Cost-effectiveness analysis of aripiprazole-escitalopram with aripiprazole-agomelatine as bipolar treatment in a pharmacy in Bandung, Indonesia

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ABSTRACT

Background: According to WHO in 2016, there are 60 million people affected by bipolar, this case continues to increase, including in Indonesia. The prevalence of bipolar disorder varies between 1-4 percent in Indonesia. At a pharmacy located in the city of Bandung, where a psychiatrist practices, this case ranks first in a variety of other mental disorders, namely 34.1% (in 2016). Aim: The aim of the study was to analyze more cost-effective therapy between the combination of aripiprazole and escitalopram with aripiprazole and agomelatine in a pharmacy in Bandung, Indonesia. Method: The outcome used was (Montgomery Asberg Depression Rating Scale/MADRS reduction) while the cost component used is direct cost. This study was conducted retrospectively in the January-December 2016 of 90 continuous phase bipolar disorder patients in a pharmacy in Bandung, using the perspective of patients and pharmacies, with direct cost components. The intention of the patient perspective means the patient cost component, and the intention of pharmacy perspective meant the pharmacy cost component. The pharmacoeconomic method was Cost Effectiveness Analysis. Data was obtained from medical records and financial division. Results: From the statistical tests performed on the outcome group, the p-value obtained was 0.293. Based on Average Cost Effectiveness Ratio (ACER), aripiprazole and escitalopram was more cost-effective than aripiprazole and agomelatine (IDR 1,057,705/MADRS score from patients perspective and IDR 842,705/MADRS scores from institutional perspective). Then Incremental Cost Effectiveness Ratio (ICER) was IDR 470,000/MADRS score from patients perspective and IDR 265,499 from pharmacy perspective. Conclusion: It indicated that aripiprazole and agomelatine is more cost effective than of aripiprazole and escitalopram in two perspective because there was a decrease in costs/MADRS score.

KEY WORDS: Agomelatine, Aripiprazole, Bipolar, Cost-effectiveness analysis, Escitalopram

INTRODUCTION

Mental disorders are skills or behavioral patterns that are clinically related to suffer and experience in one or more of the lives of human life. Bipolar disorder is a mood disorder consisting of at least one manic, hypomanic, or mixed episode which is usually accompanied by a history of major depressive episodes. According to the WHO in 2016, there are 60 million people affected by bipolar, and this case continues to increase, including in Indonesia. The prevalence of bipolar disorder varies between 1% and 4% in Indonesia. Bipolar patients must get continuous therapy, so these patients need to spend a large amount of money. Pharmacoeconomic analysis provides suggestions for patients to choose the most cost effective drug or provide suggestions for doctors in taking decisions for patient therapy. In this pharmacy, bipolar disorder is a major case that requires pharmacoeconomic studies in the treatment of the disease and inventory of drugs focused on this disease. Therefore, pharmacoeconomic research is needed to determine the best drug that this pharmacy needs to provide.

Pharmacoeconomics is also defined as a description and analysis of therapeutic costs in a health service and more specifically is a study of the process of identification, measuring and comparing costs, risks and benefits of a program, services, and therapies and determining the best alternative. Pharmacoeconomic evaluation estimates the price of a product or service based on one or more perspective.

One example of antipsychotic group is aripiprazole. As far as is known, there are no pharmacoeconomic...
studies regarding aripiprazole. One study related to that group is comparing lurasidone and quetiapine. One of the new drugs in the atypical antipsychotic group is aripiprazole. Aripiprazole is a novel antipsychotic initially approved for the treatment of schizophrenia but soon found to be effective in bipolar disorder. This drug is well studied, as randomized controlled trials have been conducted in various phases of bipolar disorders. Aripiprazole exhibits the pharmacodynamic properties of partial agonism, functional selectivity, and serotonin-dopamine activity modulation - the new exemplars in the treatment of major psychiatric disorders. Pharmacotherapy for bipolar disorder is very complex, so in its management, patients are given more than one type of drug (combination). At one of the pharmacies in Bandung, aripiprazole combined with escitalopram (serotonin–norepinephrine reuptake inhibitor) and agomelatine (metallonergic group).

Due to these considerations, in this study, a pharmacoeconomic evaluation was carried out. The aim of the study was to analyze more cost-effective therapy between the combination of aripiprazole-escitalopram with aripiprazole-agomelatine in a pharmacy in Bandung, Indonesia.

**MATERIALS AND METHODS**

**Determination of Drug Criteria**

The drugs that compared the effectiveness of therapy and the cost was a combination of aripiprazole 15 mg tablets once a day and escitalopram 10 mg tablets once a day with aripiprazole 15 mg tablets once a day and agomelatine tablets 25 mg once daily. Only these two combinations of drugs are used in this pharmacy.

**Determination of Patient Criteria**

The inclusion criteria for patients were continuous phase bipolar patients, aged 20–50 years, and patients who received combination therapy with aripiprazole and escitalopram and who received combination therapy with aripiprazole and agomelatine. Exclusion criteria were patients who were <20 years of age and >50 years old and patients who received therapy other than a combination of aripiprazole and escitalopram and a combination of aripiprazole and agomelatine.

