International Journal of Infectious Diseases 60 (2017) 35–41

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Review

Moxifloxacin is an effective and safe candidate agent for tuberculosis treatment: a meta-analysis

Ping Xu[a,b], Hui Chen[a], Junchi Xu[a,b], Minjuan Wu[a], Xiaoyan Zhu[a,b], Fengping Wang[a], Sufang Chen[a], Junhua Xu[a,b,*]

[a] The Affiliated Infectious Hospital of Soochow University, 1 Xier Road, Gusu District, Suzhou City,China
[b] Key Laboratory of Infection and Immunity of Suzhou City, Suzhou City, China

ARTICLE INFO

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Moxifloxacin
Tuberculosis
Recommended regimens
Meta-analysis

SUMMARY

Background: To evaluate the efficacy and safety of the introduction of moxifloxacin into the recommended regimen for tuberculosis (TB) treatment.
Methods: A meta-analysis was performed of nine eligible studies regarding the effect of moxifloxacin plus the recommended regimen compared to the recommended regimen alone for the treatment of TB.
Results: In the efficacy analysis, the overall odds ratio (OR) for sputum culture conversion was 1.895 (95% confidence interval (CI) 1.355–2.651, $p = 0.000$), indicating that when moxifloxacin is combined with the recommended regimen, the rate of sputum culture conversion is elevated compared to the recommended regimen alone. The overall OR for recurrence was 0.516 (95% CI 0.342–0.920, $p = 0.022$), suggesting that the introduction of moxifloxacin into the recommended regimen reduces TB relapse after treatment. In the safety analysis, the overall OR was estimated to be 1.001 (95% CI 0.855–1.172, $p = 0.989$), demonstrating that adding moxifloxacin to the recommended regimen does not cause more adverse events during TB treatment.
Conclusions: This meta-analysis suggests that the introduction of moxifloxacin into the recommended regimen for the treatment of non-drug resistant TB improves the clinical outcome by elevating the culture conversion rate and reducing the recurrence rate.

Contents

Introduction

Although the global incidence of tuberculosis (TB) has shown a recent slow decline, the number of cases remains daunting and has overwhelmed the capabilities of many health systems, especially in countries with a concomitant HIV epidemic (Vashishtha, 2009; Fonseca et al., 2015). Therefore, TB remains a major global health

* Corresponding author. Tel: +86 512 65180352; fax: +86 512 65188088.
E-mail address: xujunhua_sz@163.com (J. Xu).

http://dx.doi.org/10.1016/j.ijid.2017.05.003

threat and more effort should be directed towards improving its treatment. At present, anti-TB therapy relies on combinations of bactericidal and sterilizing drugs that protect against the development of resistance (Mitchison, 2000).

The currently implemented regimen for pulmonary TB comprises the combination of isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E) for 2 months and isoniazid plus rifampicin for the following 4 months, which is called short-course chemotherapy (Zumla et al., 2013). In order to reduce the emergence of drug resistance, the combinations of two drugs (isoniazid and rifampicin) and three drugs (isoniazid, rifampicin, and pyrazinamide) are also recommended regimens (Zumla et al., 2013). However, patient compliance is poor due to the long treatment duration (Dye et al., 2002). Consequently, new drugs that shorten the duration of TB treatment could substantially reduce the likelihood of disease recurrence and death caused by inadequate therapy.

The fluoroquinolone moxifloxacin has been shown to have potent activity against *Mycobacterium tuberculosis* in vitro (Ji et al., 1998; Gillespie and Billington, 1999). Early studies of moxifloxacin in murine models showed that moxifloxacin had good bactericidal activity and was a good substitution for isoniazid (Lounis et al., 2001; Miyazaki et al., 1999). Although positive results have been observed with the use of moxifloxacin as an addition to the recommended regimens for TB treatment, the results remain inconsistent. For example, Rustomjee et al. reported that moxifloxacin improved the sterilizing activity of therapy and might shorten the treatment duration after adding it to the recommended regimens for TB treatment, whereas Burman et al. concluded that the addition of moxifloxacin to the recommended regimens would not allow a significant shortening of the treatment duration for TB (Rustomjee et al., 2008; Burman et al., 2006).

