



Cost Effectiveness Analysis of Antipsychotics Schizophrenia of Inpatients in Mental Hospital West Java Province

(*Analisis Efektivitas Biaya Antipsikotik Pasien Skizofrenia Rawat Inap di Rumah Sakit Jiwa Provinsi Jawa Barat*)

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ABSTRACT

Background: Schizophrenia is a mental disorder that can affect behavior, emotions and communication. In the agitation phase, the patient is accompanied by destructive or violent behavior. In these conditions, the patient must immediately calm down to avoid risk. Monotherapy treatment in acute agitation schizophrenia is more recommended than combination therapy. **Aims:** The purpose of this study was to determine the effectiveness of treatment costs and the factors that influence the total cost of schizophrenia patients at the Mental Hospital of West Java Province. **Methods:** This study was observation by cross sectional study design according to the hospital perspective. This used method is retrospective data. The subject were inpatients aged 18-65 years with diagnosis of schizophrenia disorder and receiving antipsychotic therapy for at least 1 month. **Result:** The results showed that average cost-effectiveness ratio (ACER) Rp.288.659/1 score PANSS EC with an average decrease score of 9,70. There is a difference in variant data compared because p-value = 0.011<0,05. ICER calculation of A to C = (Rp. 2.800.001–Rp. 2.593.821)/(9.70 - 8.57) = Rp. 182.460. The most significant factors that influence the total cost are administration and room. **Conclusion:** A typical-atypical monotherapy is recommended as a treatment for schizophrenic in agitation acute.



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ABSTRAK

Latar Belakang: Skizofrenia merupakan gangguan jiwa yang dapat mempengaruhi perilaku, emosi, dan komunikasi. Pada fase agitasi, pasien disertai dengan perilaku destruktif atau kekerasan. Kondisi seperti ini, pasien harus segera tenang untuk menghindari risiko. Pengobatan monoterapi pada skizofrenia agitasi akut lebih direkomendasikan daripada kombinasi terapi. Tujuan: Tujuan penelitian ini adalah untuk mengetahui efektivitas biaya pengobatan dan faktor-faktor yang mempengaruhi total biaya pasien skizofrenia di Rumah Sakit Jiwa Provinsi Jawa Barat. Metode: Penelitian ini merupakan penelitian observasi dengan desain cross sectional menurut perspektif Rumah Sakit. Metode penelitian ini menggunakan data retrospektif dengan subjek penelitian adalah pasien rawat inap berusia 18-56 tahun dengan diagnosis gangguan skizofrenia dan mendapat terapi antipsikotik minimal 1 bulan. Hasil: Hasil penelitian menunjukkan bahwa Average Cost-Effectiveness Ratio (ACER) 288.659/ 1 skor PANSS EC dengan rata-rata penurunan sebesar 9,70. Terdapat perbedaan varian antara data yang dibandingkan, karena nilai $p= 0,011 < 0,05$. perhitungan ICER A to C = $(Rp\ 2.800.001 - Rp\ 2.593.821) / (9.70 - 8.57) = Rp.\ 182.460$. faktor-faktor yang paling signifikan mempengaruhi total biaya adalah administrasi dan ruangan. Kesimpulan: Monoterapi atipikal direkomendasikan sebagai pengobatan skizofrenia pada fase agitasi akut.

Kata kunci: Agitasi akut, Antipsikotik, *Average Cost-Effectiveness Ratio* (ACER), Skizofrenia.

INTRODUCTION

Schizophrenia is a severe mental disorder characterized by disorders of thinking, language, perception and sense of self (Druais et al., 2016). Characteristics of schizophrenia in the acute stage are that the patient is often restless, irritable, and sometimes shows hostility and violence. In such cases, the patient must be treated immediately to minimize the risk to others or self (Suzuki et al., 2013). The prevalence of schizophrenia in Indonesia in 2018 with the highest rates in Bali (11.1%), DI Yogyakarta (10.4%), NTB (9.6%), West Sumatra (9.1%) and Central Sulawesi (8, 2%) (Ministry of Health RI. Basic Health Research, 2018). Despite its relatively low prevalence, schizophrenia is associated with significant health, social, and economic concerns. Schizophrenia is one of the top 15 leading causes of disability worldwide (Vos et al., 2017).

