Connecticut Epidemiologist

Volume 35, No. 2 March 2015

Experience Using 12 Weekly Doses of Isoniazid and Rifapentine as Treatment for Latent Tuberculosis Infection, Connecticut—March 2012–January 2015

More than 10 million persons living in the United States are infected with *Mycobacterium tuberculosis* complex (TB) (1). Latent TB infection (LTBI) describes the presence of TB bacteria without manifestation of symptoms and is non-infectious. About 5 – 10% of people with LTBI will develop active TB disease if not treated; therefore, treating LTBI is a cornerstone of the U.S. strategy for TB control and elimination (2). However, efforts to treat LTBI have been hampered by poor treatment completion rates, attributable in part to the lengthy standard regimen of nine months of daily self-administered isoniazid (INH) (3). Of LTBI patients reported to the Connecticut Department of Public Health (DPH) during 2012-2014 who initiated INH monotherapy, 58% completed treatment.

The adoption of a shorter treatment regimen is essential to increasing completion rates. Recent studies, including one randomized controlled trial, have shown 12 weekly doses of INH and rifapentine (RPT) given by directly observed therapy (DOT) to be as effective as the standard regimen, with high patient acceptance, tolerability, and completion rates (4). Contraindications for this regimen include women who are pregnant or expecting to become pregnant within the 12-week regimen, children less than 2 years old, persons with HIV infection taking antiretroviral therapy, and persons presumed to be infected with INH or rifampin-resistant *M. tuberculosis*.

In 2011, the Centers for Disease Control and Prevention (CDC) released recommendations for treatment of LTBI with the INH-RPT regimen. In early 2012, the Connecticut Advisory Committee for the Elimination of Tuberculosis issued guidelines for Connecticut clinicians on the use of this treatment regimen, and the DPH TB Control Program began enhanced passive surveillance to monitor the effectiveness and safety of administering INH-RPT to Connecticut residents (5). Descriptive analyses of patient demographics, adverse events, and treatment completion rates are performed on an ongoing basis as part of this enhanced surveillance.

From March 2012–January 2015, 373 Connecticut residents started treatment for LTBI using INH-RPT. These patients were treated by private providers (77%), at local health departments (14%), and in school or university settings (9%). The median age of those treated was 38 years (range: 10–90 years); 55% were male. One-third of the patients were Hispanic/Latino (33%), 21% were black, 18% were white and 17% were Asian. Of patients treated with INH-RPT, 60% were foreign born, with 41% arriving in the U.S. within the past year. The top countries of birth among foreign born individuals were China, Haiti, Peru, and Dominican Republic.

Although demographics, behavioral information, and medical risk factors are requested on all patients, data were incomplete. Among 358 patients for which this information was available, 97 (27%) were students and 71 (20%) were unemployed. Nineteen (5%) were contacts to a known TB case, 17 (5%) were homeless within the past year, 9 (3%) were identified while in long-term care, and 1 was identified in a correctional facility. Data on substance use was incomplete, however approximately 2-4% report excess alcohol, injection drug use or non-injection drug use. Medical risk factors for treatment for LTBI were reported by 40 (11%) patients and included diabetes (n=17), viral hepatitis (n=9), chronic renal disease (n=5), immunosuppression (n=3), and other conditions (e.g. hypertension) (n=19). Most of these comorbidities did not significantly impact treatment completion outcomes (Figure 1, see page 6).

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Of 308 patients with final disposition data, 265 (86%) successfully completed treatment, 25 (8%) stopped treatment due to an adverse event, 12 (4%) were lost to follow-up or refused, and 6 (2%) stopped for another reason. The percentage of patients who completed treatment was significantly higher for INH-RPT when compared to INH ($p<0.001$). Half of these patients (51%) reported at least one symptom while receiving treatment; the most commonly reported complaints were nausea (30%), fatigue (24%), and soreness (22%), or a combination of multiple symptoms (Table 1, see page 7). Despite symptoms, few patients (8%) discontinued treatment due to adverse drug reactions. The most common adverse events resulting in discontinuation of treatment included elevated liver transaminases, fever, and flu-like symptoms. Three patients were hospitalized for 1–2 days during the course of treatment.

