http://ejournal.seaninstitute.or.id/index.php/healt
Jurnal eduhealth, Volume 13, No 02, 2022
E-ISSN., P-ISSN. 2087-3271

Description of Side Effects of Using Antituberculosis Drug in Pulmonary Tuberculosis Patients: Literature Review

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ARTICLE INFO

Keywords:
Pulmonary tuberculosis,
Drug side effects,
Antituberculosis drugs,
Mycobacterium tuberculosis

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ABSTRACT

Pulmonary tuberculosis (TB) is a chronic and infectious disease that is still a global concern. The bacterium that causes tuberculosis is the bacterium Mycobacterium tuberculosis. The high incidence of tuberculosis is due to the rapid spread of bacteria caused by the easy transmission of the disease, namely through the droplet nucleus containing Mycobacterium tuberculosis. Tuberculosis morbidity and mortality is a serious problems, especially due to the emergence of side effects of Anti Tuberculosis Drugs (OAT). most sufferers feel unable to tolerate the side effects of OAT experienced during the treatment process. This study aimed to determine the side effects felt by patients with pulmonary tuberculosis who used antituberculosis drugs. The most widely used method is the descriptive method with a cross-sectional approach with different data collection. The results showed that side complaints caused by OAT ranged from mild effects: nausea, abdominal pain, joint pain, tingling, and red urine to severe side effects, namely respiratory syndrome (shortness of breath), itching, and redness of the skin, deafness, jaundice. without other causes, visual disturbances, and vomiting.

1. INTRODUCTION

A chronic infectious and contagious disease that is still a concern in the world is pulmonary tuberculosis (TB). The bacteria that causes pulmonary tuberculosis, namely Mycobacterium tuberculosis (Merzistya & Rahayu, 2019). When a smear-positive pulmonary TB patient speaks, coughs, sneezes, or expels phlegm into the air, it is very possible to transmit the disease as much as ±3,000 droplets of sputum containing germs [1].

Until now, tuberculosis is one of the top 10 killers globally and is a serious infectious disease. India, China and Indonesia are the three countries with the most cases. Based on data from the World Health Organization (WHO), Indonesia is ranked third as the country with the most cases of pulmonary TB in the world. Tuberculosis cases are still the main cause of death in Indonesia [2].

Many patients have experienced Mycobacterium tuberculosis because the spread of this disease is very easy which causes transmission from individual to other individuals. Based on this, the use of the DOTS (Directly Observed Treatment of Short Course) approach for treatment is one of the methods used to control pulmonary TB [3].

Five important components make up the DOTS strategy. First, a political commitment that is supported by greater long-term finances. Second, finding cases using high-quality sputum and examining it under a microscope. Third, routine care with patient supervision and assistance. Fourth, an efficient management system and availability of anti-tuberculosis drugs (OAT). Fifth, a monitoring, recording and reporting system that can show the results of treatment and program effectiveness [4].

A very important problem with tuberculosis is the side effects caused by the use of anti-tuberculosis drugs (OAT). All pulmonary tuberculosis patients seeking treatment must be informed about the side effects of anti-tuberculosis drugs; failure to do so may result in withdrawal from the drug. Monitoring drug side effects is very important to get the best treatment results. The negative effects of

anti-TB drugs observed during treatment are often intolerable to many patients. The intensity of side effects has an effect on how well patients take their medications and can even lead to disengagement (lack of follow-up) from therapy [5].

Patients with pulmonary TB can experience adverse or severe side effects. These side effects, namely, nausea, vomiting, no appetite, stomach pain, headache, dizziness, itchy skin, tingling, visual disturbances, hearing loss, reddish urine, joint pain [6]. This causes problems in the treatment of pulmonary TB and kills tuberculosis bacteria, because it interferes with the successful effect of therapy. Interruption of therapy due to side effects causes bacterial resistance to increase the disease burden and patient burden [7].

It is very important to identify the side effects of OAT with appropriate management. Patient adherence to therapy is affected by these side effects. To identify and manage mild to severe adverse events, the patient's clinical status must be consistent throughout treatment. Therefore, I conducted this research by conducting a literature study, namely conducting a review of various journals related to the side effects of antituberculosis drugs in pulmonary tuberculosis patients to identify the side effects experienced by pulmonary tuberculosis patients who use antituberculosis drugs.

