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Cost Effectiveness Analysis of Oral Iron Chelation in Patients with Thalassemia Major at RSUP Dr. M. Djamil Padang

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Abstract:- *Thalassemia major*, as a red blood cell disorder that is passed from both parents to their children, requires high costs and the use of iron chelation drugs throughout the patient's life. Pharmacoeconomics studies in patients with *thalassemia major* needs to be conducted to determine the efficiency and effectiveness of selecting oral iron chelation drugs. This study aims to analyze the cost and cost-effectiveness of using oral iron chelation drugs such as deferasirox and deferiprone in patients with *thalassemia major* at RSUP Dr. M. Djamil Padang in 2018-2019. Data was collected retrospectively using total sampling from patient medical records and hospital information system data. Cost parameters include accommodation costs, medical treatment costs, laboratory costs, and drug costs. The effectiveness parameter used is a decrease in serum ferritin levels. Based on the results of this study, the average total cost per treatment for *thalassemia major* patients who used deferasirox (IDR 401,940,001,-) was more expensive than deferiprone (IDR 269,261,557,-). The effectiveness of deferasirox (1309 ng/mL) was bigger than that of deferiprone (830 ng/mL). The cost-effectiveness ratio of deferasirox (IDR 307,059,-/) was lower than deferiprone (IDR 324,412,-/). To change the drug from deferiprone to deferasirox requires an additional cost of IDR 276,990 per one additional unit. From the average cost-effectiveness ratio, it can be concluded that deferasirox is more cost-effective than deferiprone.

Keywords:- Thalassemia Major; Oral Iron Chelation; Cost Effectiveness Analysis; Pharmacoeconomics; Deferasirox; Deferiprone.

I. INTRODUCTION

Thalassemia major, as a group of thalassemia disease, is a blood cell disorder that is inherited from both parents. Patients with thalassemia major require routine blood transfusions and optimal administration of iron chelation drugs to maintain their quality of life. Lifelong blood transfusions are required by the patient to treat anemia and maintain hemoglobin levels of 9-10 g/dl. However, this repeated transfusion also has an unfavorable impact on the patient, namely excessive accumulation of iron in various organs of the body which causes cell damage and death [1].

Iron chelating agents/chelating agents are substances used to prevent or reverse the toxic effects of a heavy metal on enzymes or other cellular targets, or to accelerate the elimination of metals from the body [2]. In Indonesia, there are two oral iron chelation drugs, namely deferasirox and deferiprone. Both of these drugs require large financing with a fairly high cost difference. The needs for one child with thalassemia major weighing 20 kg for blood transfusions and iron chelation drugs reaches 300 million per year [3].

In line with the existence of health technology in the form of drugs, medical devices, diagnostic methods, or treatment that continues to develop, another problem arises and must be faced by users of these health/drug technologies. The problem is the relatively high prices of existing drugs. This is logically acceptable considering that the drugs used are able to provide additional value and solutions towards existing health problems. The problem regarding to the high price causes the costs needed to be able to use the new drug to be even more expensive. [4].

To compare two or more health interventions that provide different levels of effectiveness, a cost-effectiveness analysis (CEA) can be used. In CEA, treatment outcomes are not measured in monetary units, but they are defined and measured in natural units. The results of CEA are described as the cost-effectiveness ratio (C/E ratio), the numerator of the ratio represents the total cost, and the denominator of the ratio describes the effectiveness/effectiveness variable outputs. So it is presented in terms of cost to effect [5,6,7].

II. RESEARCH METHOD

Reseach Design and Data Collection

This research is a non-experimental observational cross sectional study with retrospectively retrieved data. Data collection was carried out by recording all activities related to the variables to be studied during the research time. The data

collected is secondary data from various sources, namely the medical records of the patients studied, the Pharmacy Installation, the Laboratory Installation, and the Finance Department.

