

Analysis of the Relationship of Drug Side Effects and Tuberculosis Patient's Compliance After Treating With Drug Synthesis and Herbal Medicine

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ABSTRACT

Most of the problems caused by long-term use of TB drugs are adverse drug reactions or side effects of the TB drugs. The high problem of TB in Indonesia is caused by, among other things, case finding and complete treatment, which are less rapid than the spread of the disease. The main goal of treating TB patients is to reduce mortality and morbidity and prevent transmission by curing patients. The prevalence of tuberculosis in men is 3 times higher than in women. The same is happening in other countries. This happens because men are more exposed to TB risk factors such as smoking, exposure to air in the work environment and lack of non-compliance to taking medication. The diverse composition of TB drugs with the aim of being antimicrobial makes drug side effects difficult to avoid so that patient compliance becomes a problem in carrying out TB treatment. The purpose of this study was to analyze the side effects of drugs that occur and the level of patient compliance to taking medication and to analyze the relationship between the two effects. This research was a quantitative research with a cross sectional study design. This study used a survey method using a questionnaire instrument with the aim of analyzing the relationship between drug side effects and patient compliance. The sample size in this study was 200 respondents. The research locations were 4 community health centers (Puskesmas) and 1 Makassar community lung health center. Data processing and analysis techniques in this study used univariate and multivariate analysis which can be used to confirm that there is a relationship between drug side effects and patient compliance. The results showed that the side effects of drugs greatly affect patient compliance in carrying out TB treatment.

Keywords: *Drug side effects, patient compliance and tuberculosis*

INTRODUCTION

Globally, tuberculosis is a major health problem of concern and affects individuals disproportionately in low to middle income countries. In 2017, it is estimated that in 10 million people who suffer from TB, there are 1.3 million people who die and 6.7 million are recorded as TB sufferers. A total of 3.3 million (33%) were not diagnosed as having TB or diagnosed as having TB but were not reported.¹

Indonesia is the country with the 5th most TB patients in the world after India, China, South Africa and Nigeria. It is estimated that the number of TB patients in Indonesia is around 5.8% of

the total number of TB patients in the world. The number of new TB cases in Indonesia was 420.994 cases in 2017 (data as of May 17, 2018). Based on gender, the number of new TB cases in 2017 in males was 1.4 times greater than in females. Even based on the Tuberculosis Prevalence Survey, the prevalence in men is 3 times higher than in women. The same is happening in other countries. This happens because men are more exposed to TB risk factors such as smoking, exposure to air in the work environment and lack of non-compliance to taking medication. This survey found that of all male participants who smoked as much as 68.5% and only

3.7% of female participants who smoked.^{2,3,5}

The problem of drug resistance in TB treatment is an important public health problem and needs to be addressed immediately. The incidence of drug resistance has increased since the introduction of the first TB treatment in 1943. Anti-TB drug resistance TB is basically a phenomenon as a result of inadequate treatment of TB patients and transmission from these Multi Drug Resistant (MDR) TB patients. Inadequate treatment is usually the result of one or more of the following conditions: 1. Improper regimen, dosage, and route of administration. 2. Irregularity and non-compliance of patients to take medication. 3. Discontinued availability of anti-tuberculosis drugs and 4. Low quality of drugs.⁵

The use of anti-tuberculosis drugs is often found side effects that complicate the target of treatment. The side effects of anti-tuberculosis drugs that arise will interfere with the patient's activities by 81.82%. The incidence of side effects of anti-tuberculosis drugs that occurs most often is 100% reddish urine and the lowest side effects are tingling and drowsiness at 9.09%.⁶ Multidrug-resistant TB (MDR-TB) is caused by strains of *Mycobacterium tuberculosis*. with the most observed side effects were digestive disorders (18.4%), psychiatric disorders (5.5%), arthralgia (4.7%), hepatitis (3.9%), peripheral neuropathy (3.1%), hypothyroidism (2.3%), epileptic seizures (2%), dermatological effects (2%), ototoxicity (1.6%), and nephrotoxicity (1.2).⁷

The duration of tuberculosis treatment for 6 months, 9 months, and 12 months is the reason for the Patient compliance to treatment so that the achievement of successful treatment is difficult to avoid. The treatment phase is

divided into two phases, namely the intensive phase and the continuation phase. In the intensive phase, usually the patient will get more types of drugs (three, four, or five types of drugs) depending on the tuberculosis case at hand. In the intensive phase, treatment is generally continued with only two types of drugs.⁵ Many types of TB drugs and long duration make it difficult for patients to maintain compliance so anti-tuberculosis drugs are provided in the form of Fixed Dose Combination (FDC).