2. METHOD

The first method uses judgmental sampling and analytic observation through cross-sectional sampling. To measure patient compliance, data was collected using primary data in the form of a questionnaire. In addition to questionnaires, patient medical records can be used to measure medication history factors, drug side effects, and disease history [8]. The second method, research used descriptive observational analysis. This study used a cross sectional design. Frequency distribution tables and univariate data analysis were used to show the percentage of side effects experienced by patients during therapy. This tool is a checklist listing the various side effects a patient may experience and how to manage them [3]. The third method, an analytic observational study, uses the Case Control method. Three stages of data analysis were completed: univariate analysis to determine the frequency distribution; bivariate analysis using odd ratio analysis; and multivariate analysis [9]. The fourth method is a descriptive observational study using TB patient treatment cards as the basis for retrospective data collection. Total sampling is the approach used for sampling [10]. Fifth method, literature study. Literature study is a type of research that seeks appropriate sources of discussion [2]. The sixth method, descriptive observational time series, such as routinely checking side effects every two months (early intensive) treatment [6]. The seventh method, this type of cross-sectional descriptive study uses patient questionnaires as the main source of primary data [7]. The eighth method, cross-sectional strategy and descriptive technique.For adult pulmonary TB patients, data were collected retrospectively using secondary medical record data [4].

3. RESULTS AND DISCUSSION

Table 1. Methods and results of journal review

No	Method	Result
1	Cross sectional, judgmental sampling technique.	Complaints from pulmonary TB patients who have been taking medication for more than two months about side effects such as nausea and vomiting. Attacks and distress caused by activity interruption. effects on patients from irregular drug use or discontinuation of treatment.
2	Descriptive observational. Cross Sectional Study.	Symptoms experienced by sufferers include nausea, vomiting, red urine, anorexia, fever, joint discomfort, itching, and skin redness. Nausea and red urine accounted for 71.5% of the frequently reported side symptoms.
3	Observational analytic Case Control approach.	According to the results of the analysis, the presence of drug side effects was associated with a risk of drug non-adherence 5,492 times higher than the absence of drug side effects (Odds

		Ratio = 3.853 or OR > 1 with a Lower Limit (LL) = 1.723 and an Upper Limit (UL) = 8.616 with a level 95% confidence and supported by a value of p = 0.001 (p <0.05).
4	Using TB patient cards as a basis for retrospective data collection, descriptive observation of treatment.	There are side effects of red urine, nausea, weakness, mild itching, bone pain, fever and no side effects
5	Study of literature	The gastrointestinal system is the organ system most frequently affected by pharmacological side effects, according to literature studies. The second largest organ in the body, the skin, is the most negatively affected by OAT use. It is relevant that one of the systems that is often affected by pharmacological side effects when taking antituberculosis drugs is the gastrointestinal system. Patients with pulmonary tuberculosis most often report nausea, itching, vomiting, and fatigue as side effects of OAT. Joint discomfort, peripheral neuropathy, anorexia, flu-like symptoms, urine discoloration, hepatitis, hypersensitivity, hyperuricemia and severe hepatotoxicity are other adverse effects.
6	Descriptive observational with time series design	In the first and second weeks, more patients reported having anti-TB side effects. With continued treatment, fewer patients reported having OAT side effects. Patients still often report having negative side effects from OAT. According to data, 67.2% of patients had side effects until the end of the therapy phase. Joint pain (81%) was the most common OAT side effect seen by pulmonary TB patients during treatment. Other side effects included nausea (79.3%), itching (77.6%), loss of appetite (75.9%), vertigo (67.2%), and tingling (50%). Hearing loss (6.9%) was the least visible impact.
7	Descriptive with a cross-sectional approach. Primary research data were collected from patient questionnaires.	Patients reported experiencing red urine as a side effect 22% of the time. Patients experienced nausea as a secondary side effect in 18% of cases, which started soon after treatment was finished. In addition, patients reported side effects including weakness (14%), joint discomfort and itching (8%), and vomiting (12%).
8	Cross-sectional strategy and descriptive techniques. Medical records of adult patients with pulmonary TB are used to produce retrospective data using secondary data.	Disturbance of the first line Hepatobiliary system is a side effect of OAT which occurs in 35.7% of cases. The most common side effect in category I OAT patients is hepatotoxicity. Hepatotoxicity, digestive problems, itchy skin, neurological problems, and kidney failure are among the category II side effects of OAT.