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Editorial

Tolerability and treatment completion data suggest that 12 weekly doses of INH-RPT as treatment for LTBI is a promising alternative to nine months of daily INH for Connecticut patients. Compared to the 58% completion rate for INH monotherapy, an 86% overall completion rate is a substantial improvement. Due to the shorter duration of treatment, it might be especially useful among persons who are homeless, migratory workers, and students, as well as those unwilling to stop alcohol use for nine months. Qualitative reports highlight ease of implementation and high acceptability among Connecticut providers. Ultimately, the decision to use the INH-RPT regimen depends on patient preferences and motivation to complete treatment, and provider familiarity and comfort level with administering the regimen.

Although some patients report symptoms during the course of treatment, few experience reactions severe enough to result in discontinuation of treatment. Of the 3 patients hospitalized during treatment, one went on to complete treatment, highlighting patient motivation as a key factor in the success of this regimen. Even patients with sociomedically complex backgrounds, including homelessness, unemployment, and substance use, can be treated successfully.

On a national level, the CDC is coordinating further evaluation of the use of INH-RPT in order to provide additional recommendations regarding special populations and adverse events. In an effort to expand treatment options, a clinical trial is

Figure 1. Isoniazid-rifapentine treatment completion and discontinuation by patient demographic and medical risk factors (N=308)

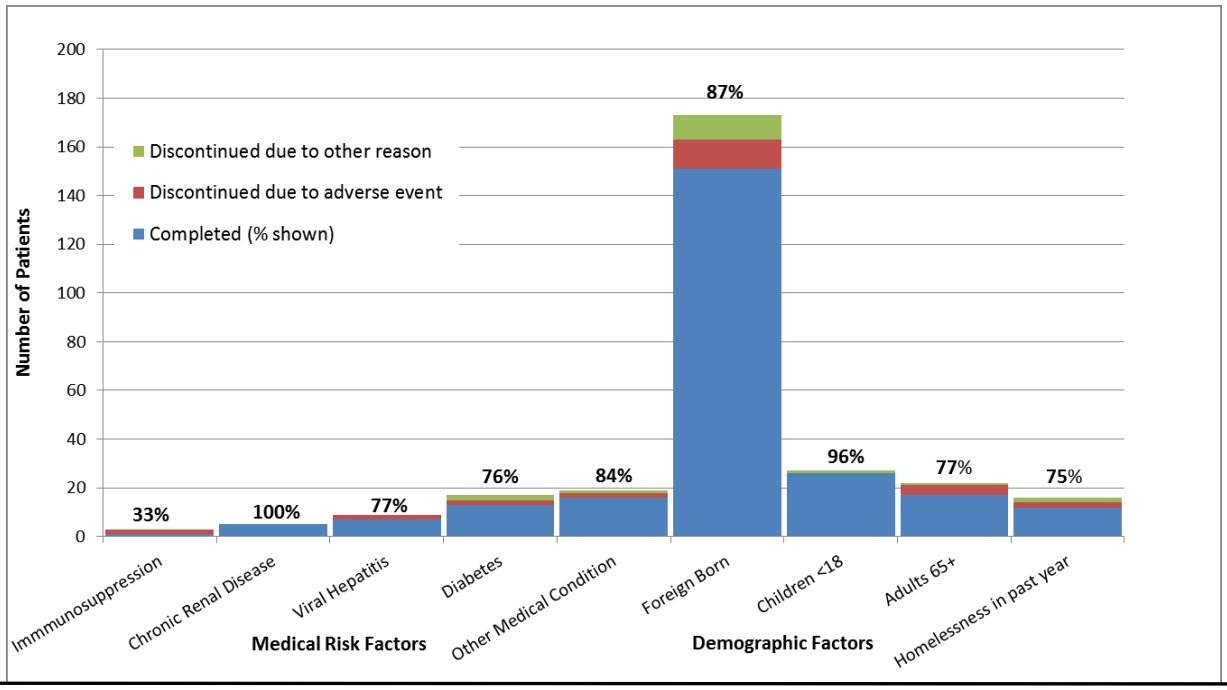

Table 1. Reported treatment-associated adverse drug reactions (N=142)

Symptom	Number of Complaints*
Nausea	42 (30%)
Fatigue	34 (24%)
Soreness	31 (22%)
Numbness/Tingling	21 (15%)
Fever	21 (15%)
Diarrhea	20 (14%)
Rash	14 (10%)
Appetite loss	13 (9%)
Abnormal lab results	8 (6%)
Yellow skin/eyes	2 (1%)
Other†	68 (48%)

*Percentages do not add up to 100%; patients can report more than 1 symptom
†Also includes multiple concurrent complaints

currently underway to compare adherence to INH-RPT given by DOT versus self-administered therapy, with or without weekly text reminders. The cost of RPT has often been cited as a significant barrier to the use of the regimen. However, recent communication between the CDC and the manufacturer of the medication has led to a decrease in price from $51 to $32 per 32-pill box, which has made treatment more cost-effective.