Patient

This research was conducted at RSUP Dr. M. Djamil Padang, West Sumatra, Indonesia. The study population was all thalassemia major patients for the period January – December 2018 and January – December 2019. The study samples that are included in the inclusion criteria were thalassemia patients who were participants of the National Health Insurance (BPJS), aged ≥ 2 years, requiring routine blood transfusions and serum ferritin examination, using the iron chelation drugs deferiprone or deferasirox. Meanwhile, the exclusion criteria were thalassemia major patients who were not participants of the National Health Insurance, thalassemia major patients under 2 years of age, thalassemia major patients receiving injection of iron chelation drugs, and thalassemia major patients receiving combination of oral iron chelation drugs.

Cost and effectiveness

Costs are calculated using a health care perspective so that the total costs calculated are direct medical costs, consisting of accommodation costs, medical treatment costs, laboratory costs, and drug costs. The parameter of effectiveness used was the decrease in serum ferritin levels in six month intervals when using deferasirox / deferiprone.

Cost analysis

The measurement results of the cost-effectiveness ratio analysis were obtained based on the average total cost of each treatment divided by the average of drug effectiveness. A lower cost-effectiveness ratio value indicates a more cost-effective choice of drug therapy.

Sensitivity analysis

The sensitivity analysis method used in this study is a one-way sensitivity analysis method. This method is a simulation of changes in cost value with a fixed effectiveness value. The analysis is carried out by simulating the increase and decrease in costs with a percentage of 5%.

III. RESULT AND DISCUSSION

A total of 114 patients with thalassemia major received treatment at RSUP Dr. M. Djamil Padang during 2018-2019, where 90 people that use deferasirox and deferiprone were subjects in this study, while 24 people were in the exclusion criteria. The flow of patient data collection can be seen in Figure 1.

