THE EVALUATION OF THE COMPARISON ANTITUBERCULOSIS DRUGS INTERACTIONS TO THE TEENAGER AND ADULT INPATIENT AT LABUANG BAJI HOSPITAL MAKASSAR IN 2019

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ABSTRACT

***Background** : The drugs interaction is a changes of the drugs due effect because of the combination with another drugs or the consumtion of the drugs in the same time. The drugs interaction will make a reduction of the drugs effect so that the result of the therapy is not as good as the expectation. The research of the drug interaction is to reduce and prevent the treatment fo the tuberculosis patient with a right treatment so it will reduce the drugs interaction during the therapy and also can increase a good therapy which is can effective, safe and efficient. The aim of the research was to known the interaction antituberculosis drugs to the teenager and adult inpatient in the RSUD Labuang Baji Makassar 2019.*

***Methods** : The method of the research was used non-experimental (observational) descriptive analysis (qualitative) and retrospective data collection. In this research, there were 62 samples by used Slovin's formula technique. The drugs interaction in terms of Drug interaction of Stockley's book in 9th edition. Checker drugs interaction application and Medscape application.*

***Result :** The result of the research showed the interaction of the antituberculosis drugs and non antituberculosis drugs ware 62 cases (100%). The evaluation of the interaction antituberculosis drugs : The severity or the significance highest level were 34 cases (75.6%), based on the data collection in the patient who consumed Isoniazid. That medicine was used for tuberculosis treatment therapy category 1, category 2 and multi drugs resistant. Based on mechanism showed pharmacodynamics were 24 cases (53.3%). Then based on the data collection showed the most of pharmacodynamics level interaction was Moxifloxacin doe to used for the treatment of multi drug resistant of tuberculosis. In this research, the most patient was multi drug resistance of tuberculosis. Based on the interaction of pharmacodynamics level showed that antagonist was the highest level with 22 cases (91.7%).*

***Conclusion** : Based on the data collection showed the most interaction of the highest antagonist was Moxifloxacin due to used as multi drug resistant of tuberculosis.*

***Keywords**: Antituberculosis, Drug Interaction, Labuang Baji Hospital.*

INTRODUCTION

Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis that can attack the lungs and other organs (Surabaya City Health Office, 2017). Pulmonary tuberculosis is tuberculosis that occurs in the lung parenchyma (tissue). Patients who suffer from pulmonary tuberculosis and at the same time suffer from extra-pulmonary tuberculosis are classified as pulmonary tuberculosis patients (Subuh, 2016).

Tuberculosis cases in 2018 were 67.2% and this figure increased compared to 2017 which was 52.6% and also in 2016

of 35.8%. Tuberculosis cases by province in 2018, the highest province was DKI Jakarta with a percentage of 122.2 %, and followed by South Sulawesi 84.0% (Indonesian Health Profile, 2019).

Drug interactions are changes in the effect of a drug due to the presence of other drugs when given simultaneously so that the effectiveness or toxicity of other drugs changes. The existence of drug interactions can cause a decrease in drug effects so that the desired therapeutic results are not optimal. The problem of drug interactions should be a concern for health workers (Widia and Marline, 2018). Pulmonary tuberculosis patients require a lot of drugs given to treat the disease they are suffering from. However, the large number of drugs used will increase the possibility of drug related problems (DRPs), especially in the identification of drug interactions.

Concurrent use of anti-tuberculosis drugs (OAT) with comorbid drugs can lead to potential drug interactions. The effect resulting from the drug interaction is that it can cause a change in the concentration of the comorbid drugor anti-tuberculosis drugs (OAT). This can lead to toxicity or reduced efficacy of anti-tuberculosis drugs (OAT) and drugs for the disease (Veryanti et al, 2019).

In this study, adolescents and adults were taken because according to (S. Andayani and Astuti, 2017) said that patients with pulmonary tuberculosis attack almost all age groups, especially those found in the productive age (15-50 years). At that age, if a person suffers from pulmonary tuberculosis, it can result in the individual being no longer productive and can even become a burden for his family. Productive age is the age where a person is at the stage to work or produce something both for himself and for others. Based on (Amin, 2017), classifying the age of adolescents 12-25 and adults 26-45.