Data in Indonesia that mental health problems cause economic losses of up to twenty trillion rupiah (Putri et al., 2015). Schizophrenia is a disease that is the most expensive to treat of all mental illnesses. The direct costs of each schizophrenic patient are twice the costs of major depression, and four times the costs of anxiety disorders (Ringgen et al., 2014). The economic burden of schizophrenia was estimated at \$155.7 billion (\$134.4 billion-\$174.3 billion based on sensitivity analyses) for 2013 and included excess direct health care costs of \$37.7 billion (24%), direct non-health care costs of \$9.3 billion (6%), and indirect costs of \$117.3 billion (76%) compared to individuals without schizophrenia. The largest components were excess costs associated with unemployment (38%), productivity loss due to caregiving (34%), and direct health care costs (24%) (Cloutier et al., 2016). Treatment of schizophrenic patients uses typical antipsychotics (fga = first generation antipsychotic)

and atypical antipsychotics (sga = second generation antipsychotic). Atypical antipsychotic monotherapy is preferred as first-line treatment (Dipiro, et al., 2015).

Research conducted at the ammanuel addis ababa special nutrition hospital, ethiopia, concluded that the high rate of antipsychotic polypharmacy was 28.2%, 27.9% used two antipsychotics, 23.3% used fga plus fga and 4.6% used in fga plus sga (Tesfaye et al., 2016). Research conducted by Shakir et al (2022), in long-term inpatients with schizophrenia, antipsychotic polypharmacy including fga and sga can be safely switched to either sga or fga monotherapy with respect to the risk of relapse. For patients who are prescribed clozapine in combination with fga, switching to clozapine monotherapy is superior in relapse prevention. (Shakir et al., 2022). The measuring instrument that sees the symptoms of agitation is the Positive and Negative Syndrome Scale Excited Component (PANSS EC). PANSS EC is a five item verified score from the PANSS consisting of items of joy, hostility, tension, uncooperative, and poor impulse control with each item rated from 1 (none) to 7 (extreme), resulting in a range of scores between 5 and 35 (Zeller et al., 2017). This study was conducted to determine the average cost of treatment and the factor that influence the total cost of schizophrenia patients at the Mental Hospital of West Java Province.

MATERIAL AND METHODS

Materials

Research Design

The research design used an observational study with cross-sectional retrospective analysis. The data collection by medical record and medical costs from finance department. From the research data, then calculation of the cost effectiveness by Average Cost Effectiveness Ratio (ACER) and Incremental Cost Effectiveness Rasio (ICER).

Subjects and Research Location

The subject of this study were patients with acute agitation of schizophrenia in the emergency department to hospitalization at the Mental Hospital of West Java Province.

Inclusion and Exclusion Criteria

The inclusion criteria in this study are:

1. Subjects are adult patients aged 18-65 years according to WHO with a diagnosis of schizophrenia spectrum disorder based on ICD and DSM V classifications.
2. Inpatients receiving atypical antipsychotic monotherapy, atypical-atypical combination therapy, and atypical-typical combination therapy for at least 1 month.

The exclusion criteria in this study are:

1. Incomplete PANSS EC records.
2. Patients who underwent a drug change
3. Incomplete or lost medical records.

Inclusion and implitation

The implementations of this study are:

1. Research permits at the Mental Hospital of West Java Province.
2. Collecting data from all research subjects who met the inclusion criteria and did not include the exclusion criteria in the medical records of patients at the West Java Mental Hospital including:
 - a. Patient characteristics data include name with initials and medical record number with last number disguised.
 - b. Research subjects were divided into two groups, who received a typical mono atypical antipsychotic and atypical antipsychotic combination therapy for at least 1 month.
 - c. Medical cost data

In each study subject, a decrease in PANSS score was recorded after using atypical antipsychotics monotherapy and combination therapy. In addition, records of drug use are also recorded to determine the amount of drug use by patients while in the inpatient room. Then the direct medical costs that have been collected are processed, to be used to measure cost effectiveness analysis (CEA).