**Determination of Perspectives**

Determination of research perspectives was seen from an individual perspective and institutional perspective. The valuation perspective is important in pharmacoeconomic studies because the chosen perspective determines the cost component. Perspective of the assessment of patients, namely patients as pharmacoeconomic studies, the example is the calculation of health care costs to achieve a certain quality of life so that patients can assess a health intervention is quite valuable or not compared to other needs (including entertainment). Pharmacy perspective is pharmacoeconomic evaluation viewed from an institutional perspective (pharmacy) in calculating the cost-effectiveness of treatment as one of the factors in the preparation of the Hospital Formulary, DOEN, and National Formulary.

**Determination of Outcome**

The outcome was determined using the Montgomery–Asberg Depression Rating Scale (MADRS) which was used to measure the effectiveness of therapy in patients with bipolar disorder. The effectiveness of therapy was the difference in the mean reduction of the patient’s initial MADRS score and the final MADRS score during therapy.

**Determine the Cost Component**

**Patient perspective**

The cost component used was direct medical costs during the 3-month time horizon, including the total cost of using a combination of drugs and the consultation fee calculated based on the number of consultation visits.

**Pharmacy perspective**

The cost component used is the costs associated with purchasing drugs from distributors or PBF, equipment costs, and equipment costs that are used as a support in carrying out inspection activities in bipolar patients during a 3-month time horizon.

**Pharmacoeconomic Analysis**

This study used a non-experimental method with retrieval retrospective data from medical records at a pharmacy in Bandung. The pharmacoeconomic method used was cost-effectiveness analysis. Pharmacoeconomic analysis was calculated by comparing the total cost of therapy with a decrease in the MADRS score obtained from each alternative. Cost-effectiveness comparisons in both alternatives were calculated using the average cost-effectiveness ratio (ACER) method, cost-effectiveness diagrams, and the incremental cost-effectiveness ratio (ICER) method.

**RESULTS AND DISCUSSION**

The population in this study was based on medical record data at one of the pharmacies in Bandung during 2016. There were 90 patients who fit the inclusion criteria. According to the data obtained, the comparison is almost the same, men (47.8%) while women (52.2%). This is consistent with the reference that the ratio of bipolar cases between women and men is 1:1 in this pharmacy. In women, the cause can be due to the hormone estrogen. This hormone has a major effect on mood changes that can be the
beginning of the onset of bipolar disorder, while in men, it can be caused by a decrease in testosterone and serotonin [Table 1].

Patients with a range of 31–40 years were the most in this study (42.2%) because patients who seek treatment at this pharmacy are continuous phase bipolar patients who have previously been treated in other places but then do not get maximum results so that the patient’s family moves the patients to this pharmacy. Hence, first therapy for these patients when the first episode appears is not treated at this pharmacy but in another place with a different doctor [Table 1]. Based on Indonesia Ministry of Health, there are 60 million people with bipolar disorder, but there is no information on the age of the patient. There are only a number of people with general depressive disorders and anxiety for ages 15 years and over by 14 million people or 6% of the total population of Indonesia.\[9\] A combination of aripiprazole and escitalopram is given to patients more (54.4%) [Table 1]. The authors have not yet obtained a study that shows the use of a combination of drugs, but that there is a single drug use.\[6,10\]

Escitalopram works to treat depression directly by inhibiting serotonin reuptake, while agomelatine works to treat depression indirectly by binding to melatonin so as to improve sleep quality. A greater decrease in the MADRS score was found in the combination of aripiprazole and escitalopram compared with aripiprazole and agomelatine (8.02). This is due to work mechanism factors that influence the effectiveness of drug combinations [Table 2]. From the statistical test, the result was that there were significant differences between patients given combination therapy of aripiprazole and escitalopram with aripiprazole and agomelatine with significant values, 0.293 (\(P > 0.05\)) [Table 2]. In testing this statistic, data processing is performed using Statistical Package for the Social Sciences.

Cost is analyzed by calculating unit costs and total therapy costs in patient perspective [Tables 3, 4, 5 and 6]. The cost of therapy included in the cost analysis with patient perspective is a direct cost consisting of the use of drugs given for three months, where for bipolar patients who are in the ongoing therapy phase