Rapid urbanization in developing countries and the economic status of individuals also affect a person's susceptibility to infection. The TB burden follows the socio-economic level. A person with low socio-economic status is exposed to several risk factors such as malnutrition, air pollution, alcohol and others. These conditions increase the risk of TB. Someone with lower economic status has a higher tendency to be exposed to crowds or overcrowding, lack of air ventilation and lack of safe cooking facilities. These factors also increase the risk of TB. The purpose of this study was to analyze the side effects of drugs that occur and the level of patient compliance to taking medication as well as to analyze the relationship between drug side effects and compliance of tuberculosis patients after treatment with synthetic drugs and medicinal herbs.

MATERIALS AND METHODS

The type of research used in this research was quantitative research with a cross sectional study design. This study uses a survey method using a questionnaire instrument with the aim of analyzing the relationship between drug side effects and patient compliance after treatment with synthetic drugs and herbal medicinals in the city of

Makassar. This research will be carried out in 4 Community Health Centers (Puskesmas) in the Makassar city area and Makassar Community Lung Health Center in 4 Makassar city areas. The research was conducted from March to October 2020.

The population in this study were TB respondents who were treated with modern medicine and herbal medicine. Respondents are Makassar people who live in Makassar City who perform TB treatment in several areas of Community Health Centers (Puskesmas) and Makassar Community Lung Health Centers. Samples were respondents who came to the Community Health Center and Makassar Community Lung Health Center to perform treatment and obtain synthetic drugs as well as perform alternative treatments using medicinal herbs. The sample size in this study used parameter estimates with proportion data as many as 200 respondents.

The sampling technique in this study was done by random sampling, namely randomly selecting respondents who came to the Community Health Center and Makassar Community Lung Health Center who received synthetic drugs and used medicinal herbs as alternative medicine. Respondents who were selected by random sampling were then given an explanation of the study and their willingness as respondents to answer the research questions contained in the questionnaire with the aim of analyzing the pattern of TB treatment used during therapy. Sampling of Puskesmas was chosen randomly in several areas of the Community Health Center in Makassar city and Makassar Community Lung Health Center. The instruments used in this research are

questionnaires and interview sheets which have been tested for validity and reliability. The questionnaire instruments and interview sheets are structured instruments, where respondents only answer questions according to the guidelines set.

Data processing and analysis techniques in this study used univariate and multivariate analysis which can be used to confirm that there is a relationship between drug side effects and patient compliance after treatment with synthetic drugs and herbal medicinals in Makassar city according to the hypothesis.

RESULTS

The research locations used as research locus were 4 Puskesmas and 1 Makassar Community Lung Health Center. For Community Health Centers (Puskesmas) in the Makassar city area, they are taken from the work area representing the positions of the west, east, north and south. The sample size in the study was 200 people with details: Puskesmas A = 35 respondents, Puskesmas B = 35 respondents, Puskesmas C = 35 respondents, Puskesmas D = 35 respondents. Makassar Community Lung Health Center = 60 respondents, but the sample obtained in the study was 204 respondents.

Table 1. Drug side effects felt by respondents after taking synthetic drugs (TB drugs) during TB treatment in 5 research locations in Makassar city

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no side effects	13	6.4	6.4	6.4
	1 drug side effect	60	29.4	29.4	35.8
	2 drug side effects	53	26.0	26.0	61.8
	3 drug side effects	49	24.0	24.0	85.8
	4 drug side effects	17	8.3	8.3	94.1
	5 drug side effects	9	4.4	4.4	98.5
	6 drug side effects	2	1.0	1.0	99.5
	7 drug side effects	1	0.5	0.5	100.0
	Total	204	100.0	100.0	

Table 1. Shows that 191 (93.6%) respondents from 204 respondents experienced drug side effects after undergoing the TB treatment process. A total of 60 (29.4%) respondents experienced 1 side effect from the drug and the most side effects were red urine, nausea and vomiting, drowsiness, dizziness, itching. 13 (6.4%) respondents did not experience any side effects during the TB treatment process.

