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RESEARCH ARTICLE

Evaluation of antipsychotic side effects on schizophrenia patients at Dr Radjiman Wediodiningrat Hospital, Indonesia

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Abstract

Background: Schizophrenia is the most common mental illness with a poor prognosis. Antipsychotics are the major treatment for Schizophrenia. **Objective:** This study examines schizophrenia patients' side effects and antipsychotic medication. **Method:** A retrospective study with cross-sectional observational analysis was conducted in June 2023, with only the data from schizophrenia patients in Dr. Radjiman Wediodiningrat Hospital, Indonesia. Data were collected from the prescription records of schizophrenia inpatients from January to June 2023. The Chi-square test was used to analyse and measure the relationship between the incidence of adverse events with antipsychotics in schizophrenia patients. **Result:** Schizophrenia inpatients were majority male (74.7%) and the age 18-35 years was 41%. This study showed that the pattern of prescription of antipsychotics is atypical monotherapy (37.6%) and combinations (24.9%) were the most antipsychotics prescribed. Most of the schizophrenia outpatients have extrapyramidal syndrome side effects (31.9%), such as rigidity (12.2%), tremor (3.5%), dystonia (6.6%), and other side effects (11.8%). **Conclusion:** This study highlighted that atypical antipsychotics were the most common choice for treatment in the inpatient setting. Atypical have a lower risk of extrapyramidal side effects than typical. The negative effects of atypical antipsychotics, including metabolic syndrome, have not been identified. Thus, more research is required.

Introduction

Schizophrenia is the most prevalent mental disorder, characterised by significant reality distortion, severe personality disorganisation, and an inability to interact with daily life (World Health Organisation, 2022). Schizophrenia has affected approximately 24 million people, or one in 300 people (0.32%) worldwide. The prevalence of schizophrenia in Indonesia is based on data from Basic Health Research in 2013, where the prevalence of mental disorders in Indonesia was 1.7% per 1000 population. In 2018, it rose to 7% per 1000 population. This is a fairly drastic increase from 2013 (Indonesian Ministry of Health, 2018). Therapeutic management for schizophrenia patients generally uses antipsychotics. These medications frequently reduce positive symptoms properly but may not greatly alleviate negative symptoms or cognitive impairments. However, monotherapy with antipsychotics does not significantly improve symptoms in at least 20% of people with schizophrenia. In addition, 70% of people with schizophrenia continue to require, for a long time, even lifelong, medication to control their symptoms. They do not fully recover despite getting treatment procedures and improvements in early diagnosis of the condition. (Lähteenvuo & Tiihonen, 2021). The choice of antipsychotic medication considers the dominant symptoms of psychosis and the side effects of the medication (Stahl, 2021). Antipsychotic drugs have a variety of side effects and often result in schizophrenia

patients not adhering to therapy, which can adversely affect "*patients*'' quality of life, even causing considerable morbidity and mortality rates. The main side effect of concern is the side effect of extrapyramidal syndrome. Extrapyramidal syndrome symptoms may appear a few days to weeks after antipsychotic use (Stroup & Gray, 2018).

The primary aim of this study was to collect information on patient characteristics, including gender and age, the type of antipsychotics given to patients, and the side effects felt by schizophrenia patients. Given the importance of selecting antipsychotic drugs used by schizophrenia patients to reduce the experienced symptoms, both positive and negative, and considering the risk of side effects of antipsychotic administration, it is necessary to confirm the relationship between the use of antipsychotics and the incidence of extrapyramidal side effects in a patient with schizophrenia.

Methods

Design

A cross-sectional observation of patient medical records was used to measure the relationship between the dependent variable, antipsychotic therapy given to schizophrenia patients, and the independent variable, i.e. the incidence of side effects caused by antipsychotics administered in Dr. Radjiman Wediodiningrat Psychiatric Hospital, Indonesia. Data were collected retrospectively from the prescription records of schizophrenia inpatients from January to June 2023.

