Effects of human immunodeficiency virus infection on recurrence of tuberculosis after rifampin-based treatment: an analytical review
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CRD summary
This complex review identified that the increased rate of recurrence of tuberculosis among patients infected with the human immunodeficiency virus probably reflects increased rates of both reinfection and relapse. The recurrence risk is especially elevated with treatment regimens involving less than 6 months' treatment with rifampin. The quality of the review was limited in terms of the literature search, quality assessment and the reporting of the review methodology.

Authors' objectives
To assess the influence of human immunodeficiency virus (HIV) infection and duration of rifampin treatment on the recurrence of pulmonary tuberculosis (TB).

Searching
PubMed was searched up to May 2002; the search terms were reported. The references from eligible recent references were checked and suggestions from experts were followed up. No language restrictions were reported.

Study selection
Study designs of evaluations included in the review
Cohort studies with at least 6 months' follow-up were eligible for inclusion in the review.

Specific interventions included in the review
Studies of patients previously treated with rifampin-based therapy were eligible for inclusion. The rifampin therapy had to have started with a minimum of 2 months' rifampin plus at least two other drugs. The overall therapy had to have involved at least two drugs for 5 to 12 months, given at least twice a week.

Participants included in the review
To be included in the review, the studies had to be of patients aged over 15 years who had been treated with rifampin-based therapy for TB. The patients had to have a history of smear or culture-positive pulmonary TB that was cured by the end of a full course of treatment.

Outcomes assessed in the review
The outcome assessed was the recurrence rate of TB by HIV status and by duration of rifampin treatment.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

The reviewers recorded sample sizes, durations of follow-up (rifampin treatment duration was categorised as at least 7 months, 5 to 6 months, or 2 to 3 months), treatment regimens, recurrence rates and times to recurrence by HIV infection status. The paper described how the background incidence of TB was estimated.
Methods of synthesis
How were the studies combined?
The studies were combined using multivariate linear regression analysis. HIV infection status and rifampin treatment duration were categorical variables, while TB incidence and follow-up duration were continuous covariates. Time patterns in recurrences were assessed by fitting Weibull survivorship functions. Studies that reported restriction fragment length polymorphism analysis were reviewed to determine the percentage of the recurrences due to reinfection or relapse. The studies were weighted by sample size.

How were differences between studies investigated?
Difference between the studies were discussed in the text and incorporated in the analysis.

Results of the review
Forty-seven studies involving 14,103 patients were included.

The mean observed TB recurrence rates were statistically significantly higher in patients with HIV (4.5 cases per 100 person-years) compared with those without (1.9 cases per 100 person-years) (P<0.0001). The multivariate analysis showed that the recurrence rate significantly decreased with increasing duration of follow-up (P<0.0001) and with increasing duration of rifampin treatment (P<0.0001). A high background TB incidence increased the risk of recurrence (P=0.048).

In persons not infected with HIV, the recurrence rate increased with decreasing duration of rifampin therapy: 1.4 cases per 100 person-years with a duration of at least 7 months compared with 2.0 and 4.0 cases per person-years with treatment durations of 5 to 6 and 2 to 3 months, respectively, over a follow-up of 34 months and TB incidence of 250 cases per 100,000 person-years (overall trend P=0.00014). The effect of rifampin duration was significantly increased in HIV-infected persons (P=0.025). For HIV-infected persons the relative risk of infection with a treatment duration of 2 to 3 months compared with 7 or more months was 4.6 (95% confidence interval: 1.7, 7.4).

Overall 30% of TB recurrences were due to reinfection.

Authors' conclusions
The increased rate of TB recurrence among HIV-infected patients probably reflects increased rates of both reinfection and relapse. The recurrence risk is especially elevated with treatment regimens involving less than 6 months' treatment with rifampin.

CRD commentary
This was a complex review of the effect of the duration of rifampin treatment, and the impact of HIV infection and background prevalence of TB, on recurrence rates of TB. The inclusion criteria were well defined except for study design, but the literature search was limited to a single electronic database, making it likely that studies were missed. The quality of the included studies was not assessed and details of the review methodology, in terms of minimising reviewer, bias were not reported. The cut-offs by which different durations were grouped together and the statistical methods used in the analysis appear appropriate. The authors' conclusions appear to follow from the findings of the review.

Implications of the review for practice and research
Practice: The authors stated that, in countries where HIV infection is endemic, TB recurrence may be reduced by the administration of rifampin-based treatment for at least 6 months, in accordance with World Health Organization recommendations.

Research: The authors did not state any implications for further research.
Bibliographic details

PubMedID
12830415

DOI
10.1086/375220

Indexing Status
Subject indexing assigned by NLM

MeSH
Antitubercular Agents /adverse effects /therapeutic use; HIV Infections; Humans; Incidence; Mycobacterium tuberculosis /drug effects; Prospective Studies; Recurrence; Rifampin /adverse effects /therapeutic use; Tuberculosis, Pulmonary /chemically induced /epidemiology

AccessionNumber
12003001475

Date bibliographic record published
31/03/2005

Date abstract record published
31/03/2005

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.