In order to determine the role of moxifloxacin in the treatment of TB, a meta-analysis of all available studies to date was performed to comprehensively investigate the efficacy and safety of moxifloxacin plus recommended regimens compared to recommended regimens alone for the treatment of TB.

Methods

Study selection

To evaluate the effect of moxifloxacin in the treatment of TB, multiple databases including the NCBI global database and Google Scholar were searched for related studies with the aim of performing a meta-analysis. Keywords were 'tuberculosis' and 'moxifloxacin'. All articles in the literature that were published before June 6; 2015 were included.

Articles that did not report human clinical trials were excluded. Study types included were randomized controlled trials (RCTs) and two-arm prospective studies. Only studies in which the drug regimen in the control group contained H, R, Z, and E were taken into consideration. The case groups underwent therapy in which one of H, R, Z, or E was replaced by moxifloxacin, or moxifloxacin was added directly to the recommended regimen. When a study was reported in more than one article such that data overlapped, only the article reporting the most extensive results was retained.

All patients in the covered studies were newly diagnosed with pulmonary TB or newly found to be sputum smear-positive for acid-fast bacilli. In order to minimize the effects of other relevant factors such as drug resistance in the assessment of the efficacy and safety of moxifloxacin, patients who had received anti-TB treatment for more than 7 days in the preceding 6 months, or more than 7 days of fluoroquinolone treatment in the preceding 3 months, were excluded. Patients with rifampicin-resistant or isoniazid-resistant TB were also excluded.

Data extraction

All the data were extracted and reviewed by two reviewers independently. The following characteristics were extracted from the eligible studies: first author, year of publication, population and age of the participants, regimens of controls and cases, drug dose of moxifloxacin, sex ratio of the participants, treatment period, type of study, and adverse effects.

Statistical analysis

The data were analyzed using STATA 12 software (STATA Corp. LP, College Station, TX, USA); a p-value of <0.05 was considered statically significant.

In this study, the efficacy of moxifloxacin in the treatment of TB was estimated by sputum culture conversion and recurrence. Sputum culture conversion was defined as two or more consecutive negative sputum cultures detected at the endpoint of treatment. Herein, the sputum culture conversion after 2 months of treatment is described, since this has been regarded as a surrogate marker of the final treatment outcome (Seddon et al., 2012; Visser et al., 2012). Recurrence of TB was defined as the Ref. Jawahar et al. (2013), and related information on recurrence during

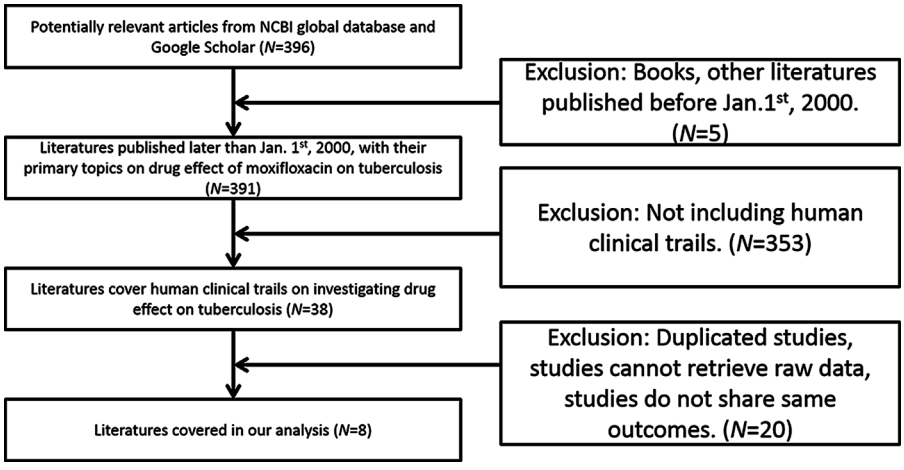

Figure 1. Flow chart of study selection and specific reasons for exclusion from the meta-analysis.