Table 2. Actions taken by respondents if they experience drug side effects after taking synthetic drugs (TB drugs) during TB treatment in 5 research locations in Makassar city

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no side effects	30	14.7	14.7	14.7
	1 drug side effect	118	57.8	57.8	72.5
	2 drug side effects	56	27.5	27.5	100.0
	Total	204	100.0	100.0	

Table 2. Shows that there are 118 (57.8%) respondents who only take 1 action when experiencing drug side effects and most of the action is to continue treatment even though they get drug side effects. 56 (27.5%) respondents took 2 countermeasures when experiencing drug side effects, the most of which were continuing to take medication and consulting a doctor. 30 (14.7%) respondents did not take action when experiencing drug side effects.

Table 3. Drug side effects felt by respondents after taking herbal medicine during TB treatment in 5 research locations in the Makassar city

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no side effects	184	90.2	90.2	90.2
	1 drug side effect	16	7.8	7.8	98.0
	2 drug side effects	2	1.0	1.0	99.0
	3 drug side effects	2	1.0	1.0	100.0
	Total	204	100.0	100.0	

Table 3. Shows that 184 (90.2%) responses did not take TB treatment using medicinal herbs so that drug side effects could not be reported. However, there were 16 (7.8%) respondents who used medicinal herbs that did not show any side effects of the drug.

Table 4. Actions taken by respondents if they experience drug side effects after taking herbal medicine during TB treatment in 5 research locations in the Makassar city

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	take no action	185	90.7	90.7	90.7
	take 1 action herbal medicine side effects	14	6.9	6.9	97.5
	take 2 actions herbal medicine side effects	4	2.0	2.0	99.5
	take 4 actions herbal medicine side effects	1	.5	.5	100.0
	Total	204	100.0	100.0	

Table 4. Shows that there are 185 (90.7%) respondents who did not take action on side effects of drugs because respondents did not take medicinal herbs for TB treatment.

The relationship between the perceived side effects of synthetic TB drugs and patient compliance

Table 5. The relationship between side effects of synthetic TB drugs felt by respondents and patient compliance during TB treatment in 5 research locations in the Makassar city

		Patient Compliance		Total
		Non-Compliance	Compliance	
synthetic drug side effects	no side effects	11	2	13
	1 drug side effect	42	18	60
	2 drug side effects	25	28	53
	3 drug side effects	35	14	49
	4 drug side effects	8	9	17
	5 drug side effects	5	4	9
	6 drug side effects	2	0	2
	7 drug side effects	1	0	1
Total		129	75	204

Table 5. Shows that there are 18 respondents (30%) with 1 side effect of the drug being compliance to taking medication during TB treatment. The number of respondents 28 (52.3%) who got 2 side effects of drugs were obedient to taking medication.

The relationship between drug side effects and patient compliance

Table 6. Relationship of actions when drug side effects occur and patient compliance during TB treatment in 5 research locations in the Makassar city

		Patient Compliance		Total
		Non-Compliance	Compliance	
	take no action	24	6	30

synthetic drug side effects	take 1 action synthetic drug side effects	61	57	118
	take 2 actions synthetic drug side effects	44	12	56
Total		129	75	204

Table 6. Shows that there are 61 (51.7%) respondents who are not compliant in carrying out the TB treatment process when choosing a choice of action when drug side effects occur and there are 44 (78.6%) respondents who are not compliant in carrying out the TB treatment process when choose two options of action when drug side effects occur.

The relationship between the perceived side effects of herbal medicine and patient compliance

Table 7. The relationship between the side effects of herbal medicine felt by respondents and patient compliance during TB treatment in 5 research locations in the Makassar city

		Patient Compliance		Total
		Non-Compliance	Compliance	
Herbal medicine side effects	No side effect of herbal medicine	113	71	184
	1 side effect of herbal medicine	12	4	16
	2 side effects of herbal medicine	2	0	2
	3 side effects of herbal medicine	2	0	2
Total		129	75	204

Table 7. Shows that there are 184 respondents who did not feel the side effects of the drug even though they had used herbal medicine but were not in the category for TB treatment.

The relationship between the side effects of herbal medicine and patient compliance

Table 8. The relationship between actions when side effects occur from herbal medicine and patient compliance during TB treatment in 5 research locations in the Makassar city

		Patient Compliance		Total
		Non-Compliance	Compliance	
Herbal medicine side effects	take no action	114	71	185
	take 1 action drug side effects of herbal medicine	10	4	14
	take 2 actions drug side effects of herbal medicine	4	0	4
	take 4 actions drug side effects of herbal medicine	1	0	1
Total		129	75	204

Table 8. Shows that 185 respondents did not take action when there were drug side effects that were felt when taking medicinal herbs. Herbal medicine are not for the purpose of treating TB.