Assessment

The sample used was all the patients diagnosed with schizophrenia who received antipsychotic therapy and met the inclusion and exclusion criteria of the study. The inclusion criteria used were patients with a primary diagnosis of schizophrenia, patients receiving antipsychotic therapy, either monotherapy or combination and male and female patients aged >18 years. Patients with a history of extrapyramidal syndrome and metabolic syndrome before receiving antipsychotic therapy or metoclopramide therapy and patients with incomplete medical record data were excluded from this study. Furthermore, this research was summarised descriptively with the results of data analysis using the chi-square test.

Statistical analysis

This study used statistical analysis in the form of a chi-square test to analyse and measure the relationship between the incidence of side effects and antipsychotics for schizophrenia patients.

Ethical approval

The ethical approval No.LB.02.03/XXVII.5.7/7086/2022 was obtained at the Health Research Ethics Commission of Dr Radjiman Wediodiningrat Hospital, Indonesia. It was obtained before the research was carried out.

Results

As shown in Table I, the sample of 229 participants who were eligible for the study had schizophrenia inpatients who were majorly male (74.7%), and the age range from 18-35 years was 41%.

Table I: Characteristics of schizophrenia patients (N=229)

Characteristic	N (%)
Gender	
Male	171 (74.75%)
Female	58 (25.3%)
Age (year)	
18 – 35	94 (41.0%)
36 – 45	88 (38.4%)
46 – 60	45 (19.7%)
> 60	2 (0.9%)

Table II showed that the pattern of prescription of antipsychotics is atypical monotherapy (37.6%), and combinations (24.9%) were the most antipsychotics prescribed.

Table II: Regiment of antipsychotic (N=229)

Regiment therapy	N (%)
Monotherapy	
Typical	43 (18.8%)
Atypical	86 (37.6%)
Combination	
Typical – Typical	11 (4.8%)
Typical – Atypical	32 (14.0%)
Atypical – Atypical	57 (24.9%)

Table III shows most of the schizophrenia outpatients have extrapyramidal syndrome side effects (31.9%), such as rigidity (12.2%), tremor (3.5%), dystonia (6.6%), general extrapyramidal side effect (9.6%) and other side effects (11.8%) such as anaemia, dizziness, digestive problems, and diarrhoea.

Table IV shows that the Chi-square analysis p-value was less than 0.05. Regarding extrapyramidal side effects, there was no difference between monotherapy and combination therapy (p = 0.000).

Table III: Frequency of side effects[†](N=229)

Side effects	N (%)
No-present side effects	156 (68.1%)
Extrapyramidal Side Effect (EPS)	
Rigidity	28 (12.2%)
Tremor	8 (3.5%)
Dystonia	15 (6.6%)
General extrapyramidal side Effect	22 (9.6%)
Other side effects[‡]	27 (11.8%)

[†] One patient may experience more than one side effect; [‡] Other side effects such as anaemia, dizziness, gastrointestinal problems, and diarrhoea.

Table IV: Chi-square analysis (N=229)

Variable	Extrapyramidal side effect		Significance
	Present	No-present	
Gender			
Male	46 (26.9%)	125 (73.1%)	0.006
Female	27 (46.5%)	31 (53.4%)	
Age (year)			
18 – 35	23 (24.4%)	71 (75.5%)	
36 – 45	27 (30.65)	61 (69.3%)	0.012
46 – 60	23 (51.1%)	22 (48.8%)	
>60	0 (0.0%)	2 (0.9%)	
Type of antipsychotic			
Typical monotherapy	19 (44.2%)	24 (55.8%)	
Atypical monotherapy	14 (16.3%)	72 (83.7%)	
Typical – Typical combination	10 (90.9%)	1 (9.1%)	0.000
Typical – Atypical combination	8 (25.0%)	24 (75.0%)	
Atypical – Atypical combination	22 (38.6%)	35 (61.4%)	

Discussion

It is impossible to treat schizophrenia without the use of medications. For most patients, antipsychotic medication is required for the successful implementation of a psychosocial rehabilitation program (Doane *et al.*, 2020). Therefore, the use of typical antipsychotics and atypical antipsychotics is important in treating schizophrenia. Treatment with antipsychotics affects several receptors that can control the acute symptoms of schizophrenia, both positive and negative. Therefore, administering antipsychotic therapy to patients considers the condition and dominant symptoms that the patient is experiencing (Julaeha *et al.*, 2020).