This research was conducted at the Labuang Baji Regional General Hospital (RSUD) Makassar city because based on data obtained from medical records it said that the number of pulmonary tuberculosis patients for hospitalization in 2019 was 363 patients and the highest compared to other diseases.

Therefore, a drug interaction study was conducted to reduce and prevent the risk of treatment in tuberculosis patients by being given appropriate drug therapy so as to reduce the incidence of drug interactions during therapy and also increase optimal therapy in order to obtain effective, safe and efficient therapy.

METHODS

Place and Time Design

The type of research used in this research is non-experimental (observational) with descriptive analysis (qualitative) and data collection is retrospective. Research and data collection were carried out at the Labuang Baji Regional General Hospital (RSUD) Makassar City on June 25-July 25 2020.

Population And Sample

The population is the whole of the unit of analysis in accordance with the information to be desired. The population in this study was all data on inpatient tuberculosis patients at the Labuang Baji Regional General Hospital (RSUD) Makassar city throughout 2019.

The sample is part of the selected population and represents the population. Samples were taken from inpatient pulmonary tuberculosis patients aged adolescents and adults at the Labuang Baji Regional General Hospital (RSUD) Makassar city in 2019. While the sample in the form of tuberculosis patient data met the following criteria:

1. Inclusion, among others

a. Hospitalized patients with a diagnosis of pulmonary tuberculosis.
b. Adolescents (ages 15-24) and adults (ages 25-44).
c. Patients with 1-18 days of treatment.
d. Patients without comorbidities or with comorbidities, including diabetes mellitus, gastritis, hypoalbuminemia, hypokalemia, hyponatremia, septicemiaanemia, anxiety disorders, poor nutrition, abdominal colic, hypertension, hypoosmolality, hyperbilirubinemia, drug-induced hepatitis, hyperuricemia, melena, pneumonia, chronic obstructive pulmonary disease and urticaria.
e. Patients with the number of drugs 2-12 types of drugs.

2. Exclusion among others: outpatients, patients under five, children and the elderly.

The sampling technique is purposive sampling. Purposive sampling is a technique for determining the sample according to certain criteria determined based on the research objectives.

Data Analysis

Data analysis is presented in tabular form with descriptive exposure and analysis using SPSS (statistical package for the social sciences, descriptive statistics). Potential drug interactions are reviewed from the book Stockley's Drug Interaction 9th Edition (2010), the drug interaction checker application and the Medscape application.

RESULT

Table 1. Distribution of Pulmonary Tuberculosis Patients by Gender

Gender	*Number (Patient)*	*Percent (%)*
Man	*40*	*64.5*
Woman	*22*	*35.5*
Total	*62*	*100.0*

Data source: Labuang Baji Hospital in 2019

Based on Table.1, there are male tuberculosis patients, 40 patients (64.5%) and women 22 patients (35.5%).

Based on the Table.2, the highest patients were aged 45-64 years (35.5%), then those aged 25-44 years (35.0%) and those over 65 years old were 57 patients (15.7).

Table 2. Distribution of Tuberculosis Patients by Age

Age	*Number (Patient)*	*Percent (%)*
38 days > 1 year	*1*	*0.3*
1-4 years	*2*	*0.6*
5-14 years old	*9*	*2.5*
15-24 years old	*38*	*10.5*
25-44 years old	*127*	*35.0*
45-64 years old	*129*	*35.5*
> 65 years old	*57*	*15.7*
Total	*363*	*100.0*

Data source: Labuang Baji Hospital 2019`

Table 3. Distribution of Tuberculosis Patients based on Duration of Treatment

Treatment Duration	Number (Patient)	Percent (%)
1-5 days	29	46.8
6-10 days	29	46.8
11-15 days	3	4.8
16 days	1	1.6
Total	62	100.0

Data source: Labuang Baji Hospital in 2019

Based on table 16 the highest percentage is 1-5 days and 6-10 days (46.8%) of treatment while the lowest is 16 days (1.6%) maintenance. Based on table 4 the highest percentage with the number of drugs is 5 types of drugs (29.0%) while the lowest is 2 types of drugs (1.6%). Based on the data obtained that many drugs depend on the many comorbidities suffered by the patient.