Moving forward, the DPH TB Control Program will be working to expand the use of this treatment regimen in Connecticut. Strategies to reach this goal include actively engaging community health centers and other partners in patient management and DOT administration. Additionally, remote and electronic technologies such as video DOT may offer opportunities to increase the use of this treatment regimen across the state. Interested providers should contact the TB Control Program at (860) 509-7722. State-specific guidance and reporting forms are available at http://www.ct.gov/dph/tb.

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This study/report was supported in part by an appointment to the Applied Epidemiology Fellowship Program administered by the Council of State and Territorial Epidemiologists (CTSE) and funded by the Centers for Disease Control and Prevention (CDC) Cooperative Agreement Number 1U38OT000143-02.

Table. Summary of Tuberculosis Cases Reported in Connecticut*, 2014.

Classification	n= 60 No. (%)
Age (years)	
<5	1 (2)
5–14	1 (2)
15–24	13 (22)
25–44	19 (32)
45–64	13 (22)
≥65	13 (22)
Race/Ethnicity	
Asian	18 (30)
Black	14 (23)
White	12 (20)
Hispanic	16 (27)
Gender	
Male	41 (68)
Female	19 (32)
Birth Origin	
U.S. and Territories	14 (23)
Other Nations (21 different Nations)	46 (77)
Pulmonary cases	41 (68)
HIV positive	0 (0)
Multi-drug resistant (resistance to at least isoniazid and rifampin)	1 (2)
Birth Nations with ≥5 Cases	
Haiti	6
China	5
India	5
Towns with ≥5 cases	Rate**
Hartford	8 (6.4)
Norwalk	5 (5.7)
New Haven	5 (3.8)

* Cases were reported from 34 towns.
** Rate per 100,000 population.

Monitoring of Travelers for Ebola Virus Disease, Connecticut, October 2014 – February 2015

On September 30, 2014, the first laboratory-confirmed case of Ebola in the United States was diagnosed. On October 11, 2014, in an effort to identify travelers from West African countries with widespread Ebola transmission, the Centers for Disease Control and Prevention, working with domestic partners, established an entry screening program at five U.S. international airports (1).

Screening allows public health authorities to identify and medically evaluate ill travelers upon U.S. arrival, educate travelers on reporting fever and other symptoms to public health authorities, and provide the travelers' contact information to state public health authorities to facilitate monitoring. These actions are necessary to facilitate rapid detection of illness and implementation of public health control measures.

The Connecticut Department of Public Health interviews all travelers to determine appropriate monitoring and movement restrictions (2). For 21-days after departure from the Ebola-affected country, travelers check their temperature twice a day and report daily to the local health department in the town they are staying in. This active monitoring allows rapid identification and medical evaluation of travelers who develop signs and symptoms of Ebola.

During October 11, 2014–February 28, 2015, 75 persons arrived in Connecticut who were monitored (Table 1). The majority of persons monitored were aged >18 years. The mean number of monitored travelers per month was 15 (range 12-20) (Table 2).

Reported by

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Table 1. Travelers monitored for Ebola by countries visited, Connecticut, October 1, 2014-February 28, 2015

Country	Number of travelers (%)
Liberia	36 (48)
Guinea	17 (23)
Mali*	10 (13)
Sierra Leone	9 (12)
Multiple Countries	3 (4)
Total	**75**

*Only travelers who departed Mali between 11/17/2014-1/5/2015 required monitoring.

Table 2. Travelers monitored for Ebola by month and age group, Connecticut, October 1, 2014-February 28, 2015

Month Monitoring Started	Age Group		Total
	≤18 years	>18 years	
October	3	11	**14**
November	5	12	**17**
December	5	15	**20**
January	0	12	**12**
February	0	12	**12**
Total	**13**	**62**	**75**