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Mini Review

A Mini Review on the Efficacy of First-line regimen for Pulmonary Drug-Susceptible Tuberculosis

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Abstract

Drug-susceptible pulmonary tuberculosis is a major concern in developing economies. This review is intended to briefly discuss the efficacy of isoniazid, rifampicin, pyrazinamide, and ethambutol as first line regimen for drug-susceptible pulmonary tuberculosis. These drugs show a remarkable inhibitory activity against mycobacterium tuberculosis, as stated in literature.

Keywords: Efficacy, First-line treatment, Pulmonary, Drug-Susceptible, Tuberculosis, Patients, Treatment, Targeting

Abbreviations: DSP-TB: Drug-Susceptible Pulmonary Tuberculosis; LMICs: Low and Middle-Income Countries; TB: Tuberculosis; HRZE: isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E); PLHIV: people living with HIV; HIV: Human Immune Virus; RNA: Ribonucleic Acid; DNA: Deoxyribonucleic Acid; ART: Antiretroviral Therapy.

Introduction

Drug-Susceptible Pulmonary Tuberculosis (DS-TB) is highly prevalent in Low and Middle-Income Countries (LMICs), where it remains a leading cause of morbidity and mortality [1,2]. Key risk factors for this communicable disease, include socioeconomic status, health conditions, and environmental factors. In particular, low rifapentine exposure and higher baseline disease severity are associated with unfavourable outcomes [1,3]. Major parts of the respiratory system are lungs, airways, and associated structures that facilitate breathing and gaseous exchange. The DS-TB primarily targets the lung parenchyma, where the Mycobacterium tuberculosis bacteria form granulomas and can switch between replicating and non-replicating states [1]. Effectiveness of the treatment is important in preventing emerging drug-resistant strains. The standard isoniazid (H), rifampicin (R), pyrazinamide (Z), and

ethambutol (E), (HRZE), regimen is typically administered over a 6-month period, with a 2-month intensive phase followed by a 4-month maintenance phase [2,4] (*Riccardi, et al.,* [2]). Thus, the first two months involve the uptake of all four drugs. The subsequent treatment for the remaining four months, follows a continuation phase administering isoniazid (H) and rifampicin (R) against the disease. This combination is designed to rapidly reduce the bacterial load, prevent relapse, and minimize the development of drug resistance. This first line regimen, has been effective in treating DS-TB in LMICs, with treatment success rates aligning with global standards. This regimen is widely recommended and used globally due to its effectiveness in treating DS-TB. However, challenges such as side effects and treatment adherence remain [4,5]. The HRZE regimen is more effective than prehistoric treatments, for example, sanatorium care, which were less structured and often resulted in higher rates of drug resistance, treatment failure and resistance development [5,6]. These challenges highlight the need for continued research and innovation in TB management. Therefore, this prompted investigating the efficacy of the first line HRZE drugs for managing DS-TB.

The development of shorter and more effective treatment regimens, like the rifapentine-moxifloxacin combination, offers promising future alternatives, shortening treatment duration from six to four months [4,7]. The H drug inhibits synthesis of mycolic acids, essential components of the mycobacterial cell wall and is a cornerstone of TB treatment due to its potent bactericidal activity against actively dividing TB bacteria [8,9]. Secondly, the R drug effectiveness emanates from its inhibitory mechanisms towards synthesis of bacterial Ribonucleic Acid (RNA) by binding to the Deoxyribonucleic Acid (DNA)-dependent (RNA) polymerase. It is crucial for its sterilizing activity, which helps in preventing relapse by eliminating dormant bacteria [8,9]. Under the first line treatment regimen for DS-TB, is Z drug, which works effectively in acidic environments, similar to those found within macrophages and necrotic tissue. It is particularly effective during the initial phase of treatment, contributing to the shortening of therapy duration [8,9]. Another equally as important drug towards the management of DSP-TB, is E drug, which inhibits the synthesis of the mycobacterial cell wall by obstructing arabinosyl transferases. It is primarily used to prevent the development of drug resistance during the initial treatment phase [8,9].

