Acceptability of Short-Course Rifampin and Pyrazinamide Treatment of Latent Tuberculosis Infection Among Jail Inmates*

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Study objectives: To determine whether short-course treatment of latent tuberculosis infection (LTBI) with 2 months of rifampin and pyrazinamide (2RZ) is well tolerated and leads to increased treatment completion among jail inmates, a group who may benefit from targeted testing and treatment for LTBI but for whom completion of ≥ 6 months of isoniazid treatment is difficult because of the short duration of incarceration.

Design: Prospective cohort.

Setting: Large, urban county jail.

Patients: All inmates admitted to the Fulton County Jail who had positive tuberculin skin test results, normal findings on chest radiography, and expected duration of incarceration of at least 60 days.

Intervention: Inmates were offered 2RZ via daily directly observed therapy for 60 doses as an alternative to isoniazid therapy.

Measurements and results: We measured the completion of 2RZ treatment and toxicity due to 2RZ treatment during incarceration. From December 14, 1998, through December 13, 1999, 1,360 new inmates had positive tuberculin skin test results and normal findings on chest radiography, and 168 new inmates had an expected duration of incarceration of ≥ 60 days. One hundred sixty-six inmates (> 99%) were HIV-negative. Eighty-one inmates (48%) completed 60 doses of 2RZ treatment while incarcerated. Seventy-four inmates (44%) were released before completion. Treatment was stopped in 1 inmate (< 1%) for asymptomatic elevation of aspartate ami

2RZ was acceptable to and well tolerated by inmates, and led to a marked increase in the number of inmates completing treatment of LTBI during incarceration. (CHEST 2001; 119:833–837)

Key words: correctional institutions; treatment of latent tuberculosis infection

Abbreviations: AST = aspartate aminotransferase; LTBI = latent tuberculosis infection; 2RZ = rifampin and pyrazinamide

Decreasing tuberculosis morbidity in the United States has led to increasing challenges for tuberculosis control. Although tuberculosis disease is likely to occur in certain well-defined risk groups that can be targeted for control efforts, the recognized groups often lack access to health-care services, have high rates of substance abuse, or spend time in congregate settings where individual identification and evaluation as case contacts are difficult.1–3

Correctional institutions have been frequently recognized as sites of Mycobacterium tuberculosis transmission and disease outbreaks in the last decade.4–6

Public health priority has been appropriately given to
case detection, isolation, and treatment within facilities. However, as correctional health and public health are increasingly recognized to be intertwined, targeted testing for and treatment of latent tuberculosis infection (LTBI) among persons in correctional institutions will be given higher priority.

Jails, which house persons who are awaiting arraignment or court action, or persons sentenced to terms of < 1 year, pose a particularly challenging opportunity for treatment of LTBI. The short duration of incarceration and high turnover rate in jails make completion of treatment difficult. However, the jail population includes persons at high risk for tuberculosis with little access to preventive healthcare services.

Short-course treatment of LTBI with 2 months of daily doses of rifampin and pyrazinamide (2RZ), which has equivalent efficacy as 12 months of daily isoniazid therapy among tuberculin skin test-positive, HIV-infected persons, has recently been recommended as an acceptable alternative to isoniazid therapy for HIV-uninfected persons. However, experience with implementing this regimen in HIV-uninfected persons, including persons in congregate settings such as jails, is limited. We describe a collaborative effort of the Fulton County Sheriff’s Department, the Fulton County TB Program, and the Georgia TB Control Program to use 2RZ in the Fulton County Jail, an urban jail that was the 16th largest in the United States in 1997–98, with an average daily census of 4,276 inmates.

**Materials and Methods**

All inmates admitted to the jail undergo medical screening through the jail medical services at the time of booking, including a brief medical history. Inmates complaining of symptoms suspicious for pulmonary tuberculosis are placed in respiratory isolation at the jail and undergo further evaluation. Individuals without complaints receive a tuberculin skin test unless they give a history of a previous positive test result or previous tuberculosis disease. Tuberculin testing is performed using the Mantoux method. Skin tests are read in 48 to 72 h by medical staff. Inmates with a skin-test induration of ≥ 5 mm undergo chest radiography, as do those who report HIV infection (regardless of skin test results), a history of previous positive tuberculin test result, or previous active tuberculosis.

Beginning December 14, 1998, inmates were eligible to receive 2RZ, rather than isoniazid, if they had a current or previously documented positive tuberculin skin test result (≥ 5 mm induration for those with HIV infection, recent case contact, or fibrotic changes on chest radiography, and ≥ 10 mm induration for all others), a chest radiograph without evidence of active tuberculosis, an expected duration of incarceration of 60 days from the time their chest radiograph report was available, and no history of previous adequate treatment for LTBI. Pregnant women and persons with gout were not eligible for 2RZ treatment.

