Research Article

IDENTIFICATION OF DRUG-RELATED PROBLEMS IN ADULTS WITH TUBERCULOSIS AT THE TEBET SUBDISTRICT HEALTH CENTER FROM JULY TO DECEMBER 2018

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ABSTRACT

Objective: Tuberculosis (TB) is a highly prevalent infectious disease caused by *Mycobacterium tuberculosis.* The recommended TB treatment is a combination of various antibiotics in the form of a fixed-dose combination tablet or kombipak; however, this increases the prevalence of drug-related problems. Therefore, this study aimed to identify drug-related problems of patients receiving TB therapy at the Tebet Subdistrict Health Center from July 2018 to December 2018.

Methods: The study was designed as a cross-sectional study using the retrospective data retrieval method from prescriptions of patients with TB from July 2018 to December 2018. The classification system prepared by Cipolle, Strand, and Morley was used for the classification of drug-related problems; this system includes unnecessary drug therapy, required additional drug therapy, ineffective drug, dosage error, and drug interaction.

Results: The percentage of unnecessary drug therapy, required additional drug therapy, ineffective drug, dosage error, and drug interaction was 2.85%, 6.89%, 1.54%, 12.46%, and 66.18%, respectively, with the occurrence of drug-related problems being the highest.

Conclusion: The administration of anti-TB drugs can potentially cause drug-related problems. Therefore, the assessment needs to be optimized before the administration of medications to patients and medications should be prescribed and monitored regularly to achieve rational drug use.

Keywords: Tuberculosis, *Mycobacterium tuberculosis*, Antituberculosis, Drug-related problems, Cipolle.

INTRODUCTION

Tuberculosis (TB) is a highly prevalent communicable disease caused by *Mycobacterium tuberculosis* [1]. The World Health Organization [2] stated that 9 million individuals were infected by *M. tuberculosis* in 2013 worldwide. Moreover, 1.5 million individuals worldwide die due to *M. tuberculosis* infection annually. In 2017, 87% of new TB cases occurred in 30 countries and >95% cases of TB-infected individuals in developing countries such as India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa [2]. Indonesia, with 842,000 cases, is the third country with the highest number of cases of TB worldwide after India and China [2-5].

The compliance with medication intake in patients infected with TB and with other diseases is challenging, leading to multidrug- or rifampicin-resistant (RR) TB (Multidrug resistance [MDR]/RR-TB) [4,5]. Some reasons for this include failure in dose use, indiscipline, and drug interaction with other medicines [6]. Recently, the treatment success rate of patients with TB has decreased from 89.5% in 2008 to 85.1% in 2017 [7]. Furthermore, although drug interaction can occur, the combination drug therapy is still effective in treating TB [8]. Problems mentioned earlier are part of the problems observed in treating patients with TB [2,9,10].

Problems related to drug resistance can possibly occur or can potentially become a problem in treatment. Moreover, it can influence quality of life and affect the socioeconomic status of patients. To date, there have been many issues in the management of patients with MDR/RR-TB related to indication, efficacy, safety, and discipline [11,12]. Therefore, pharmacists have an important role in providing drug rationally to patients to tackle and reduce problems [13].

Successful treatment of patients with TB can be achieved by complex treatment with long-term duration. This study aimed to analyze and identify anti-TB drug-related problems at the Tebet Subdistrict Health Center in 2018.

METHODS

This study used cross-sectional, descriptive, and secondary data analysis from adult prescription medicine from July 2018 to December 2018 at the Tebet Subdistrict Health Center. The study was conducted from February 2019 to July 2019. The study has received a research permit from Unit Pelaksana Pelayanan Terpadu Satu Pintu, Kota Administrasi Jakarta Selatan by number 237/082.61.

The samples of this study were randomly selected from the prescription of patients with TB aged 18–64 years. The diagnosis was coded using the International Classification of Diseases-10 (ICD-10). ICD-10 A15.0 indicates patients with TB confirmed by sputum microscopic test with or without sputum culture, ICD-10 A15.1 indicates patients with TB diagnosed only by sputum culture, ICD-10 A15.2 indicates patients with TB confirmed by histologic examination, and ICD-10 A15.3 indicates patients with TB diagnosed by unpredictable test. Exclusion criteria were incomplete prescriptions, prescription for MDR/RR-TB, pregnant women with TB, patients with HIV, patients with TB, TB with more than one code of ICD-10, and respiratory TB.

