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BRIEF REPORT

Completion Rate and Side-Effect Profile of Three-Month Isoniazid and Rifapentine Treatment for Latent Tuberculosis Infection in an Urban County Jail

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In an urban jail population, 3 months of isoniazid and rifapentine (3HP) was associated with an 85% latent tuberculosis infection treatment completion rate compared with 18% in a standard 9-month isoniazid treatment group. Among the 91 patients who started 3HP therapy, there were 2 treatment discontinuations from adverse drug reactions.

Keywords. correctional healthcare; prevention; tuberculosis.

The estimated prevalence of active tuberculosis (TB) among inmates in correctional facilities is 4 to 17 times greater than the general US population, and over 7% of inmates have latent TB infection (LTBI) [1]. In 2012, there were more than 9900 active TB cases reported in the United States, and 4% of cases occurred among incarcerated persons [2]. Because many TB outbreaks have been reported in correctional facilities [3, 4], treatment of LTBI in correctional settings is a priority.

Implementing a 9-month isoniazid (9H) regimen for LTBI in jails is challenging due to short durations of incarceration. Historically, 9H treatment completion rates in correctional settings have been low, between 31% and 37% [5, 6]. In addition, patient education and monetary incentives to increase postincarceration LTBI treatment completion have been ineffective [7].

A recent clinical trial implementing 3 months of isoniazid and rifapentine (3HP) given as 12 once-weekly doses by directly observed therapy (DOT) was found to be noninferior to 9H in preventing progression of LTBI to active TB and resulted in higher completion rates [8]. However, there was an increased discontinuation rate from adverse drug reactions (ADRs) with 3HP [8]. Although this clinical trial was conducted among close contacts to individuals with active TB disease [8], the performance of 3HP in an incarcerated population with high rates of substance abuse, human immunodeficiency virus (HIV), and hepatitis that could potentially increase medication intolerance and ADR is unclear [1]. The goals of the current study were to determine the safety, tolerability, and completion rates of 3HP in an urban county jail population.

METHODS

Santa Clara jail has an average daily population of 4632 inmates with an average length of stay of 110 days. Latent TB infection treatment in the jail was 9H until implementation of 3HP in June 2012. We prospectively observed 3HP patients and compared LTBI treatment completion rates to a historic cohort that received 9H. The primary endpoint was treatment completion. The secondary endpoint was permanent 3HP discontinuation due to ADRs. Statistical analyses were conducted using SAS, version 9.3 (SAS Institute Inc., Cary, NC). The study was approved by Santa Clara Valley Medical Center Research and Human Subjects Review Committee with waiver of informed consent. The Centers for Disease Control and Prevention (CDC) determined the project was not human subjects research and did not require approval by an institutional review board.

Patients included in both cohorts were those who were asymptomatic with a tuberculin skin test (TST) of ≥10 mm and normal chest radiographs. Exclusion criteria for both cohorts included the following: TB disease, known treatment drug allergy, liver function tests (LFTs) including aspartate or alanine transaminase levels greater than 3 times the laboratory normal range, pregnancy, or previously completed LTBI treatment. Patients were clinically evaluated monthly. Upon discovery of an ADR, medical providers assessed severity and determined whether treatment could be continued. If patients agreed and providers determined continuation safe, treatment was continued. Treatment was discontinued if LFTs were greater than 5 times baseline. Because patients were unable to be observed after they were released or transferred to other facilities, only data of patients completing treatment at this facility were analyzed.

Retrospective 9-Month Isoniazid Cohort

Patients who initiated 9H between January 1, 2010 and December 31, 2011 were included in this analysis. Patients were eligible if the anticipated incarceration time was >3 months. Patients received 900 mg of isoniazid (INH) and 50 mg of pyridoxine twice weekly for 9 months by DOT. Liver function tests were evaluated at baseline, 1 month after treatment initiation and

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as clinically indicated. Completion was defined as receiving 72 doses of INH within 12 months. The number of INH administered doses and reasons for discontinuation were abstracted from medication administration records.

Prospective 3-Month Isoniazid and Rifapentine Cohort

Patients with both positive TST and subsequent positive whole blood interferon gamma-release assay who initiated 3HP between June 11, 2012 and March 18, 2014 were included in the analysis. Patients were not eligible to start 3HP if they were HIV positive and on antiretroviral medications consistent with the CDC guidelines or had an expected incarceration of <4 months [9].

Patients received 900 mg of rifapentine, 900 mg of INH, and 50 mg of pyridoxine weekly by DOT for 12 doses. Monthly LFTs and complete blood counts were obtained. In addition to previously described discontinuation parameters for 9H, treatment was discontinued for new leukopenia (white blood cell $<3.9 \times 1000$/mcL) or thrombocytopenia (platelets $<100 \times 1000$/mcL). Completion was defined as receiving 11 doses within 16 weeks. Data were abstracted from electronic medical records.

RESULTS

Patients in the 2 cohorts differed in age, but not gender, race, ethnicity, or body mass index (Table 1).