Daily rifampin dosage was 600 mg and pyrazinamide dosage was 15 to 20 mg/kg. Medication was administered by directly observed therapy to the inmates in their cell blocks 7 days a week. Measures of asparginine aminotransferase (AST), bilirubin, uric acid, and CBC with platelets were obtained at baseline and repeated every 4 weeks while the inmate was receiving treatment, or sooner if any abnormality, including elevation of AST three or more times normal, was noted. Inmates with minor complaints of side effects from the medications were evaluated by the program coordinator; those with more serious complaints were seen in the jail clinic by medical services. Inmates were told that if they were released from jail while still receiving treatment, they should go to the Fulton County TB Clinic to complete treatment.

To evaluate the feasibility of using 2RZ treatment in tuberculosis-infected inmates in this setting, we assessed the proportion of inmates admitted to the jail who were eligible and willing to take treatment, the proportion among those starting treatment who completed treatment while incarcerated, the proportion who developed adverse events, and the proportion of those released from jail before completing treatment who completed treatment while in the community.

**Results**

Each month in 1999, on average, 1,758 inmates, 75% of those admitted to the jail, had a tuberculin skin test placed, and 1,197 (68%) were read within 48 to 72 h. On average, 502 inmates (28%) were released each month before their skin tests were read, and an additional 4% of tests were not read for other reasons, although the inmates were still incarcerated. Of the skin tests read, 7.3% were ≥ 10 mm of induration.

From December 14, 1998, through December 13, 1999, 1,360 new inmates had positive tuberculin skin test results and normal chest radiographic findings. Of these, 529 inmates (38.9%) were released before being interviewed by the 2RZ program coordinator, 358 inmates (26.3%) reported previous adequate treatment for LTBI, and 305 inmates (22.4%) had an expected duration of incarceration of < 60 days. The 168 inmates (12.3%) eligible for the program all agreed to start 2RZ treatment. The 168 inmates who started 2RZ treatment were 97% black, 93% male, and 7% Hispanic. Their ages ranged from 17 to 60 years, with a median of 38 years and a mean of 37 years. Thirty-one inmates consented to HIV testing after counseling; all were HIV-seronegative. Two others reported being HIV-infected.

The number of doses of medication received before stopping because of release from jail or adverse event is shown in Figure 1. Eighty-one inmates (48%) completed 60 doses of 2RZ treatment while incarcerated; 74 inmates (44%) were released before completion. Medication treatment was stopped in 13 inmates because of adverse events: 1 inmate had an asymptomatic elevation of AST ≥ 10 times normal (553 U/L) after 4 weeks of treatment, and 12 inmates (7%) had minor complaints of rash and/or pruritus, paresthesias, headaches, or nausea. Ten of the 13 adverse events occurred within the
first 10 days of starting treatment, whereas the unexpected releases before completion of treatment occurred throughout the 60-day period.

Laboratory abnormalities were infrequent. Five inmates had AST values increasing to ≥ 3 times the upper limit of normal after 4 weeks receiving treatment: three values increased ≥ 3 to ≤ 5 times normal, one value increased to ≥ 5 to ≤ 10 times normal, and one value increased to ≥ 10 times normal. All inmates had normal baseline AST values. The mean age in those developing elevated AST while receiving 2RZ was not different from that of the population as a whole. Among these five inmates, two inmates completed treatment with improvement in AST and two inmates were released without completing treatment or further follow-up of AST. The inmate with AST > 10 times the upper limit of normal (553 U/L) had treatment permanently discontinued, but then was released before further follow-up.

An additional seven inmates had elevated AST values at baseline, before starting 2RZ treatment: four inmates had baseline AST of ≥ 3 to ≤ 5 times upper-limit normal, and three inmates had ≥ 5 to ≤ 10 times upper-limit normal. Five of these inmates completed 2RZ treatment while incarcerated; all had a decrease of AST while receiving treatment.

There were no significant changes in total bilirubin, WBC count, hematocrit, or platelet count while receiving treatment. Only one inmate had a significant elevation of uric acid, from a baseline of 9.3 mg/dL to 11.5 mg/dL after 4 weeks. There were no complaints of joint pains or precipitation of acute gout.

Of the 74 inmates released or transferred while receiving 2RZ, 11 inmates (15%) came to the Fulton County TB Clinic at least once to continue treatment, although none completed treatment while under the care of the clinic.

Based on pharmacy dispensing records, during the same 12-month period that the 2RZ program was in operation, 232 inmates at the jail started receiving isoniazid treatment for LTBI and 9 inmates (3.9%) received ≥ 6 months of isoniazid treatment. During the 12-month period before the initiation of the 2RZ program, December 1997 through December 1998, 21 of 517 inmates (4.1%) who had been started on treatment received ≥ 6 months of isoniazid treatment for LTBI. In that year, 143 inmates (28.8%) of those who did not complete an adequate course of isoniazid treatment did complete at least 60 doses, enough to have completed the 2RZ regimen if that had been an option.