Data were analyzed using univariate analysis using Microsoft Excel 2013. Analysis was performed to examine the incidence distribution related to drug problems of patients with TB classified by Cipolle *et al.* [14]. Furthermore, the data used to analyze the percentage of problems related to medicine and medicine interaction caused from drug therapy

using online IBM Micromedex Web Access Application and/or Drug Interaction Checker Medscape.

RESULTS

The total sample was 2023 prescriptions. However, only 483 prescriptions were included in the final analysis. Other prescriptions were excluded because they did not meet the inclusion criteria. Tables 1 and 2 summarize patient characteristics.

The result showed that the TB status in men at 62.41% was higher than that in women. Based on age, patients with TB were aged 18-<36 years. Table 2 shows characteristics of patient with TB based on age.

Table 3 shows the description of prescriptions.

The problem identification of this study used the classification system from Cipolle *et al.* [14]. The classification consisted of seven classifications, such as treatment requiring other additional medicines, unnecessary prescription of drugs, overdose, less dose, wrong medicine, unwanted drug reaction, and patient compliance [14]. Table 4 shows the drug problems. Tables 5-9 show the description of drug problems per category.

DISCUSSION

Population and sample
In this study, the number of male patients with TB was more than that of women. First, this may be due to the patriarchal culture in Indonesia,

where men can generally access TB treatment more easily [15]. Second, more men smoke and consume alcohol compared with women. Higher male mobility also increases men's risk for being more exposed to TB-causing bacteria [15]. Women's immunity to TB is higher than in men [16]. Third, the biological microbiological examination of sputum in men is more sensitive than that in women; hence, the detection of TB in men is easier [17].

TB is highly prevalent in the 18–<36 years of age group. This may be due to the high mobility of the reproductive age, and a dense work environment causes a patient with TB to potentially transmit the disease to his colleagues [15]. In addition, TB can develop potentially more in the reproductive age compared with latent TB [18].

Anti-TB drugs are the most prescribed drugs in TB therapy. This condition is in accordance with the treatment needed, namely, TB therapy with anti-TB drug in the form of fixed dose combination (FDC) and kombipak.

Identification of drug-related problems
Unnecessary drug therapy
Drug therapy is unnecessary when the patient has no clinical indication. Providing unnecessary therapy can cause resistance, particularly in

Table 1: Characteristics of patient with tuberculosis based on sex

Sex	Total patients (n=133)	Percentage
Male	83	62.41
Female	50	37.59

Table 2: Characteristics of patients with tuberculosis based on age

Group of age	Number (n=133)	Percentage
Group 1 (18–<36 years)	76	57.14
Group 2 (36–<56 years)	37	27.82
Group 3 (56–<65 years)	20	15.04

Table 3: Prescription conditions of patients with TB

Name of drug	Frequency (n=843)	Percentage
Anti-TB drugs	529	62.75
FDC	270	32.03
Anti-TB drug Category 1	232	27.52
Anti-TB drug Category 2	37	4.39
Anti-TB drug category for children	1	0.12
Kombipak	121	14.35
Isoniazid	44	5.22
Rifampicin	44	5.22
Ethambutol	26	3.08
Pyrazinamide	7	0.83
Injection	138	16.37
Streptomycin sulfate	138	16.37
Other than anti-TB drugs	314	37.25

FDC: Fixed-dose combination, TB: Tuberculosis

Table 4: Description of drug problems

Drug-related problems category	Recipe sheet (n=479)	Percentage of recipe sheet
With drug-related problems	383	79.30
Without drug-related problems	96	19.70

Table 5: Description of unnecessary drug therapy

Drug therapy	Recipe sheet (n=843)	Percentage
Drug therapy is not needed	24	2.85
Drug therapy is needed	819	97.15

Table 6: Prescription conditions of patients with tuberculosis

Additional drug therapy	Recipe sheet (n=479)	Percentage of recipe sheet
Need for additional therapy	33	6,89
No need for additional therapy	446	93,11

Table 7: Ineffective drug prescription

Effective drug	Recipe sheet (n=843)	Percentage of recipe sheet	Recipe sheet (n=479)	Percentage of recipe
Ineffective drug	13	1.54	9	1.88
Effective drug	843	98,46	470	98.12

Table 8: Description of the accuracy of tuberculosis therapy doses at the Tebet Subdistrict Health Center

Ketepatan dose	Recipe sheet (n=843)	Percentage of recipe sheet	Recipe sheet (n=479)	Percentage of recipe
Accuracy of dosing	738	87.54	391	81.63
Inappropriate dose	105	12.46	88	18.37
Overdose	46	5.46		
Low dose	59	7.00		

Table 9: Description of potential drug interactions in tuberculosis therapy at the Tebet Subdistrict Health Center

Interaction	Recipe sheet (n=479)	Percentage
With interaction	317	66.18
No interaction	162	33.82

prescribing antibiotics. In addition, the administration of unnecessary therapy can also cause undesirable effects. The administration of unnecessary drug therapy is due to physicians focusing on the symptoms of the patient, not based on diagnosis. In addition, demands from patients who desire that their symptoms disappear quickly encourage doctors to prescribe medications to treat symptoms.

