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Efficacy and safety of daily treatments for drug-susceptible pulmonary tuberculosis: a systematic review and network meta-analysis

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Abstract

Objectives To evaluate and update the evidence on the comparative efficacy and safety of antimicrobial drugs regimens for treating pulmonary drug-susceptible tuberculosis (DS-TB).

Methods A systematic review was performed with searches in PubMed and Scopus (PROSPERO-CRD42019141463). We included randomised controlled trials comparing the effect of any antimicrobial regimen lasting at least 2 weeks. The outcomes of interest were culture conversion and incidence of adverse events. Bayesian network meta-analyses and surface under the cumulative ranking curve (SUCRA) analyses were performed. Results were reported as odds ratio with 95% credibility intervals.

Key findings Fifteen studies were included the meta-analysis (n = 7560 patients). No regimen was statistically more effective than the WHO standard approach (rifampicin, isoniazid, ethambutol, and pyrazinamide). The use of rifapentine 450 mg instead of rifampicin in the standard regimen demonstrated to be statistically safer than all other options for serious adverse events (e.g. hepatotoxicity, arthralgia) (OR ranging from 0.0 [CrI 0.00–0.04] to 0.0 [0.00–0.97]; SUCRA probabilities of 10%). Therapies containing rifapentine (Rp1500HEZ, Rp900HEZ) and moxifloxacin (RMEZ, RHMZ) are effective regarding culture conversion, but statistical uncertainty on their safety profile exists.

Conclusion The WHO standard regimen remains an overall effective and safe alternative for DS-TB. For intensive phase treatments, drugs combinations with rifapentine and moxifloxacin seem to reduce treatment duration while maintaining efficacy.

Keywords: tuberculosis, antitubercular agents, drug-susceptible, systematic review, network meta-analysis

Introduction

Tuberculosis (TB), a chronic infectious disease caused by airborne transmission of aerosolised droplets of *Mycobacterium tuberculosis*, is one of the top 10 leading causes of death worldwide.[1] According to the World Health Organization (WHO), an estimated 10 million new cases of the disease (incidence rate of about 130 cases per 100 000 inhabitants) and more than 1.2 million related deaths occurred in 2018. Around 90% of cases are of adults (age ≥15 years), males (57%), and almost 1/10 occur in people living with HIV.[2]

Drug-susceptible tuberculosis (DS-TB) is defined as a disease with no resistance to TB drugs and no history of antituberculous chemotherapy.[3] Currently, the standard therapy recommended by the WHO for treating DS-TB includes the use of four antimicrobial drugs (rifampicin, isoniazid, ethambutol and pyrazinamide – RHEZ regimen) for a period of at least 6 months.[4] However, around 15%-20% of patients progress to resistant forms of the disease, requiring longer treatments that may range from 9 to 20 months and whose average success rate is of around 55%.[2] This occurs mainly due patient's lack of adherence, which for socioeconomic or drug-related reasons (e.g. adverse effects, duration of treatment and recurrence of symptoms) discontinues therapy without complete cure of the disease.[5,6] The need for re-treatment is common, and therefore, new therapeutic regimens and combinations with antitubercular drugs, such as delamanid and bedaquiline, have been developed aiming at shortening the overall time of drug therapy and improve success rates.[7]

The selection of the best therapeutic approach considering drugs' clinical profile, patient's preferences and access in each scenario should be grounded in updated evidence. Currently, the comparative efficacy and safety of TB drug regimens

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