Patients undergoing OAT treatment experience mild to severe side effects and these side effects are unwanted conditions even though the drug has been used according to the dosage and usage and affects patients in taking the drug obediently [11].

When treating pulmonary tuberculosis, side effects play an important role in ensuring that patients take their medications as prescribed. Patients who do not experience drug side effects will feel calm and motivated to complete their treatment, while those who experience them will experience discomfort due to the side effects of the drugs they are taking and may give up on continuing treatment [8]. Handling side effects, including providing pharmacological information along with complaints received and administering drugs in response to complaints [3].

Patients who take OAT because of unpleasant symptoms can experience drug side effects, such as symptoms. The side effects of OAT range from mild (nausea, stomach discomfort, tingling, pain on urine color) to severe (respiratory syndrome, itching and redness of the skin, jaundice without other causes, vision, hearing problems, and vomiting) [9].

The 2014 Ministry of Health guidelines do not apply to the management of OAT KDT 1 category of side effects. For example, the recommended amount for treating pyridoxine deficiency is 20-50 mg, but patients in trials are receiving only 2-10 mg of pyridoxine, which should be used as a prophylactic dose for nausea. Due to nausea, pyridoxine cannot have its full effect [10].

Rifampicin is responsible for the side effects of nausea, stomach discomfort and anorexia. nausea caused by streptomycin. Isoniazid-induced effects include tingling and itching. Isoniazid can interact with drugs that cause vitamin deficiencies because it has the same chemical structure in the body as pyridoxine (Vitamin B6). Vitamin deficiencies can make you feel sick, tired, weak, and lose your appetite [2].

Because this was the first time taking OAT, the first and second weeks had the most negative effects. Patients are most susceptible to side effects at this time. KDT OAT side effects can be caused by one or more of the drugs included in it. Rifampicin (R), isoniazid (H), pyrazinamide (Z), streptomycin (S), and ethambutol (E) are the various types of drugs found in KDT. Pyrazinamide is the drug that most often causes side effects. When an allergic reaction occurs, histamine and body acid levels can increase, causing inflammation and pain in the muscles and joints of people with pulmonary tuberculosis.

Side effects of rifampin include decreased appetite and stomach upset. Streptomycin-induced vertigo or balance problems. Side effects of isoniazid include tingling and itching of the skin. There are several factors that can affect how you respond when OAT side effects occur. Susceptibility to isoniazid is seen in Asian races, one of which is Indonesia, which is genotypically categorized as a fast acetylator. Because isoniazid, one of the ingredients in KDT, has the same chemical formula as pyridoxine in the body, isoniazid can combine with other drugs to produce vitamin deficiency (anorexia) [6].

Red urine is the most common side effect, occurring in 100% of individuals receiving therapy for pulmonary tuberculosis. Although not dangerous for the patient, the side effect of this colored urine is rather disturbing. occurs as a result of metabolism of the drug rifampicin. A macrocyclic antibiotic compound called rifampicin inhibits the formation of ribonucleic acid in various infections. has a local and extracellular sterilizing effect and a strong bactericidal action against tubercle bacilli. drugs, especially isoniazid, which can have nausea as a side effect. The main mechanism is that isoniazid prevents the manufacture of mycolic acid, an essential component of the mycobacterial cell wall [7].

Hepatotoxicity caused by anti-TB drugs including pyrazinamide, isoniazid and rifampicin. Hepatotoxicity is a side effect of the hepatic metabolism of these three drugs. During the intensive phase, which includes the first two months of category I TB and the first three months of category II TB, rifampicin, isoniazid, and pyrazinamide are administered together. In the intense stage, the combination of these three drugs increases the risk of hepatotoxicity [4].

4. CONCLUSION

The most commonly reported side effects were nausea, red urine, itching, weakness and joint discomfort. By providing pharmacological information, listening to patient complaints, and adjusting drug therapy to these complaints, side effects can be managed.

The percentage of patients experiencing OAT side effects was higher in the first and second weeks of treatment. The most common organ systems in the body to deal with drug side effects are the skin and digestive tract. Everyone experiences different side effects, and not everyone who uses OAT experiences them. OAT category I and category II both experience hepatotoxicity as one or more side effects. In the intensive phase, there are many side effects of category I and II OAT.

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