Systematic Review and Meta-Analysis of Treatment of Latent TB Infection to Reduce Progression to Multidrug-Resistant Tuberculosis

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RESULTS

Comparison Study #1


- **Setting:** Australia
- **Time period:** 1994-2009
- **Subjects:** N=69 with LTBI of contacts to MDR-TB patients, median age 27
- **Study type:** Prospective observational study, released isolates of index cases, ≥3 years of follow up
- **n=11 received effective (≥1 med to which their strain was susceptible) treatment with 1-2 mds for 9 months**
  - treated mostly multidrug alone or with EMB; EMB vs. EMB, INH, or RIF; CIP alone or with PZA
  - Outcomes: No (0%) TB cases
- **n=38 considered not effectively treated**
  - Outcomes: 2 (5%) TB cases

Comparison Study #2


- **Setting:** Micronesia
- **Time period:** 2009-2012
- **Subjects:** N=119 with LTBI of contacts of MDR-TB patients, median age of those starting treatment was 24
- **Study type:** Prospective observational study with 36 months of follow up
- **n=104 received 12 months daily treatment (mostly FQ): Mox, EMB, EMB, combo**
  - 89% completed
  - Outcomes: No (0%) TB cases; No serious adverse events (hospitalization, irreversible morbidity), although 15% reported adverse events
- **n=15 refused or discontinued treatment within 2 weeks.**
  - Outcomes: 3 (20%) TB cases

Comparison Study #3


- **Setting:** Western Cape Province, South Africa
- **Time period:** 1994-2000
- **Subjects:** N=105 children < 5 yrs. of age, household contacts
- **Study type:** prospective observational study with 30 months of follow up
- **n=41 received 3-4 drug combinations of INH/PZA/EMB/Eth [6 with OFL] for 6-12 months**
  - Outcomes: 2 (5%) TB cases
- **n=64 no treatment**
  - Outcomes: 13 (20%) TB cases

Complete Data from 3 Comparison Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>LTBI Tx</th>
<th>No LTBI Tx</th>
<th>Total</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparison Study #1</td>
<td>11</td>
<td>11</td>
<td>22</td>
<td>1.00 (0.16-6.33)</td>
</tr>
<tr>
<td>Comparison Study #2</td>
<td>36</td>
<td>38</td>
<td>74</td>
<td>1.00 (0.16-6.33)</td>
</tr>
<tr>
<td>Comparison Study #3</td>
<td>104</td>
<td>104</td>
<td>208</td>
<td>1.00 (0.16-6.33)</td>
</tr>
</tbody>
</table>

Pooled RR=0.052 (0.020-0.137)

Possible reasons for some heterogeneity:
- Sample size (49, 119, 105)
- Overall TB incidence (4% Australia, 3% Chuuk, 14% S. Africa)

Systematic Review Process

- Evidence-based recommendations for treatment of contacts to multidrug-resistant (MDR) TB patients are lacking because of small studies, TB incidence in contacts to MDR-TB patients treated for latent MDR-TB infection (LTBI) is unknown
- To conduct a systematic review of published studies to assess TB incidence with and without LTBI treatment in contacts to infectious MDR-TB patients
- To conduct a meta-analysis of the association of latent MDR TB infection treatment with TB incidence

METHODS

- In December 2014, we conducted a systematic review of published studies in PubMed, EMBASE, and Cochrane Library.
- We searched for the key words: tuberculosis, multidrug resistant, contacts, and treatment.
- We considered contacts effectively treated if they were on one medication to which their likely MDR-TB strain was susceptible.
- We estimated a pooled random effects relative risk (RR) and its 95% confidence interval.

CONCLUSIONS

- Very few studies met the inclusion criteria, so results should be cautiously interpreted.
- However, we found, by using meta-analysis, some empirical evidence for the effectiveness of LTBI treatment to prevent MDR TB.

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RESULTS of Meta-analysis of 3 Studies (Pooled Random Effects Relative Risk=0.179 (0.034-0.929)

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Citation: Lesoir C, Lecuyer J, Berjen OA, et al. Long-term follow-up of contacts exposed to multidrug-resistant tuberculosis in Victoria, Australia. 1994-2009. 10.1371/journal.pmed.1001208

December 20, 2015

Citation: Bamrah S, Brostrom R, Klein FJ, et al. Treatment for Multidrug-Resistant Latent Tuberculosis Infections—Auburn State of Micronesia, 2008-2012. 10.1371/journal.pmed.1001308

December 20, 2015

Citation: Schaaf et al. Evaluation of Young Children in Contact with Adult Multidrug-resistant Pulmonary Tuberculosis. A 36-Month Follow-up. Pediatrics. 2002; 109:765

December 20, 2015

Citation: Axelrod AS, Halsey NA, Tegtmeier SM, et al. Treatment for Multidrug-Resistant Latent Tuberculosis Infections—Auburn State of Micronesia, 2008-2012. 10.1371/journal.pmed.1001308

December 20, 2015

Citation: Schaaf et al. Evaluation of Young Children in Contact with Adult Multidrug-resistant Pulmonary Tuberculosis. A 36-Month Follow-up. Pediatrics. 2002; 109:765