A Critical Thinking of Antipsychotic Medication and Side Effects Schizophrenia Patients

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Keywords: Antipsychotics, Extrapyramidal Syndrome, Metabolic Syndrome, Schizophrenia, Side Effects.

Background: Schizophrenia is the most common mental illness with a poor prognosis. Antipsychotic drugs are the main treatment for schizophrenia, but the administration of this therapy can sometimes cause side effects that are quite detrimental to the patient. Antipsychotic drugs are used to manage the treatment of schizophrenia. The main goals in the treatment of schizophrenia are to reduce the frequency and severity of psychotic exacerbations, to improve symptoms, and to improve patients' functional capacity and quality of life. Objectives: This narrative review aims to describe the administration of antipsychotic therapy and assess the relationship between antipsychotic therapy and the incidence of adverse events in patients with schizophrenia. Methods: The research method used is a narrative review by searching for published articles on the relationship between antipsychotic treatment and the incidence of extrapyramidal syndrome adverse events in patients with schizophrenia. Results: A narrative review of 20 published journals showed that symptoms of extrapyramidal syndrome can occur after a few days to weeks of use of typical antipsychotics. While metabolic syndrome side effects occur after a few weeks in patients receiving atypical antipsychotics. Conclusion: Patients on typical antipsychotic therapy experienced more extrapyramidal syndrome side effects than patients on atypical antipsychotic therapy. However, the side effects of atypical antipsychotics were found to be more dangerous, with a risk of death due to the metabolic syndrome side effects they caused.

1 INTRODUCTIONS

Schizophrenia is the most common mental disorder. Mental disorders do not directly cause death, but these disorders can make people unproductive and dependent on others, causing prolonged suffering for individuals, families, communities and the state. Schizophrenia is characterised by a number of symptoms that include significant disturbance of reality, distortion of reality, severe personality disorganization, and the inability of individuals to interact with everyday life (Organization, 2022). Schizophrenia is characterised by other more specific symptoms, namely positive and negative symptoms. Positive symptoms include chaotic speech, delusions, hallucinations, and cognitive and perceptual impairments. Negative symptoms include avolition (decreased interest and drive), decreased desire to talk and poor content, flat affect, and disruption of personal relationships. People with schizophrenia have great difficulty communicating and being around other people. They also experience hallucinations and illusions, so they seem to see things that are not real (Lähteenvuo & Tiihonen, 2021).

Schizophrenia affects approximately 24 million people worldwide, or 1 in 300 people (0.32%) (World Health Organization, 2022). While the prevalence of schizophrenia in Indonesia is based on data from Riskesdas in 2013, where the prevalence of mental disorders in Indonesia was 1.7% per 1000 population, in 2018 it increased to 7% per 1000 population. This is a rather drastic increase compared to 2013 (Kementrian Kesehatan RI, 2018).

Antipsychotic medications are used to treat patients with schizophrenia. The main goals in the treatment of schizophrenia are to reduce the frequency and severity of psychotic exacerbations, improve symptoms, and improve patients' functioning and quality of life (Bahar et al., 20-21). Antipsychotic medications are drugs that suppress specific psychological functions without affecting general functions such as normal thinking and behaviour. The choice of antipsychotic medication takes into account the predominant symptoms of psychosis and the side effects of the medication

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(Haafizah Dania, Melisa I. Barliana & Abdulah, 2019). Antipsychotic medications have a variety of side effects and often lead to non-adherence in patients with schizophrenia, which can negatively affect the patient's quality of life and even cause significant morbidity and mortality. The main side effects of concern are the extrapyramidal syndrome caused by typical antipsychotic therapy and the metabolic syndrome caused by atypical antipsychotic therapy. Symptoms of extrapyramidal syndrome side effects or metabolic syndrome side effects may appear several weeks after the administration of antipsychotic medication (Sass et al., 20-23; Stroup & Gray, 2018).

The main objective of this review of scientific articles is to describe the pattern of antipsychotic use and to review the incidence of antipsychotic side effects that may occur as a result of antipsychotic therapy during long-term treatment.