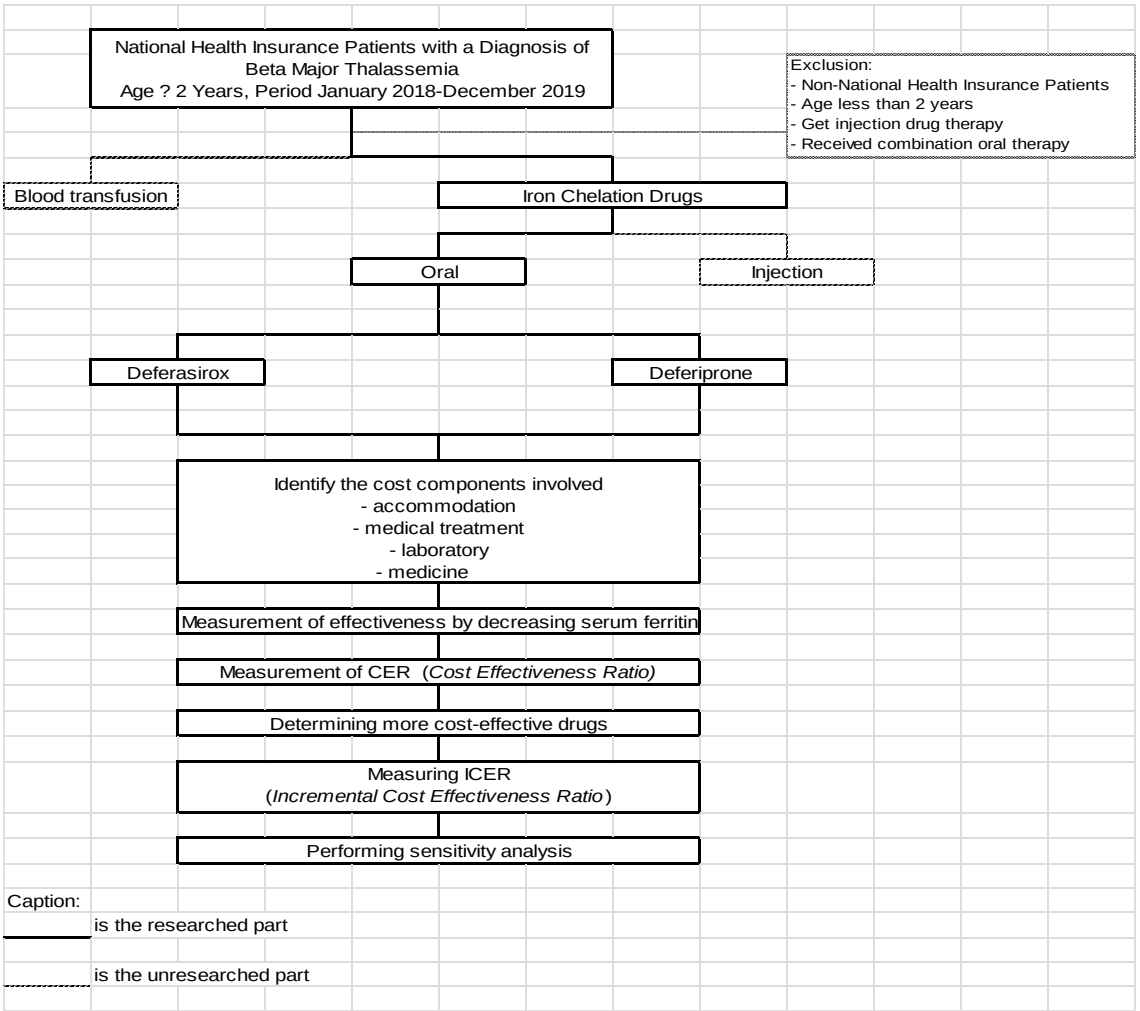

Figure 1. Patients data collection flow

From Figure 2, it can be seen that the majority of the patients involved in this study were children. This is in line with data on the life span of thalassemia patients according to research which states that thalassemia major patients have an average age of 9.82 years, with the highest age category in the range of 6-15 years (65.8%) [8].

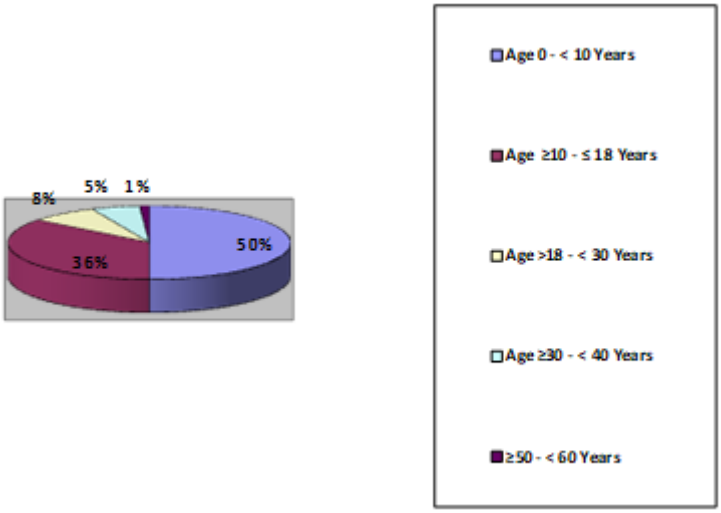

Figure 2. Characteristics of patients by age

Figure 3 shows the characteristics of thalassemia major patients at RSUP Dr. M. Djamil Padang by gender. Data on the gender of patients with thalassemia major according to research in Aceh and Medan, there are more male patients than female patients (63.3%) [8,9]. In this study, it is obtained that the number of male and female patients is equal (50% each). The distribution of the use of oral iron chelation drugs is shown in Figure 4.