Comorbidities and HIV Coinfection

A retrospective cohort study in Eswatini reported a high TB-related mortality amongst patients with HIV. The statistics, show a case fatality ratio of 11.7% for People Living with HIV (PLHIV) contrasting with 7.5% for HIV-negative patients. Among PLHIV, lacking Antiretroviral Therapy (ART), significantly increased the risk of death during TB treatment [10]. A higher mortality risk was observed in Zimbabwe amongst TB patients with HIV coinfection, despite a high uptake of ART. The study results show a 22% mortality rate among TB patients, with HIV infection being a significant risk factor [11]. Other reports, indicate resistance towards first-line TB drugs, particularly R drug, posing a significant challenge. In the east African country of Guinea, rifampicin-resistant TB was noted with 18.9% patient mortality during treatment, with older age and HIV infection being notable risk factors [12]. Despite a decline in TB mortality at the population level in Eswatini, the case fatality among TB treatment cases remained high, indicating that current treatment strategies may not be sufficient to address all risk factors associated with mortality [10]. The need for improved TB therapies and strategies to reduce active TB disease is evident, as highlighted by the sustained high fatality rates during TB therapy [10].

Conclusion

The mini review was intended to report the efficacy of the first line treatment on DS-TB using HRZE drugs. Combinational therapy is used for DS-TB management where isoniazid acts as an inhibitor of mycolic acid synthesis, while rifampicin inhibits RNA polymerase. In the successful management of pulmonary related TB, pyrazinamide disrupts membrane and energy production whereas ethambutol inhibits arabinogalactan synthesis. This first line treatment has shown to be effective against this communicable disease. Nonetheless, an extensive investigation on HRZE drugs is required to improve on their effectiveness in managing DSTB to avoid mortality and resistance while taking the drugs.

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Conflicts of Interest

The authors declare there is no conflict of interest regarding the publication of this research manuscript.

References

1. Putri O, Salim MA, Gunawan A, Devin D, Amaris E, et al. (2023) Drug-Resistant Pulmonary Tuberculosis. Indones J Life Sci 5(1): 10-40.
2. Riccardi N, Occhineri S, Vanino E, Antonello RM, Pontarelli A, et al. (2023) How We Treat Drug-Susceptible Pulmonary Tuberculosis: A Practical Guide for Clinicians. Antibiotics 12(12): 1733.
3. Chang VK, Imperial MZ, Phillips PPJ, Velásquez GE, Nahid P, et al. (2024) Risk-stratified treatment for drug-susceptible pulmonary tuberculosis. Nat Commun 15(1): 9400.
4. Lyu J, Shim TS (2021) Recent Advances in Drug Susceptible Pulmonary Tuberculosis Diagnosis and Treatment. Korean J Med 96(5): 390-399.
5. Migliori GB, Marx FM, Ambrosino N, Zampogna E, Schaaf HS, et al. (2021) Clinical standards for the assessment, management and rehabilitation of post-TB lung disease. Int J Tuberc Lung Dis 25(10):797-813.
6. Maher D, Nunn P (1998) Commentary: making tuberculosis treatment available for all. Bull World Health Organ 76(2): 125-126.
7. Louie JK, Agraz Lara R, Velásquez GE, Phillips A, Szumowski JD (2024) Experience With Four-Month Rifapentine and Moxifloxacin-Based Tuberculosis Treatment in San Francisco. Open Forum Infect Dis 11(4): ofae178.

8. Meghji J, Kon OM (2021) TB Treatment and Complications. In: Kon OM, editor. Tuberculosis in Clinical Practice. Cham: Springer International Publishing pp. 263-278.

9. Du Preez I, Loots DT (2018) Novel insights into the pharmacometabonomics of first-line tuberculosis drugs relating to metabolism, mechanism of action and drug-resistance. Drug Metab Rev 50(4): 466-481.

10. Kerschberger B, Vambe D, Schomaker M, Mabhena E, Daka M, et al. (2024) Sustained high fatality during TB therapy amid rapid decline in TB mortality at population level: A retrospective cohort and ecological analysis from Shiselweni, Eswatini. Trop Med Int Health 29(3): 192-205.

11. Takarinda KC, Sandy C, Masuka N, Hazangwe P, Choto RC, et al. (2017) Factors Associated with Mortality among Patients on TB Treatment in the Southern Region of Zimbabwe, 2013. Tuberc Res Treat 2017: 6232071.

12. Bangoura ST, Diallo BD, Diaby M, Camara A, Hounmenou CG, et al. (2024) Predictors of Death in Rifampicin Resistant Tuberculosis Patients Treated with the Short Course in Conakry, Guinea. Am J Trop Med Hyg 110(1): 117-122.