2 METHODS

The method used to write this article is a narrative review. Unlike a systematic review, a narrative review does not necessarily require a systematic, structured and validated literature search method. Therefore, the flow of article selection is not necessarily presented (Pae, 2015). However, in this narrative review, published articles obtained from a literature search using the scientific research database PubMed were used. In this narrative review, articles published up to August 2023 and not older than 5 years are used. Literature searches used as references in published articles were also conducted to enrich the study.

3 RESULTS AND DISCUSSION

Schizophrenia is a chronic illness that takes a long time to treat. People with schizophrenia can be given different therapies. These are given in combination over a long period of time (Doane et al, 2020; Neill et al, 2022). Treatment for schizophrenia consists of medication, psychotherapy and rehabilitation. Psychosocial therapy for schizophrenia includes family therapy, group therapy, individual therapy, psychiatric rehabilitation, social skills training and case management. The treatment of schizophrenia with antipsychotics is based on the psychotic phase, namely the acute phase with a duration of 4 to 8 weeks, followed by a stabilisation phase with a duration of 2 to 6 months, in which symptoms begin to decrease and there is an improvement in individual functioning, but individuals are still likely to have a relapse, which is then a stable phase of unlimited duration, while in this phase positive symptoms are minimal or absent, but negative symptoms are still dominant (Jia et al., 2022; Saharuddin et al., 2021).

There are more male than female patients with schizophrenia. This is because women physiologically have the hormone estrogen, which acts as an antidopaminergic, so it inhibits the release of dopamine in the nucleus accumbens, and the hormone oxytocin in women can also reduce symptoms of psychosis by inhibiting dopamine in the mesolimbic and improving thinking and social perception (Handayani et al., 2017). Sex and gender differences lead to important differences in preferences, pharmacokinetics and kinetics (Li et al., 2022). One study found that at the same dose of antipsychotics (except lurasidone and quetiapine), women had higher plasma levels than men. In addition, the effects of antipsychotics are greater because oestrogen increases the brain's sensitivity to dopamine. As a result, these drugs are more likely to be overdosed in women, and women are more likely to have side effects from antipsychotics. This is also because oestrogen is an important contributor to the sex differences we see in the efficacy and tolerability of antipsychotics (de Boer et al, 2023).

4 TYPICAL ANTIPSYCHOTIC THERAPY

The mechanism of antipsychotics is a A drug that inhibits dopamine D1 and D2 receptors and/or serotonin pathways in the central nervous system and acts on multiple receptors that can control acute symptoms of schizophrenia, both positive and negative symptoms. Therefore, the administration of antipsychotic therapy to patients takes into account the condition and the dominant symptoms experienced by the patient. Antipsychotic drugs are divided into two groups: first-generation antipsychotics (APG-I), also known as typical antipsychotics, and second-generation antipsychotics (APG-II), also known as atypical antipsychotics. Typical antipsychotics work by blocking dopamine receptors, particularly in the mesolimbic dopamine pathway, so they are often called dopamine receptor antagonists. This means that antipsychotics are able to reduce the hyperactivity of dopamine in the mesolimbic pathway so that it is effective in overcoming positive symptoms. However, these

antipsychotics also block dopamine receptors in the mesocortical, nigrostriatal and tuberoinfundibular pathways. Blocking these pathways is the reason why typical antipsychotics often cause the side effects of extrapyramidal syndrome and tardive dyskinesia, and further exacerbate negative symptoms and cognitive symptoms in schizophrenia patients (Julaeha et al, 2021).