<table>
<thead>
<tr>
<th>Table 1: Number of patients by gender, age, and drug</th>
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<tr>
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<td>Total</td>
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<tr>
<td>Drug</td>
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<td>Aripiprazole and escitalopram</td>
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<td>Aripiprazole and agomelatine</td>
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<th>Table 2: Outcome and statistical test of the combination of aripiprazole and escitalopram with aripiprazole and agomelatine</th>
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<tbody>
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<td>Drug</td>
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<tr>
<td>Aripiprazole and escitalopram</td>
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<td>Aripiprazole and agomelatine</td>
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<td>Statistical test</td>
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<th>Table 3: Cost per drug unit of patient perspective</th>
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<td>Cost components</td>
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<td>Cost per tablet (IDR)</td>
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<td>Number of drug (tablets)</td>
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<td>Total cost (IDR)</td>
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<th>Table 4: Total therapy cost of patient perspective</th>
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<td>Cost components</td>
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<td>Consultation cost</td>
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<td>Drug</td>
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<td>Cost total</td>
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requires 2-6 months in their treatment, so that therapy shows effects.\textsuperscript{[11,12]} The calculated cost is the cost per one type of drug before it is combined. The cost of therapy included in the unit cost analysis with the pharmacy perspective is the cost of drug purchases from PBF or the distributor, equipment and supplies. The time of research was 3 months [Tables 5 and 6]. The calculation done to get the results of equipment costs is to compare the time horizon divided by the economic age times the price of the equipment when first purchased. The cost per component unit is then added so that the total cost of therapy is obtained. The total cost of therapy is the total cost incurred during therapy during the 3-month time horizon in both alternatives.

The pharmacoeconomic method used is a cost-effectiveness analysis. In this method, ACER calculations are carried out. ACER formula is the comparison of the average total cost compared to the average outcome of the MADRS score reduction. [Tables 7 and 8]. From the cost-effectiveness diagram, the first alternative is the combination of aripiprazole and escitalopram as standard therapeutic references, while the second alternative, the combination of aripiprazole and agomelatine, is placed by calculating the cost-effectiveness ratio when compared with standard alternatives. From the diagram above, the combination of aripiprazole and agomelatine belongs to quadrant III interventions where these alternatives

\begin{table}[h]
\centering
\caption{ACER of the combination of aripiprazole and escitalopram with aripiprazole and agomelatine of patient perspective}
\begin{tabular}{|c|c|c|}
\hline
\textbf{Parameters} & \textbf{Aripiprazole and escitalopram} & \textbf{Aripiprazole and agomelatine} \\
\hline
Total cost (IDR) & 8,482,800 & 8,163,200 \\
Outcome & 8.02 & 7.34 \\
ACER & 1,057,705.7 & 1,112,152.6 \\
\hline
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\textit{Table 6: Total cost of pharmacy perspective}

\begin{table}[h]
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\caption{Cost components (IDR) of aripiprazole and escitalopram with aripiprazole and agomelatine}
\begin{tabular}{|c|c|c|}
\hline
\textbf{Components} & \textbf{Aripiprazole and escitalopram} & \textbf{Aripiprazole and agomelatine} \\
\hline
Drugs & 6,444,000 & 6,178,500 \\
Equipment & 299,500 & 299,500 \\
Supplies & 15,000 & 15,000 \\
Total cost & 6,758,500 & 6,493,000 \\
\hline
\end{tabular}
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\begin{table}[h]
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\caption{Cost per drug unit of pharmacy perspective}
\begin{tabular}{|c|c|c|c|}
\hline
\textbf{Components} & \textbf{Aripiprazole} & \textbf{Escitalopram} & \textbf{Agomelatine} \\
\hline
Drug & & & \\
Purchase cost per tablet (IDR) & 52,000 & 19,000 & 16,650 \\
Total of using (tablet) & 90 & 90 & 90 \\
Total cost (IDR) & 4,680,000 & 1,764,000 & 1,498,000 \\
Equipment & & & \\
Bed & - & 200,000 & - \\
Chair & - & 57,000 & - \\
Stethoscoop & - & 30,000 & - \\
Tensimeter & - & 12,500 & - \\
Supplies & - & 10,000 & - \\
Paper (Recipe, medical record, MADRS score) & - & - & - \\
dan stationary (IDR) & - & - & - \\
Plastic medicine packaging (IDR) & - & 5,000 & - \\
\hline
\end{tabular}
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\textit{MADRS: Montgomery Asberg Depression Rating Scale}

\begin{table}[h]
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\caption{ACER of the combination of aripiprazole and escitalopram with aripiprazole and agomelatine of pharmacy perspective}
\begin{tabular}{|c|c|c|}
\hline
\textbf{Parameters} & \textbf{Aripiprazole and escitalopram} & \textbf{Aripiprazole and agomelatine} \\
\hline
Total cost (IDR) & 6,758,500 & 6,493,000 \\
Outcome & 8.02 & 7.34 \\
ACER & 842,705.7 & 884,604.9 \\
\hline
\end{tabular}
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\textit{ACER: Average cost effectiveness ratio}
offer lower costs but lower effectiveness so that it is necessary to calculate the ICER [Figure 1].

Based on the patient’s perspective, the combination of aripiprazole and escitalopram is more cost effective than aripiprazole and agomelatine, with reducing cost IDR. 470,000 for each change in score. Based on the pharmacy perspective, the combination of aripiprazole and escitalopram is more cost effective than aripiprazole and agomelatine, with reducing cost IDR. 265,499 for each change in score.

CONCLUSION

The combination of aripiprazole and escitalopram is more cost effective than a combination of aripiprazole and agomelatine in the patient and pharmacy perspective in a pharmacy in Bandung, Indonesia.

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REFERENCES


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