**DISCUSSION**

Jail inmates are an important group for targeted tuberculin skin testing and treatment of LTBI. Nationally, the majority of jail inmates are adult men from racial or ethnic minorities with increased risk for tuberculosis. A 25-site national survey of tuberculosis infection in correctional facilities found that 24.6% of inmates being discharged annually may have had tuberculosis infection. Previous reports have documented tuberculosis incidence rates among incarcerated persons to be 6 to 10 times greater than those in the general population. Inmates who become infected while incarcerated may develop active tuberculosis after their release to the community, and transmission to others, including children, can occur. Persons with tuberculosis disease often have little access to preventive health-care services other than jail health services. However,
Early studies have tried to facilitate completion of isoniazid therapy among released inmates, but with limited success. Nolan et al. treated 483 inmates at the King County Jail through a jail outreach project. During a 30-month period, only 37 inmates (7.6%) completed isoniazid therapy while incarcerated; another 182 inmates transferred to other facilities. Of 262 inmates released to the community while still receiving isoniazid, 78 inmates (30%) completed therapy. The subset of released inmates who had chosen to take directly observed isoniazid preventive therapy had a higher completion rate (63 of 105 inmates; 60%) than those who chose self-administered treatment (15 of 52 inmates; 29%), but overall the results were disappointing. White et al. enrolled 79 inmates at the San Francisco City and County Jail into a randomized trial of two incentives to encourage them to go to the tuberculosis clinic after release from jail to finish isoniazid preventive therapy. Eighteen inmates (23%) completed their isoniazid treatment before release. Four of 61 inmates (6%) completed treatment after release to the community. Bock et al. started 143 inmates at the Atlanta Pre-Trial Detention Center on isoniazid preventive therapy. None completed treatment while incarcerated at that facility; 11 inmates (8%) completed treatment after release to the community.

In the first year after instituting 2RZ as a treatment option for inmates with LTBI in the Fulton County Jail, we found the regimen was acceptable to and well tolerated by inmates. In a 12-month period, 81 inmates completed treatment of LTBI while incarcerated, a greater than fourfold increase in numbers completing treatment compared with previously published reports. Also, the number of inmates who completed 2RZ treatment in this jail was almost four times greater than the number who had completed isoniazid therapy the previous year. Only a few inmates stopped 2RZ treatment because of minor adverse events, and only one inmate stopped because of serious hepatotoxicity. Because 2RZ is a relatively new regimen, the risk of hepatotoxicity is not as well defined as that associated with isoniazid treatment. Potential hepatotoxicity is of particular concern among correctional institution inmates, who have been shown to have a high prevalence of chronic hepatitis B and C, and of alcohol abuse. We did not have data on the prevalence of chronic hepatitis or alcoholism in this cohort, but it may well have been similar to other inmate populations. Despite this risk, the overall incidence of AST elevations during treatment was low, and compared favorably with that seen with isoniazid treatment. Also reassuring was the finding that, among inmates who had AST elevations before starting treatment, presumably because of alcohol abuse before incarceration, all showed improvement in liver function test results while receiving treatment.

Despite our efforts to treat only those with an expected duration of incarceration of 60 days after initiation of therapy, 74 inmates (44%) of those started on 2RZ treatment were released before completion of treatment. Release dates are difficult to predict, as more than half the inmates in jail are awaiting court action, such as trial or sentencing, and court dates and bail-bond status change frequently. Also, inmates often waited ≥10 days for chest radiograph readings after detection of a positive tuberculin skin test finding, a loss of crucial treatment days.

Now that 2RZ treatment has been shown to be acceptable to and well tolerated by jail inmates, and to facilitate markedly increased treatment completion rates for LTBI, jail and public health programs can build on these successes to expand its successful use. Evaluation for LTBI in the jail setting should be expedited. Staff should target tuberculin testing to only those inmates who will be incarcerated long enough to have it read (about two thirds of those tested in this cohort), and should focus on getting inmates who are skin test-positive among that group a radiographic evaluation and quick treatment. Because many infected inmates who would benefit from treatment of LTBI will still be released before completion of treatment, innovative outreach programs to complete treatment in the community must be integrated with the jail program. The Centers for Disease Control and Prevention is currently collaborating with five jails nationally to facilitate continuation of 2RZ treatment among released inmates with daily directly observed therapy. 2RZ appears to be a promising regimen for improving completion of treatment of LTBI in this difficult-to-reach, high-risk population, and its expanded use could contribute to our goal to eliminate tuberculosis in the United States.

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