In TB therapy, side effects are nausea, vomiting, and epigastric pain; increased liver enzyme levels; arthralgia; acne; and cutaneous pruritus or fever [8]. Therefore, in addition to anti-TB drug, additional drugs are also prescribed that are intended to overcome the side effects of TB therapy. Prescribing loratadine, cetirizine, and chlorpheniramine maleate are intended to overcome the side effects of pruritus or itching and rashes. Domperidone, ranitidine, omeprazole, and antacids are prescribed to overcome the side effects of nausea and vomiting.

Required additional therapeutic drugs

Additional therapeutic drugs are required to prevent the occurrence of a clinical condition or disease and to administer initial therapy for a medical condition. Additional drug therapy required in this study is the provision of anti-TB drug in the form of injection, FDC, or kombipak. Prescriptions considered to require additional therapeutic drugs are those that only relieve TB symptoms but do not treat TB bacterial infections; for example, patients are only prescribed guaifenesin and Vitamin B or are only prescribed salbutamol without being prescribed anti-TB drug in accordance with TB management guidelines. TB therapy without antibiotics can result in more severe infections, recurrence, and resistance if patients only undergo some TB therapy procedures with anti-TB drug.

Ineffective medicine

Ineffective medicine is when the drug administered does not provide the expected effect suitable for a medical condition. One of the cases found was dexamethasone prescription, wherein the drug was contraindicated for patients with TB. Dexamethasone is an anti-inflammatory agent that works by inhibiting cytokines and decreasing cellular immunity. With decreased immunity, patients with TB become more susceptible to the infectious bacteria. In addition, the administration of dexamethasone can also eliminate the symptoms of TB so the patient feels healed after its administration although the infection still exists if the patient does not undergo therapy with anti-TB drug.

Anti-TB drug for the children category was also prescribed for patients aged 59 years who weigh 41 kg. This case is considered as ineffective drug administration because anti-TB drug for the children category is intended for patients aged 0–14 years based on the management used at the Tebet Subdistrict Health Center, the National Guidelines for TB Control [19]. For these cases, there are other more effective drug choices, namely, Category 1 or 2 anti-TB drug intended for adult patients weighing at least 30 kg.

Dosage accuracy

Appropriate dosage is the administration of drugs in accordance with the dose based on the patient's body weight and age, as well as the frequency of administration based on official management. The accuracy of the dose in TB therapy is still a problem because the low dose can result in resistance and lead to failure of therapy, whereas it can result in poisoning in cases of overdose if the dose reaches toxic levels or can even result in death if the dose given reaches the lethal dose.

Drug interaction

Drug interactions are conditions, wherein the effects of a drug change with the presence of other drugs, herbal medicines, food, drinks, or chemicals in the surrounding environment. The effects of drug interactions can be dangerous if the reaction increases the toxicity of a drug. Reduced drug efficacy is sometimes also as dangerous as increased toxicity.

Most of the interactions that occur in TB management cause hepatotoxicity. However, the use of a combination of interacting drugs cannot be avoided; hence, liver function must be monitored by checking the levels of alanine aminotransferase (ALT) and aspartate aminotransferase to prevent hepatotoxicity. A hepatoprotector, such as curcumin, can also be prescribed to protect the liver from damage. The administration of anti-TB drug can be stopped if the increase in ALT levels exceeds thrice the upper limit of normal (ULN), with an increase in bilirubin levels, or an increase in the ALT levels exceeds 5 times the ULN without increasing the bilirubin level [20].

CONCLUSION

Patients undergoing TB therapy at the Tebet Subdistrict Health Center from July 2018 to December 2018 are mostly men in the 18–<36 years of age group. The percentage of unnecessary drug therapy and required additional therapeutic drugs for TB therapy is 2.85% and 6.89%, respectively. Therefore, prescriptions with writing errors should be immediately revised and updated in the Puskesmas information system so that the data used for further research can actually reflect prescription. The diagnosis in the ICD-10 code should be written in full in accordance with the patient's medical condition to provide the appropriate therapy in accordance with the diagnosis of the physician.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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