3. Data Collection Method

All research subjects recorded their identities, namely names with initials and medical record numbers with the last number disguised. From the medical record, it can be seen that there is a decrease in the PANSS score and the patient's treatment records. Then the medical costs are obtained directly from the finance department and then calculated the cost of drugs, doctor fees, administration and room costs as well as supporting costs.

4. Measurement of Cost Effectiveness Analysis (CEA)

Cost-effectiveness was analyzed using the Average Cost Effectiveness Ratio (ACER) formula which was calculated based on the total cost of direct treatment to patients given mono atypical antipsychotic therapy and combination therapy with therapeutic effectiveness based on decreasing the PANSS score using the following formula:

$$ACER = \frac{\text{Average total costs of therapy}}{\text{Effectiveness of drug use}}$$

5. The three antipsychotic therapy groups were compared with each other using ICER (Incremental Cost Effectiveness Ratio) with the following formula:

$$ICER = \frac{Cost_A - Cost_B}{Effect_A - Effect_B}$$

Where;

Cost A = Average total cost of monotherapy

Cost B = Average total cost of combination therapy

Effect A = Effectiveness of using monotherapy

Effect B = Effectiveness of using combination therapy

Data analysis

All data obtained were recorded and tabulated. The data obtained were analyzed using one way ANOVA to see significant differences. The significance was determined based on the *p* value < 0.05 (Dahlan, 2014)

RESULTS AND DISCUSSION

Table 1. ACER calculations

Therapy	Ratio	<i>p</i>	Average total cost	Average	Therapy
Atypical monotherapy	-Atypical-atypical Combination Therapy	0,116			
Male 8					Rp. 288.659/ 1 score
Female 3			Rp. 2.800.001	9.70	PANSS EC
	-Atypical-typical Combination Therapy	0,879			
Atypical-atypical Combination Therapy	- Atypical monotherapy	0,116			
Male 8					Rp. 661.475/ 1 score
Female 4	- Atypical-typical Combination Therapy	0,083	Rp. 5.232.275	7.91	PANSS EC
Atypical-typical Combination Therapy	- Atypical-atypical Combination Therapy	0,879			
Male 18					Rp. 302.662 / 1 score
Female 9	- Atypical monotherapy	0,083	Rp. 2.593.821	8.57	PANSS EC

The ACER results show that the atypical monotherapy treatment is Rp. 288,659 / 1 PANSS EC score with an average decrease in PANSS EC score of 9.70. Then for the treatment of atypical- atypical combination therapy is Rp.661.475 / 1 PANSS EC scores with an average decrease in PANSS EC score of 7.91 (Table 1). While the atypical-typical combination therapy was Rp. 302,662 / 1 PANSS EC score with an average total decrease in PANSS EC score of 8,57 (Table 1).

Table 2. Alternative of cost groupings

	Lower Costs	Equal Costs	Higher Costs
Lower Effectiveness	(Need ICER Calculation)		B Against A B Against C
Equal Effectiveness			
Higher Effectiveness			A Against C (Need Calculation ICER)
Atypical Monotherapy		= A	
Atypical-atypical Combination Therapy		= B	
Atypical- typical Combination Therapy		= C	

According on table 2, A against C goes into column I, which means that ICER calculations are needed
 $A \text{ Against } C = (\text{Rp. } 2.800.001 - \text{Rp. } 2.593.821) / (9.70 - 8.57) = \text{Rp. } 182.466$

ACER calculation between treatment A and C, if treatment C is choosen, it will cost more than Rp. 182,466 to increase 1 unit of effectiveness.