Table 4. Distribution of tuberculosis patients by number of drugs at Labuang Baji Hospital, Makassar City in 2019

Amount of medicine	*Number (Patient)*	*percent %*
2	*1*	*1.6*
3	*6*	*9.7*
4	*16*	*25.8*
5	*18*	*29.0*
6	*9*	*14.5*
7	*12*	*19.4*
Total	*62*	*100.0*

Data source: Labuang Baji Hospital in 2019

Based on table 5, the potential for drug interactions between OAT (anti-tuberculosis drugs) and non-Antituberculosis drugs (antituberculosis drugs) included 62 patients (100%)

Table 5. Distribution of Potential Drug Interactions in Inpatients

Potential Drug Interactions	Number (Case)	Percent (%)
Drug Interaction Occurs	343	67.4
No Drug Interactions	166	32.6
Total	509	100.0

Data source: www.drug.com, www.medscape.com, Stockley's drug interaction 9th edition.

Based on table 6, the highest interaction drug pharmacodynamic mechanism was antagonist in 22 cases (91.7%) if the effect was reducing and the lowest was synergistic in 2 cases (8.3%) synergistic pharmacodynamic interaction if the effect was strengthening. Pharmacodynamic interactions is an interaction between drugs that have similar (synergistic) or opposite (antagonist) pharmacological effects

Table 6. Distribution by Pharmacodynamics

Pharmacodynamics	Number (case)	Percent (%)
Antagonist	22	91.7
Synergistic	2	8.3
Total	24	100.0

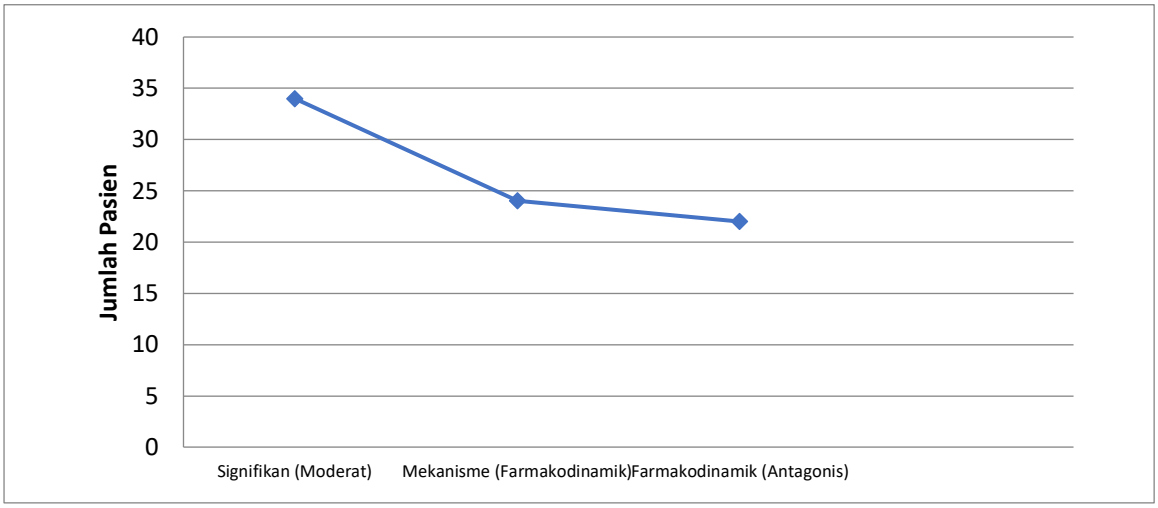
Data source: Stockley's drug interaction 9th edition

Based on table 7, the highest interaction drug pharmacokinetic mechanism is metabolism in 12 cases (57.1%) induction of the liver microsomal enzyme system by one drug can cause changes in the rate of metabolism of other drugs gradually, resulting in low plasma levels and reduced drug effects and lowest absorption. 3 cases (14.3%) interactions affect absorption, absorption rate or total amount absorbed, distribution 3 cases (14.3%) one drug can replace another drug so that the free form increases and can diffuse from plasma to the site of action of the drug and excretion In 3 cases (14.3%) the drug was eliminated by the kidneys, by glomerular filtration and by active secretion in the renal tubules. Competition occurs between drugs that use a transport mechanism.