The characteristics of research subjects at Dr Radjiman Wediodiningrat Hospital, Indonesia, are presented in Table I. Patients with schizophrenia disorder in this study were more female (74.7%) compared to females (25.3%). There is a considerable difference. There is a significant difference between male and female patients with schizophrenia. Generally, patients with schizophrenia are dominated by men, and this is because women physiologically have the hormone oestrogen, which works as an antidopaminergic, thus inhibiting the release of dopamine in the accumbent nucleus and the oxytocin hormone in women. The hormone oxytocin in women can also reduce symptoms of psychosis by inhibiting dopamine in the mesolimbic and improving mindset, social mindset, and social perception (Dania *et al.*, 2019).

With a ratio of almost 1.4:1 in this study, men are more likely than women to have schizophrenia. At the same time, several reviews could not identify sex differences in the lifetime prevalence of the illness. Schizophrenia strikes men 3.2–4.1 years earlier than it does women (Li *et al.,* 2022). At various phases of life, males and females have demonstrated varying susceptibilities to

schizophrenia. With two incidence peaks—the first in the 20–39 age group and the second after perimenopause—schizophrenia was more prevalent among men in the 40–64 age group. The condition's prevalence in women considerably rises beyond 40, which may be related to lower estrogen levels during menopause (Li *et al*., 2022; Yu *et al*., 2022). Additionally, various psychosocial factors, such as loneliness, negative life events, and a lack of social or familial support, may contribute to the development of psychosis. These conditions are typically present in menopausal and postmenopausal women (Li *et al.*, 2022).

The characteristics of patients with schizophrenia aged 18–35 years were found to be higher (41.0%) and did not differ further from the age group in the 36–45 years range (38.4%). This aligns with research conducted in North Jakarta, which showed that patients were dominated by the productive age, namely 42.05% (Winarti, 2019). Other findings examined the relationship between age in schizophrenia patients and cognitive decline (Lee *et al*., 2020; Tang *et al*., 2020). Accelerated brain ageing in schizophrenia patients can lead to cognitive decline, as indicated by neuroimaging showing faster brain ageing across various brain regions. (Lee *et al.*, 2020).

In this study, the most common types of antipsychotics given to patients with schizophrenia were atypical antipsychotics. This is because atypical antipsychotics are the first line of therapy for patients with schizophrenia (Defronzo & Thier, 1980). Atypical antipsychotics result in greater treatment retention and prevent second episodes in first-episode patients more effectively than typical antipsychotics (Hayhurst *et al*., 2014; Julaeha *et al*., 2020). Atypical antipsychotics reduce the risk of extrapyramidal syndrome and improve quality of life and productivity. The results of this study are similar to studies conducted in which the most common prescribing pattern in patients with schizophrenia was the atypical antipsychotic group in the form of risperidone (Julaeha *et al.*, 2020).

The most widely recommended antipsychotics become the first choice in administering antipsychotics for the treatment of schizophrenia because of the advantages of atypical antipsychotics in being able to improve patient adherence and quality of life; unfortunately, atypical antipsychotics have drawbacks in the form of side effects that increase the risk of metabolic syndrome such as weight gain, hypertension, dyslipidemia, and hyperglycemia (Julaeha *et al.*, 2021). Atypical antipsychotics can induce glucose abnormalities such as hyperglycemia by appearing after six weeks of taking atypical antipsychotics in patients with schizophrenia (Holt, 2019).