The results of this study indicate that therapy using the antipsychotic atypical monotherapy is more effective in patients with acute agitation schizophrenia than atypical-atypical combination therapy and atypical-typical combination therapy.

Tabel 3. Average total costs patients

Therapy	N	Average total costs	p
Atypical Monotherapy	11	Rp 2.800.001	
Atypical-atypical Combination Therapy	12	Rp 5.232.275	0,011
Atypical-typical Combination Therapy	27	Rp 2.593.821	

From the table 3, it can be seen that the significance value is $0,011 < 0.05$, which means that there is a significant difference between the average total cost of Schizophrenia patients.

Sensitivity Analysis

This research, conducted a sensitivity analysis to take into account the uncertainty aspect (uncertainty) of the various data used or generated.

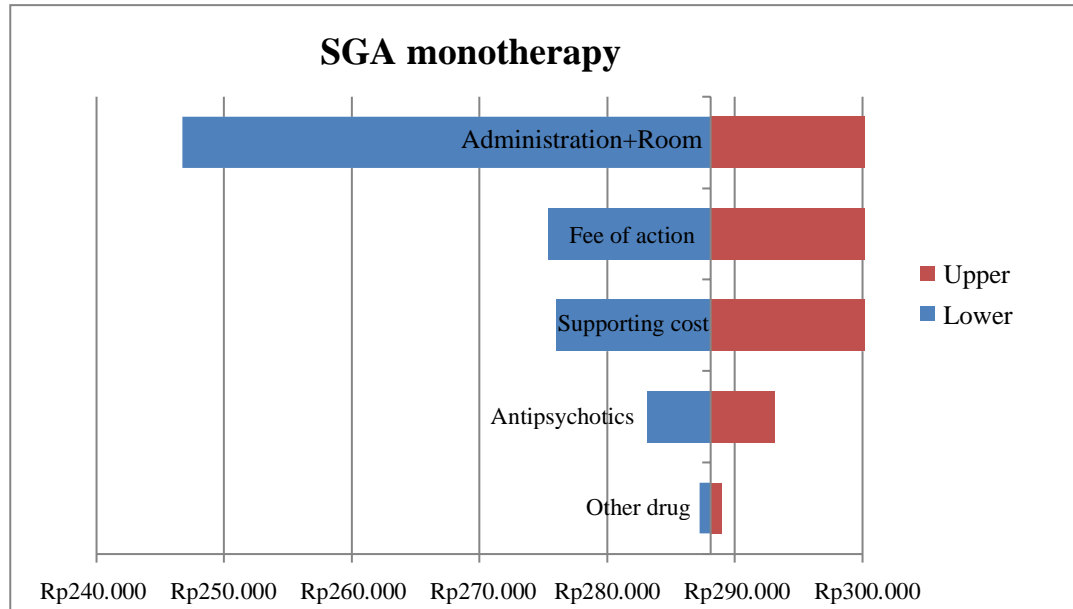


Figure.1 Sensitivity Chart SGA Monotherapy

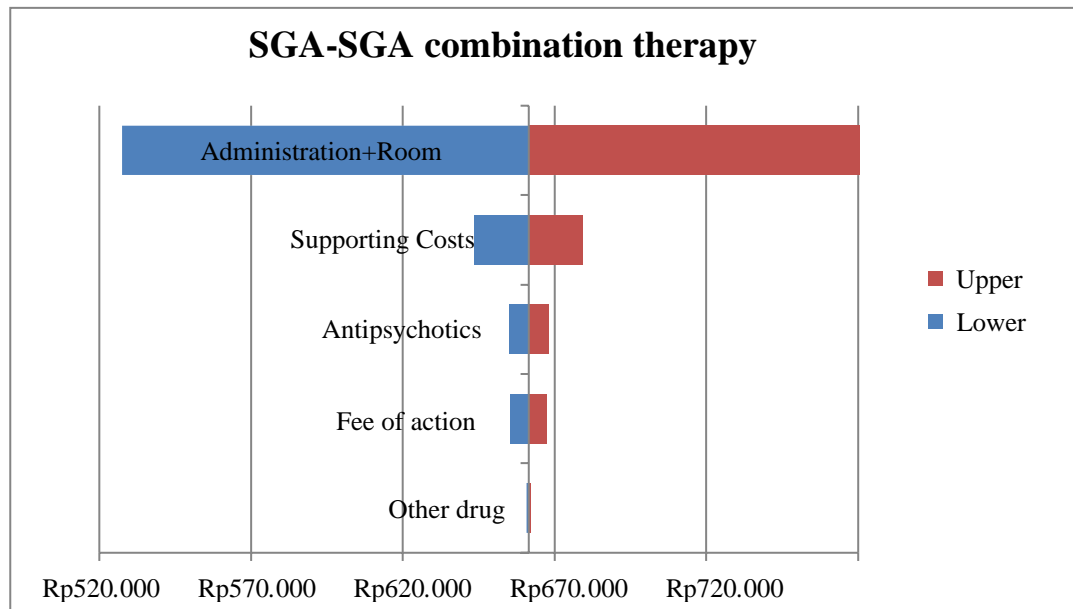


Figure.2 Sensitivity Chart SGA-SGA Combination Therapy

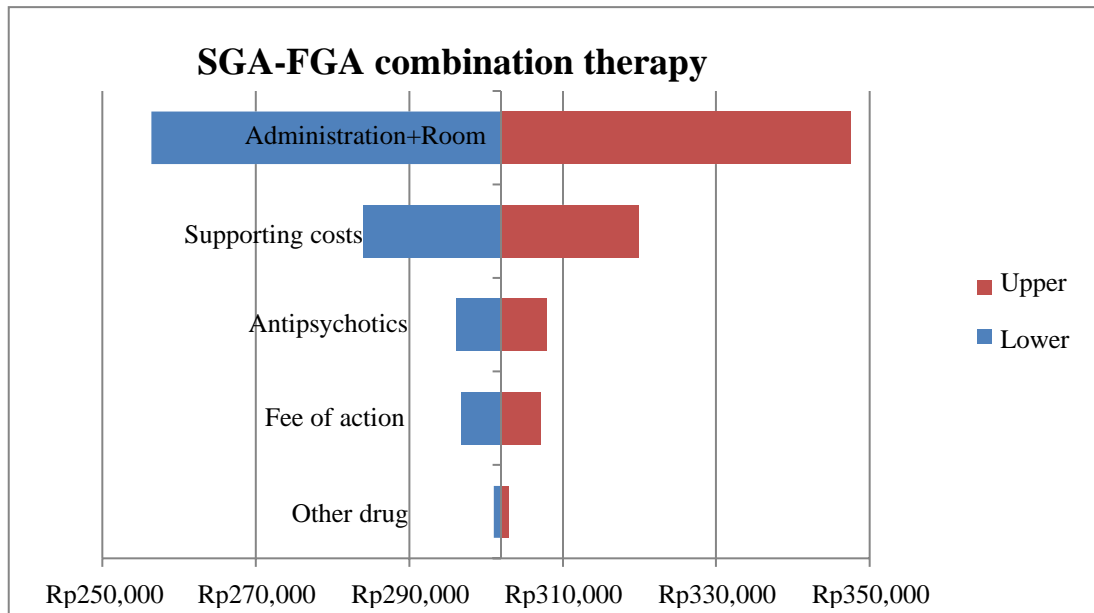


Figure.3 Sensitivity Chart SGA-FGA Combination Therapy

The sensitivity analysis of the three drug groups has been carried out by changing the value of a variable within a possible range against the calculated average while keeping the values of the other variables at a constant condition (Figure 1-3). The result with the largest number is the variable with the greatest impact on the cost-effectiveness analysis. Based on the three groups of drug diagrams, it can be seen that the largest variables are administration and room costs. This has a big impact on the costs that must be incurred.