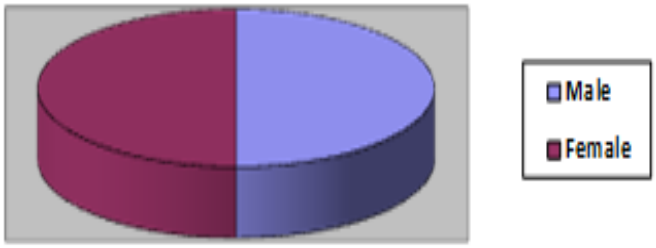

Figure 3. Characteristics of patients by gender

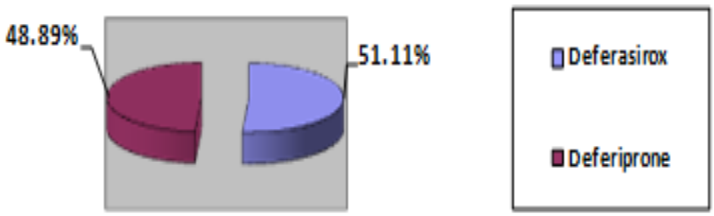

Figure 4. Distribution of oral iron chelation drug use

Data on the cost of thalassemia major patients during 2018-2019 shows that the average cost of each treatment required for patients using deferasirox (Rp 8,737,826,-) is greater than for patients using deferiprone (Rp 6,119,581,-). This is in line with research conducted in Tangerang which showed that the cost of using deferasirox was bigger than deferiprone [10]. The average effectiveness of deferasirox (1309 ng/mL) was bigger than deferiprone (830 ng/mL). This is also in line with previous studies showing that deferasirox was more effective than deferiprone [10,11]. Deferasirox showed effectiveness by lowering serum ferritin levels which was better than deferiprone because it has a very high affinity and specificity for Fe3+. The potential and specific ability of deferasirox to mobilize iron tissue and to increase its excretion has been demonstrated in several studies [12].

Table 1 shows the value of the Average Cost Effectiveness Ratio (ACER) for deferasirox which is smaller than deferiprone according to a study conducted at the Tangerang Hospital [10], but another study at the Banda Aceh Hospital stated that the ACER value for deferiprone was larger than deferiprone [13]. From the ACER value, it was concluded that deferasirox was more cost-effective than deferiprone.

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Table 1.ACER calculation results using deferasirox and deferiprone:

No	Medicine name	Average total cost per treatment	Effectiveness/average decrease in serum ferritin level	ACER
1	Deferasirox	401,940,001	1309	307,059
2	Deferiprone	269,261,557	830	324,412

Note: ACER= *average cost effectiveness ratio*

In the use of cost analysis, it is necessary to calculate the incremental cost-effectiveness ratio (ICER). With ICER, it can be seen the amount of additional costs for each change in one unit of cost-effectiveness. In addition, to make it easier to draw conclusions about which alternative provides the best cost-effectiveness in the study using the cost-effectiveness analysis method, a cost-effectiveness table can be used [4]. Deferasirox and deferiprone are present in cells that require ICER calculations. The ICER value is set to determine the additional cost for each increase in the effectiveness of a drug. The ICER value obtained is IDR 276,990 per effectiveness. The ICER value shows that there is an additional cost required if there is switched therapy from deferiprone to deferasirox. In other words, if the hospital needs to increase the effectiveness of treatment using deferasirox, the hospital must incur additional costs of Rp. 276,990 per effectiveness. The effectiveness of deferasirox is better than that of deferiprone, but the cost of using deferasirox is also higher. Hospitals need to consider whether a budget policy is needed if financing problems are found in the use of deferasirox.

The sensitivity analysis in Table 2 shows that the choice of deferasirox is sensitive towards a 25% cost increase, where the ACER value of deferasirox will be higher than the baseline deferiprone. Choosing deferasirox is also sensitive towards a 25% cost reduction of where the ACER value of deferiprone will be lower than the ACER value of deferipron. A lower ACER value for deferasirox with a better reduction in serum ferritin levels makes deferasirox more cost-effective.

Table 2.Sensitivity analysis of deferasirox and deferiprone in patients with thalassemia major

Sensitivity	Cost (A)	Decreased serum ferritin level (B)	ACER (A/B)
Deferasirox			
Baseline value	401,940,001	1309	307,059
25% drop	301,455,001	1309	230,294
25% increase	502,425,001	1309	383,824
Deferiprone			
Baseline value	269,261,557	830	324,412
25 % drop	201,946,168	830	243,309
25 % increase	336,576,946	830	405,514

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IV. CONCLUSION

From the average value of the cost-effectiveness ratio, it can be concluded that deferasirox is more cost-effective than deferiprone. Changing the drug from deferiprone to deferasirox requires an additional cost of IDR 276,990 per one additional unit of effectiveness.

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