Atypical antipsychotics may also trigger dyslipidemia (Wu *et al*., 2016; Kanagasundaram *et al*., 2021). One of the unfavourable metabolic effects of psychiatric drugs is dyslipidemia, and antipsychotic drugs such as olanzapine and clozapine are widely recognised for their propensity to induce hyperlipidemia and hypertriglyceridemia. Antipsychotics exacerbate dyslipidemia by causing oxidative stress due to changes in the activity of the enzymes superoxide dismutase, catalase, and glutathione peroxidase. Dyslipidemia can be caused by increased body weight (Hirigo *et al.*, 2021).

The utilisation of typical antipsychotic treatment was correlated with a greater incidence of extrapyramidal syndrome adverse effects among individuals. The initial manifestation is characterised by severe muscular rigidity. Impaired sweating, a common occurrence during anticholinergic medication treatment, can lead to fever, which may escalate to hazardous levels. This syndrome -stress, leukocytosis, and high fever may wrongly imply an infectious condition. Autonomic instability with a changed heart rate and blood pressure is frequently observed. Creatine kinase of the muscle type is typically high and indicates muscle injury. Postsynaptic dopamine receptors are thought to be blocked rapidly enough to cause this condition (Wells *et al*., 2017).

Following this is a severe kind of extrapyramidal syndrome (Strain, 2002). Antipsychotic medications entered clinical use shortly after extrapyramidal side effects (EPS) were discovered. There are four recognised common extrapyramidal syndromes: parkinsonism, akathisia, acute dystonia, and tardive dyskinesia. Extrapyramidal Side Effects (EPS) are as crucial as it is a risk factor for poor antipsychotic adherence, stigmatisation of patients, and relapses (Haddad *et al.*, 2012). The most frequent side effects of first-generation antipsychotics include sedation and extrapyramidal side effects (Pringsheim *et al.*, 2011). Depending on the type of side effect that develops, typical antipsychotic side effects may be managed using a variety of strategies, including a lower antipsychotic dose, the administration of anticholinergic drugs (such as trihexyphenidyl for extrapyramidal reactions and parkinsonian syndrome), switching to a lower-potency antipsychotic medication, and the provision of supportive treatment (Wubeshet *et al.*, 2019).

Most schizophrenia patients with extra-pyramidal side effects receive additional therapy, namely anticholinergics such as trihexyphenidyl. Anticholinergics are a group of drugs that block the

action of the neurotransmitter acetylcholine. (Wells *et al*., 2017). Besides being useful for treating EPS, anticholinergic drugs also have detrimental effects, such as decreased cognitive function, behavioural changes, and decreased memory function. Therefore, caution is needed when administering these drugs to patients (Hori *et al.*, 2022).

According to the correlation test analysis results, there is an association between gender and the frequency of extrapyramidal syndrome side effects. Extrapyramidal side effects are more prominently observed in patients of the male gender, primarily due to the higher prevalence of male patients within the schizophrenia population (Aichhorn *et al*., 2005; Abu-Naser *et al*., 2021; Seeman, 2021). Subsequent correlation tests also showed a relationship between the side effects of extrapyramidal syndrome and the type of antipsychotic. Atypical antipsychotic patients experienced fewer extrapyramidal adverse effects than individuals receiving typical antipsychotic medication (Ali *et al*., 2021; Kameg & Champion, 2022). This refers to the typical antipsychotic theory, where typical antipsychotics result in more significant side effects of extrapyramidal syndrome compared to atypical antipsychotics (Ramsi & Zulaikha, 2022).

Conclusion

This study showed that the pattern of most prescriptions of antipsychotics is atypical monotherapy and combination. Most schizophrenia inpatients have extrapyramidal syndrome side-effects, such as rigidity, tremors, dystonia, and other side effects, such as anaemia, dizziness, digestive problems, and diarrhoea. However, further research is needed to assess the long-term side effects of atypical antipsychotics, particularly the risk of metabolic syndrome.

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