5 ATYPICAL ANTIPSYCHOTIC THERAPY

Atypical antipsychotics act as dopamine (D2) and serotonin 5HT2 antagonists in the mesolimbic pathway. Through this mode of action, atypical antipsychotics are more effective in reducing or eliminating both positive and negative symptoms. As a result, risperidone is currently the first-line treatment for patients with schizophrenia, replacing typical antipsychotics (Saharuddin et al., 2021). Although atypical antipsychotics are very good at managing both positive and negative symptoms in patients, atypical antipsychotics can also cause extrapyramidal symptoms, but these are very rare compared with typical antipsychotics. Side effects of atypical antipsychotics include increased prolactin levels, which can cause galactorrhoea and menstrual problems in women and sexual problems in men. Other possible side effects include constipation, tachycardia and weight gain (Hirigo et al, 2021).

6 SIDE EFFECTS OF TYPICAL ANTIPSYCHOTICS

Typical antipsychotics such as haloperidol and chlorpromazine differ in the affinity with which they bind to dopamine D2 receptors. Haloperidol is estimated to be 50 times more potent than chlorpromazine. Each has a different affinity for binding to D2 receptors in the striatum, which is 70% for chlorpromazine and 90% for haloperidol. As a result, treatment with first-generation antipsychotics often causes side effects in the form of extrapyramidal syndromes that are more severe (Yulianty et al., 2017). In addition, the anticholinergic effects that occur with both haloperidol and chlorpromazine monotherapy are constipation, dry mouth, blurred vision and cognitive dullness. As a result, the addition of anticholinergic drugs is given to schizophrenia patients because of the side effects that affect cognitive function in chronic schizophrenia patients (Haddad et al., 2023).

Another common side effect of typical antipsychotics, especially chlorpromazine, is orthostatic hypotension. The use of antipsychotics can increase the risk of fractures through several mechanisms, one of which is that antipsychotics block dopamine D2 receptors, thereby inhibiting the effect of dopamine on the secretion of prolactin produced in hyperprolactinemia. This can affect bone cell metabolism and accelerate the rate of bone loss, increasing the risk of fracture (Azimi Manavi et al, 2023).

Typical antipsychotics also have a greater sedative effect than atypical antipsychotics, which will affect the sleep patterns of schizophrenia patients receiving typical antipsychotic therapy more than the sleep patterns of schizophrenia patients receiving atypical antipsychotic therapy (Valencia Carlo et al., 2023).

7 SIDE EFFECTS OF ATYPICAL ANTIPSYCHOTICS

Atypical antipsychotics are the most recommended treatment for positive and negative symptoms in people with schizophrenia (Julaeha et al, 2020). However, antipsychotics are quite scary when you look at the side effects they cause, namely the risk of sudden cardiovascular death. The risk of sudden cardiovascular death increases in proportion to the dose given. In addition to increasing the risk of sudden cardiovascular death, atypical antipsychotics also have the side effect of increasing body weight and can increase glucose and lipid levels in the body. Elevated glucose and lipid levels are among the characteristics of patients at risk for adverse effects of metabolic syndrome (Julaeha et al, 2021; Meyer & Correll, 2023). In addition to causing adverse metabolic effects (e.g. obesity and diabetes). One study found that there are adverse effects of atypical antipsychotics on adipocyte differentiation and metabolism. This is because therapeutic concentrations of aripiprazole or its active metabolite dehydroaripiprazole during adipocyte differentiation in the body interfere with glucose uptake, while fatty acid oxidation genes increase. In addition, the obesogenic olanzapine directly increases leptin gene expression but does not affect adipocyte differentiation and metabolism, potentially causing a switch from glucose to lipid utilisation in adipocytes in the body (Stelmach et al, 2023; Vranic et al, 2023). Because agranulocytosis is often a serious side effect,

clozapine should only be given to schizophrenic patients who have not responded adequately to antipsychotics other than clozapine. Clozapine may also be given to schizophrenic patients who are at risk of suicide or violence against themselves or others (Rafizadeh et al., 20-23; Soiza et al., 2018).

8 CONCLUSIONS

Patients on typical antipsychotic therapy experienced more extrapyramidal syndrome side effects than patients on atypical antipsychotic therapy. However, the side effects of atypical antipsychotics were found to be more dangerous, with a risk of death due to the metabolic syndrome side effects they cause.

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