COMPREHENSIVE REVIEW OF TUBERCULOSIS TREATMENT AND MANAGEMENT : DOSAGE, SIDE EFFECTS, AND POST-TREATMENT

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Abstract

Background. Tuberculosis (TB) is an infectious disease that remains a global health problem. TB treatment requires lengthy drug regimens with varying doses and side effects, which can affect patient adherence to therapy.

Objective. This review aims to provide a comprehensive overview of TB treatment, including dosage, side effects, and expected response after treatment.

Methods. This study collected data from 21 journals downloaded from the Mendeley platform, covering studies that addressed common aspects of TB treatment.

Results. TB treatment involves a combination of major drugs such as isoniazid, rifampicin, pyrazinamide, and ethambutol. Common side effects are gastrointestinal disorders, hepatotoxicity, and neuropathy. Adherence to dosage and management of side effects are key to successful TB therapy.

Conclusion. Proper dosing and monitoring of side effects are important factors in improving patient adherence to TB treatment, which in turn can improve treatment response.

Keywords. Tuberculosis, Treatment, Dosage, Side Effects, Patient Adherence, Treatment Response

Introduction

Tuberculosis (TB) is a contagious infectious disease caused by the bacterium Mycobacterium tuberculosis.[1] It remains a global health problem, with millions of new cases each year, especially in developing countries.[2] TB treatment is complex and takes a long time. This is due to the nature of the bacteria which requires treatment with a combination of multiple drugs to ensure complete elimination, prevent drug resistance, and reduce the risk of relapse.[5]

The standard TB treatment regime usually consists of several drugs, including isoniazid, rifampicin, pyrazinamide, and ethambutol.[3] Each drug has a different mechanism of action and the dosage must be adjusted according to the patient's clinical condition.[4,9] However, this treatment is often faced with various challenges, including the emergence of significant side effects. Side effects can include gastrointestinal disorders, hepatotoxicity, neuropathy, and hypersensitivity reactions, which can affect patient adherence to therapy.[13]

Previous studies have shown that adherence to TB treatment is one of the determinants of therapeutic success.[11] The presence of side effects, inappropriate dosing, and long treatment duration can cause patients to discontinue treatment prematurely, which in turn contributes to the development of drug-resistant TB.[14] Therefore, it is important to understand the optimal dose, side effect management, and how response to treatment can be optimized to achieve cure.[13]

Methods

This literature review was conducted using 21 journals obtained through a search in Mendeley. The journals included studies related to TB treatment, side effects, dosage, and expected response to treatment. The selected articles addressed common aspects of TB treatment in different populations in different countries.

Results

Tuberculosis (TB) treatment is generally divided into two main groups: treatment for drug-susceptible TB and treatment for drug-resistant TB (MDR-TB and XDR-TB).[6] From the analysis of journals obtained from Mendeley, several key aspects related to dosage, side effects, adherence rates, and expected clinical response after TB therapy were found.

1. TB Drug Dosage

TB treatment doses are adjusted according to the patient's weight, age, and comorbid conditions.[11] A combination of four first-line drugs-isoniazid, rifampicin, pyrazinamide,

and ethambutol-has been used as standard therapy for decades :

- **Isoniazid** : The general recommended dose is 5 mg/kg body weight. Isoniazid is known as a highly effective drug, but has a high risk of hepatotoxicity, especially when combined with rifampicin.[13]
- **Rifampisin** : A dose of 10 mg/kg body weight is used for most patients. Rifampicin also has hepatotoxic effects, but is important as a bactericidal drug that accelerates the elimination process of bacteria.[9]
- **Pyrazinamid** : Administered at a dose of 25 mg/kg body weight. Although highly effective in killing TB bacteria in acidic environments (e.g., within TB lesions), pyrazinamide can cause hyperuricemia and liver dysfunction.[8]
- **Ethambutol** : This drug is given at a dose of 15 mg/kg body weight and serves to prevent resistance to isoniazid. The main side effect to watch out for is optic neuritis, especially on long-term treatment.[6]

For drug-resistant TB (MDR-TB and XDR-TB), drug combinations used include bedaquiline, delamanid, linezolid, and levofloxacin. The dosage and duration of treatment vary depending on the type of drug resistance and the patient's.[19] For example, bedaquiline is given at a dose of 400 mg once daily for two weeks, followed by 200 mg three times a week for 24 weeks.[9]

