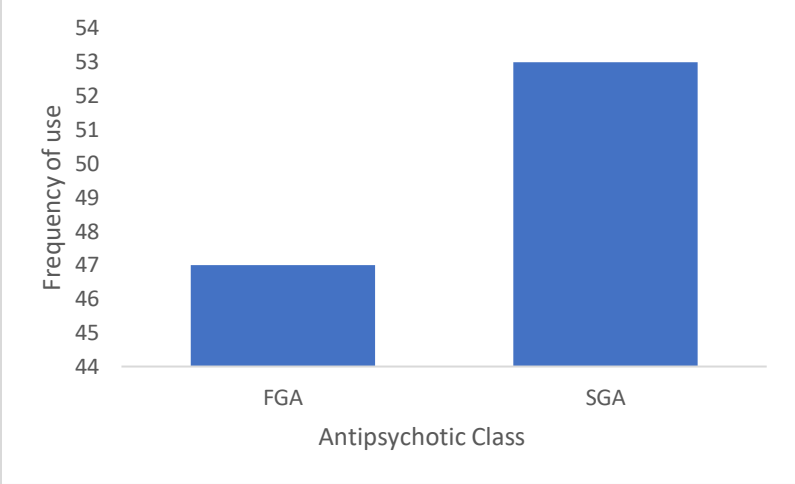

Fig 1. Frequency of antipsychotic use by class Frequency of Use

A graph shows antipsychotic use in schizophrenia patients. The study found that second-generation antipsychotics (SGAs) were more commonly used than first-generation antipsychotics (FGAs). Based on this classification, the most commonly used SGA was clozapine, while the most commonly used FGA was trifluoperazine.

IV. CONCLUSION

Based on the results of a study of antipsychotic use in schizophrenia patients conducted from July to September 2023 (n=66) at Menur Mental Hospital, it can be concluded that the pattern of antipsychotic use, found that the second generation antipsychotic (SGA) most widely used in inpatient schizophrenia patients is clozapine via the oral route with a dose of 25 mg twice a day, half to one tablet, and risperidone via the oral route with a dose of 3 mg twice a day, one tablet. Meanwhile, the first generation antipsychotic (FGA) most widely used is oral trifluoperazine with a dose of 5 mg twice a day, half to one tablet, and oral chlorpromazine with a dose of 100 mg once a day, one tablet. The most frequently used antipsychotic combination pattern in this population is risperidone combined with clozapine orally.

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VI. CONFLICT OF INTEREST

PThe author declares that there is no conflict of interest related to this publication.

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