DISCUSSION

The results of the study with a sample size of 204 respondents obtained from 5 research locations, namely the Makassar Community Lung Health Center, Puskesmas Kassi-Kassi, Puskesmas Sudiang, Puskesmas Jumpandang Baru, Puskesmas Pertiwi. This study analyzes the side effects of drugs that occur and the level of patient compliance to taking medication and analyzes the relationship between drug side effects and tuberculosis patient compliance after treatment with synthetic drugs and herbal medicine.

Drug Side Effects

A drug side effect is an unwanted effect of a drug that has been previously predicted and within the therapeutic dose limit. Side effects are impossible to avoid in treatment, but are prevented to a minimum by avoiding known risk factors. Drugs may cause side effects, as well as pharmacological effects. Drug side effects are also the result of complex interactions between drug molecules and specific sites of action in the body's biological systems. If a pharmacological effect occurs to an extreme, it will have a negative effect on the body's biological system. The mortality rate due to drug side effects is 0.24%-2.9% and the age group most often exposed to drug side effects is the elderly age group 60 years and over due to imbalanced pharmacokinetic and pharmacodynamic responses.^{23,24} In this case, most of the respondents felt 2 side effects of drugs that occurred after the treatment process. The most common side effects of TB drugs in respondents were red urine, nausea/vomiting and dizziness, while the 2 side effects of drugs that occurred

simultaneously were red urine and dizziness. The content of TB drugs that give side effects of red urine is rifampicin which is a class of antibiotics that inhibits bacterial growth by inhibiting protein synthesis, especially at the transcription stage. Rifampicin blocks the attachment of the RNA polymerase enzyme by binding to the active site of the enzyme. Rifampicin has a red powder or tablet, this is what causes the filtrate of the drug to be released with red urine.²⁵

Likewise, TB drugs whose side effects cause dizziness or nausea/vomiting are isoniazid and pyrazinamide.^{19,22,25} In this study, analyzing the actions taken by respondents when experiencing drug side effects, the results showed that there were 118 (57,8%) respondents took 1 action when experiencing drug side effects and most of the actions were continuing treatment despite getting drug side effects. 30 (14.7%) respondents did not take action when experiencing drug side effects. The length of treatment duration and patient compliance will determine the success of TB treatment so that respondents who experience drug side effects continue to take TB treatment.

Patient Compliance

TB treatment is inseparable from one of the success factors of the treatment, namely compliance. Compliance is a cooperative attitude or behavioral accuracy shown by patients in carrying out drug therapy so that goals can be achieved.¹⁹ This study showed that of the 204 respondents who took TB treatment there were 129 (63.2%) respondents who did not comply in

carrying out the treatment process. Non-compliance results in the use of drug doses being reduced so that patients lose the benefits of drug therapy. The duration of TB treatment (6-8 months) resulted in a high rate of non-compliance to drug use. Several interaction factors influence the patient's decision to stop taking the drug. Compliance with tuberculosis treatment is so complex, the phenomenon is dynamic with various factors interacting with each other, so that it has an impact on behavioral selection decisions.²²

The relationship between drug side effects and patient compliance

Drug side effects and patient compliance are two things that are related to the success of TB treatment. The results showed that drug side effects greatly affect patient compliance, of the 204 respondents who took TB treatment 129 (63.2%) did not comply with the treatment due to the side effects they experienced. Drug side effects are adverse effects of a drug that have an impact on the patient compliance process in carrying out treatment.^{24,26,27}

The relationship between the respondents actions when experiencing drug side effects and patient compliance

Efforts made by respondents in carrying out TB treatment so that drug side effects do not have an impact on non-compliance in carrying out treatment do not show the success of patient compliance. The results showed that of the 204 respondents who took TB treatment, even though measures were taken to overcome the side effects of drugs that occurred, the level of non-compliance was still higher than compliance.

CONCLUSION

1. Drug side effects greatly affect patient compliance in carrying out TB treatment
2. The level of patient compliance in the TB treatment process is still low
3. The actions taken by respondents in overcoming the side effects of drugs that occur do not have an impact on increasing drug compliance.
4. The pattern of using TB drugs using herbal medicine has not been of interest to respondents as an alternative to TB treatment.

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