DISCUSSION

In this study, the number of samples obtained in each group was different (Table 2), but this did not affect the results of the analysis, because each patient was calculated on the average of the use of direct medical costs. The ACER results in table 2 show that SGA atypical monotherapy is the most effective treatment indicated by the lowest value of Rp. 288,659 / 1 PANSS EC score with an average decrease in PANSS EC score of 9.70. This is similar to a study on the analysis of the cost of treatment for acute agitation in schizophrenic patients in China, which resulted in a higher cost of monotherapy atypical antipsychotics but offset by a shorter LOS. This affects the total cost of treatment. The total cost during hospitalization from the lowest was (¥ 11,157 ziprasidone and 11,923 haloperidol) (Yeh et al., 2018). A study conducted by Grunder et.al stated that patients who used SGA had a higher quality of life improvement than FGA. FGA had at least one adverse event compared to SGA, the most commonly seen being nervous system disorders (Gründer et al., 2016).

Paliperidone ER and risperidone are the dominant treatment options compared to haloperidol in Spain. This is indicated by the quality adjusted life years (QALY) obtained per patient of (0.7573) on paliperidone ER therapy. In addition, paliperidone was an inexpensive treatment strategy (€3,062), followed by risperidone (€3,194), haloperidol (€3,322), olanzapine (€3,893), amisulpride (€4,247) and aripiprazole (€4,712). (García-Ruiz et al., 2012). In another study the ziprasidone and risperidone strategies were the most effective options with a willingness to pay between \$5,200 and \$542,500 per QALY. This strategy has an ICER of \$5,200/QALY and is a cost-effective option over other, more expensive and less effective treatments (Park & Kuntz, 2014).

Side effects that are often found in FGA are blockade of D2 receptors that cause EPS, eg acute parkinsonism, akathisia, withdrawal dyskinesia [rebound D2 blockade], tardive dyskinesia [D2 receptor super sensitization], hyperprolactinemia, seizures, cognitive impairment. However, this is very rarely found in SGA users. This is because SGA has serotonin 5HT-2A receptor blockade which increases nigrostriatal dopamine. This is also related to the possibility of more rapid dissociation of SGA from dopamine receptors where dopamine antagonism is sufficient to exert antipsychotic effects but does not induce EPS. This is also related to patient compliance in taking antipsychotics (Schwartz, 2018).

The difference in the efficacy of FGA and SGA, can be seen from the pharmacodynamic profile of different clinical responses in schizophrenic patients. According to Seeman, typical antipsychotics bind more tightly to dopamine D2 receptors, with a lower dissociation constant. Whereas atypical antipsychotics bind more loosely to dopamine D2 receptors and have a higher dissociation constant than dopamine. This is due to the fact that typical antipsychotics dissociate very slowly, ie within 30 minutes, while atypical antipsychotics dissociate more rapidly, in less than 60 seconds. These data are supported by clinical brain imaging findings showing haloperidol bound to human D2 undergoing 2 positron emission tomography (PET) scans for 24 hours. In contrast, neither clozapine nor quetiapine were substantially lost after 24 hours of 2 PET. This is in accordance with the research being conducted, which is looking at the differences in the effectiveness of FGA and SGA (Mauri, 2014).

CONCLUSION

Atypical antipsychotic monotherapy showed cost effectiveness in schizophrenic patients compared to atypical-atypical combination therapy and atypical-typical combination therapy as indicated by decreasing the PANSS EC scale through reducing acute agitated symptoms of schizophrenia with an ACER value of Rp 288,659/1 PANSS EC score with an average decrease in PANSS score by 9.70.

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CONFLICT OF INTEREST

All authors state that there is no potential conflict of interest with the research, authorship, and/or publication of this article.

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