DSEN ABSTRACT

A Systematic Review with Network Meta-Analyses Comparing Efficacy, Completion Rates and Harms among Competing Regimens for Latent Tuberculosis Infection

What is the issue?

- The treatment of latent tuberculosis infection (LTBI) is a vital component of the overall strategy to reduce tuberculosis (TB) in a population. Treatment prevents ongoing transmission by preventing the development of active TB disease.
- A key impediment to treatment is the lengthy 9-month course of treatment with isoniazid (INH), which is the current international standard. The efficacy, completion rates and harms of more recently developed regimens, such as a 3-month regimen of INH and rifapentine (INH/RPT-3), need to be compared.

Review Questions Addressed

- Is the INH/RPT-3m regimen for LTBI associated with greater efficacy and rates of regimen completion compared to the standard 252 dose INH (9 months daily) treatment currently used in Canada, 78 dose INH (9 month) treatment used in Nunavut, 180 dose INH (6 months daily), 3-4 months daily isoniazid and rifampin, and a 4-month regimen of rifampin given daily for 4 months?
- Is the INH/RPT-3m regimen associated with lesser rates of harms compared to the standard 252 dose INH (9 month daily) treatment currently used in Canada, 78 dose INH (9 month) treatment used in Nunavut, 180 dose INH (6 months daily), 3-4 months daily isoniazid and rifampin, and a 4-month regimen of rifampin given daily for 4 months?

How was the study conducted?

- We leveraged an existing review to identify RCTs that compared LTBI interventions and reported on cases of active TB, regimen completion rates, and harms. A de novo search for non-randomized data regarding harms was performed. Studies in patients with a confirmed LTBI diagnosis were included if they studied relevant treatment regimens, and if relevant outcomes were reported. Network meta-analyses of RCTs were used to compare efficacy and completion rates between regimens. Summaries of reported harms including hepatotoxicity, mortality, flu-like symptoms, gastrointestinal symptoms, and other events were also prepared.

What did the study find?

- A total of 28 RCTs and 47 non-randomized studies met eligibility criteria: 16 RCTs reported on efficacy (n=44,149) while 20 RCTs reported on completion rates (n=39,787). Regarding harms, many outcomes were assessed, including general harms and withdrawals, hypersensitivity reactions, flu-like symptoms, gastrointestinal symptoms, mortality and hospitalization; for many harms, reporting was limited, with few data available. Overall, there was substantial variability in study populations with some enrolling prisoners, homeless individuals, children, and/or patients with HIV, renal transplantation or silicosis. Publication dates ranged from 1968-2015. Studies involving no treatment, INH-9m, INH-6m, INH 3-4m, INH 12-72m, INH/RPT-3m, INH/RFMP3-4m, RFMP 3-4m, INH/RFMP/PZA-3m and RFMP/PZA-2m were included. Reporting of findings is focused upon a subset of regimens identified a priori as being of greatest relevance to Nunavut based on duration, current status and awareness of side effect profiles; these included INH-9m, INH-6m, INH/RPT-3m, INH/RFMP 3-4m, and RFMP 3-4m.

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