2. Side Effects

Side effects of TB treatment are often a major cause of patient non-adherence. A study by Sant'Anna et al. showed that hepatotoxicity is the most common side effect of standard TB treatment, especially with the combination of isoniazid and rifampicin.[13] Other frequently reported side effects include :

- **Peripheral neuropathy** : Mainly caused by isoniazid, this neuropathy can be prevented by vitamin B6 (pyridoxine) supplementation.[2]
- **Gastrointestinal disorders** : Pyrazinamide often causes complaints such as nausea, vomiting, and anorexia.[12]
- **Optic neuritis** : Ethambutol can cause visual disturbances, which are generally reversible if treatment is stopped as soon as symptoms appear.[4]

In the treatment of MDR-TB and XDR-TB, side effects are more severe, such as cardiotoxicity from bedaquiline, myelosuppression from linezolid, and nephrotoxicity and ototoxicity from aminoglycosides.

3. Patient Adherence

Adherence to TB treatment is one of the main challenges in achieving therapeutic success. A study conducted by Potty et al. in India showed that the level of patient adherence was strongly influenced by side effect management and the social support patients received.[11] Community-based treatment programs, such as DOTS (Directly Observed Treatment, Short-Course), have successfully improved patient adherence in many developing countries.[17] However, in some countries, such as Ethiopia and India, limited access to health services, social stigma, and lack of health education are major barriers.[7]

4. Clinical Response

Clinical response to TB treatment is generally seen after 2 months of initial treatment, especially in drug-sensitive TB.[15] After the intensive phase, sputum examination results are often negative. Patients with good treatment response usually experience improvement in clinical symptoms such as decreased cough, fever, and weight loss.[18] However, in patients with drug-resistant TB, clinical response is often slower and can take 12 to 24 months for sputum results to become negative.[6]

The study by Belachew et al. showed that patients with MDR-TB treated in Ethiopia had lower cure rates compared to patients undergoing drug-sensitive TB treatment.[3] This highlights the importance of using more effective regimens and good side effect management to improve clinical outcomes.[16]

Discussion

The treatment of tuberculosis has gone through many changes along with the development of new drugs and the emergence of drug resistance.[5] Although first-line treatment for drug-sensitive TB has proven effective in eradicating the infection, the issue of adherence to treatment remains a major challenge, especially in developing countries.[4]

1. Adherence and Social Support

Adherence to TB treatment is strongly linked to side effect management and the support patients receive during therapy. A study by Ting et al. revealed that the psychological and physical burden of drug side effects can decrease patients' motivation to continue treatment.[15] Programs such as DOTS have proven to be very helpful in ensuring patients complete their treatment, but resource limitations are often a barrier to effective implementation.[17] Research by Ali et al. also showed that financial incentives and the provision of psychosocial support can improve patient adherence, especially in

communities with low education levels.[1]

2. Side effect management

Side effect management is key to maintaining treatment continuity. In the treatment of drug-sensitive TB, hepatotoxicity is a major concern, and some studies recommend regular monitoring of liver function, especially in patients with a history of liver disease or excessive alcohol use.[13] In the treatment of MDR-TB and XDR-TB, side effects are more serious, and administration of drugs such as bedaquiline requires electrocardiogram (ECG) monitoring to prevent arrhythmias. The study by Pedersen et al. showed that the use of long-term regimens with bedaquiline and linezolid in patients with MDR-TB resulted in good cure rates, but required close monitoring of side effects.[9]

3. Clinical Response to Tuberculosis (TB) Treatment

Based on several journals analyzed, the clinical response to TB treatment depends on the type of TB and the patient's condition :

1. Drug Sensitive TB

Patients with drug-sensitive TB generally show clinical improvement within the first 2 months of treatment, with symptoms such as cough and fever significantly reduced. Cure rates exceed 85% if patients adhere to the treatment regimen.[9,15]

2. Drug-resistant tuberculosis (MDR-TB and XDR-TB)

MDR-TB and XDR-TB treatment response is slower, with cure rates only around 50-60%. Treatment can last up to 12 months or more, and the risk of serious side effects such as neuropathy and hearing loss is higher.[6,8]

3. Influence of HIV and Drug Interactions

Patients with comorbidities such as HIV experience slower clinical responses, especially due to drug interactions between anti-TB and ARV therapy, which can reduce the effectiveness of TB treatment.[10]

Conclusions

Appropriate dosing and good management of side effects are critical for successful TB treatment. Treatment that lasts for 6 months or more demands high adherence from patients. With good monitoring, TB treatment can provide a significant clinical response and reduce the burden of the disease in the community.

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