Table 7. Distribution by Pharmacokinetics

Pharmacokinetics	Number (case)	Percent (%)
Absorption	3	14.3
Distribution	3	14.3
Metabolism	12	57.1
Excretion	3	14.3
Total	21	100.0

Data source: Stockley's drug interaction 9th edition



Graph 1. Drug Interaction Chart

Based on graph 1, the results of the study showed that the level of drug interaction was of severity or significant, namely moderate 34 cases (75.6%) of drugs, because moderate interactions can cause changes in the clinical status of patients such as organ damage. Meanwhile, based on the mechanism, namely pharmacodynamics in 24 cases (53.3%) of drugs, this interaction can be caused by competition at the same receptor or occurs between drugs that work on the same physiological system. Meanwhile, based on pharmacodynamics, there were 22 cases of antagonist (91.7) drugs, because pharmacodynamics occurred at the receptor level and resulted in changes in the effect of drugs that were antagonistic if the effect was reduced.

DISCUSSION

Based on the theory, pulmonary tuberculosis is an infectious lung disease caused by air contamination by Mycobacterium tuberculosis bacteria, where each gender has the same opportunity to infection with pulmonary tuberculosis (Surakhmi and Rini, 2016).

The prevalence of tuberculosis is more found in male than female. And globally there are more than 70% of men with AFB (acid-fast bacilli) positive compared to women (Puspita et al., 2016). Because men have a smoking habit, there will be a reduction in the phagocytic ability of alveolar macrophages and a decrease in the immune response and/or CD4+ lymphopenia due to the nicotine content in cigarettes, which is the reason for the increased susceptibility to pulmonary tuberculosis due to smoking. And also the habit of consuming alcohol which can cause changes in the immune system, especially changes in signaling molecules that are responsible for the production of cytokines that cause an increased risk of tuberculosis. Pulmonary tuberculosis patients, male gender, are more often

active outside the home. The task of men as the head of the family who is in charge of earning a living for the needs of his family. The patient works from morning to night and works quite hard, such as construction workers, working as a truck driver who goes out of town or province, so he is at risk of being easily infected with pulmonary tuberculosis. The impact is that the patient lacks rest, pays less attention to nutritious food, excessive stress and gets tired easily so that the patient is easily infected with pulmonary tuberculosis (Gunawan and Simbolon, 2017).

Older age can increase the incidence of pulmonary tuberculosis. This can occur due to agent factors, hosts and unhealthy housing environmental factors. Host factors include body resistance. Patients with pulmonary tuberculosis attack almost all age groups, especially those found in the productive age (15-50 years). At that age, if a person suffers from pulmonary tuberculosis, it can result in the individual being no longer productive and can even become a burden for his family. Productive age is the age where a person is at the stage of working or producing something both for himself and for others (S. Andayani and Astuti, 2017).

Based on the data obtained in table 3 above, the length of patient care is related to comorbidities in these patients. The longest treatment was 18 days with concomitant diseases of septicemia/sepsis. Sepsis is organ dysfunction due to impaired regulation of the body's response to infection. Aseptic conditions are disorders that cause death. The end result of tissue response to infection is the development of diffuse endovascular wounds, microvascular thrombosis, organ ischemia, multiorgan dysfunction and death. Septis is still the leading cause of death in several European countries after acute myocardial infarction, stroke, and trauma. Almost 50% of intensive care unit (ICU) patients are septic patients. The mortality rate due to sepsis in the ICU of Dr Kandou Hospital Manado is 65.7%. At Dr. Soetomo Hospital Surabaya, the rate of septic shock was 14.58%,

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CONCLUSION

1. There are drug interactions between OAT (drugs) anti tuberculosis) and not OAT (drugs) anti tuberculosis) as many as 62 cases (100%).
2. Evaluation of antituberculosis drug interactions include:
   a. The highest level of severity or significance was moderate in 34 cases (75.6 %), because based on the data obtained, the number of patients taking isoniazid because this drug is used for the treatment of tuberculosis category 1, category 2 and multidrug resistant.
   b. Based on the interaction level of pharmacodynamics, namely the highest antagonist level with a total of 22 cases (91.7 %), based on the data obtained the highest level of antagonist interaction was moxifloxacin because this drug is used for the treatment of multidrug resistant tuberculosis. and in this study the most patients were multidrug resistant tuberculosis patients.

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