Retrospective 9-Month Isoniazid Cohort

Among 154 patients, 28 patients (18%) completed treatment and 126 (82%) did not. Of those not completing treatment, 82% (n = 103) transferred out of jail, 13% (n = 16) had no identifiable reason, 5% (n = 6) declined treatment after initiation, and 1 discontinued medication due to hepatotoxicity and was subsequently transferred out of the facility for further evaluation. The median time on 9H for all patients was 3 months (interquartile range, 1.5–6.0) and 2 months for noncompleters (interquartile range, 1.0–4.0).

Prospective 3-Month Isoniazid and Rifapentine Cohort

Among 91 patients, 77 (85%) completed treatment and 14 (15%) did not complete treatment. Of those not completing treatment, 11 (79%) were transferred out of jail, 2 (14%) discontinued treatment because of rash, and 1 (7%) had an unrelated illness and declined further treatment. Of 11 transferred patients, 5 were released to the community and 6 were transferred to another correctional facility. The 3HP completion rate was significantly higher compared with 9H (85% vs 18%, respectively; χ^2, $P < .001$).

Of 91 3HP patients, 5 (6%) had hepatitis C and 1 (1%) had hepatitis B. In addition, 33 (37%) reported consuming more than 2 alcoholic beverages per day before incarceration, 55 (60%) reported a history of noninjection drug use, and 4 (4%) reported a history of injection drug use.

Table 1. Sociodemographic and Clinical Characteristics of 9H and 3HP Patients in an Urban County Jail[a]

Characteristic	9H Cohort (N = 154) n (%)	3HP Cohort (N = 91) n (%)	*P* Value
Median age, years (IQR)	32 (26–42)	39 (31–47.5)	<.001
Sex			
Male	151 (98.1)	87 (95.6)	.43
Race/ethnicity			.10
Hispanic ethnicity	107 (69.5)	63 (69.2)	
Asian, non-Hispanic	21 (13.6)	17 (18.7)	
White, non-Hispanic	13 (8.4)	4 (4.4)	
Other, non-Hispanic	12 (7.8)	3 (3.3)	
Unknown	1 (0.6)	4 (4.4)	
Body mass index[b]			
Median (IQR)	25.7 (23.8–29.0)	25.8 (23.5–29.0)	.39
Medical risk factors and habits			N/A
Hepatitis B	NC	1 (1.1)	
Hepatitis C	NC	5 (5.5)	
Diabetes	NC	8 (8.8)	
HIV positive	NC	0 (0.0)	
Current or past smoker	NC	39 (43.9)	
History of alcoholism[c]	NC	33 (36.3)	
History of noninjection drug use	NC	55 (60.4)	
History of injection drug use	NC	4 (4.4)	
Any adverse event			N/A
Hepatotoxicity[d]	NC[e]	1 (1.1)	
Dizziness	NC	4 (4.4)	
Fever or chills	NC	5 (5.5)	
Rash/hives	NC	4 (4.4)	
Abdominal pain	NC	1 (1.1)	
Numbness or tingling	NC	2 (2.2)	
Nausea	NC	3 (3.3)	

Abbreviations: BMI, body mass index; IQR, interquartile range; NA, not applicable; NC, data not collected; 3HP, 3 months of isoniazid and rifapentine; 9H, 9-month isoniazid.

[a] Significance was by Pearson χ^2 test for sex, Fisher's exact test for race/ethnicity, and Mann–Whitney *U* test for age and BMI.

[b] The BMI is the weight in kilograms divided by the square of the height in meters.

[c] Patient reported consuming more than 2 alcoholic beverages per day before incarceration.

[d] Liver function tests included aspartate transaminase or alanine transaminase levels >3 times normal range.

[e] Data were not collected on adverse drug reactions for 9H cohort, but 1 patient did not complete treatment due to hepatotoxicity.

Common ADRs included fever or chills (n = 5, 5.5%) and dizziness and rash (n = 4 each, 4.4%; Table 1). All episodes were mild and transient and required no medical intervention or change in treatment. Nausea (n = 3, 3.3%), numbness and tingling (n = 2, 2.2%), and abdominal pain (n = 1, 1.1%) were infrequently reported. Post hoc analysis of LFTs showed that 1 patient had LFTs greater than 3 times baseline; however, the LFTs returned to baseline and treatment was completed.

DISCUSSION

Latent TB infection completion rates increased after 3HP implementation compared with 9H. In addition, our 3HP completion rate (85%) was higher than rates in another 9H jail population (32%) and similar to the community 3HP clinical trial (82%) [7, 8]. Frequency and severity of ADRs were low in our 3HP cohort. Although we had a small sample size, our study did not replicate ADR rates reported in the community 3H trial [8].

Previous studies reported lower rates of hepatotoxicity with 3HP compared with 9H and rifampin/pyrazinamide [8, 10]; we found similarly low rates of hepatotoxicity in an incarcerated population. Post hoc analysis showed no significant difference between baseline and treatment LFTs in the 3HP cohort, suggesting a very limited effect of 3HP on LFTs. Our experience suggests that this regimen may be used in populations with a similar history of substance abuse.

In cost studies, 3HP is more expensive than 9H primarily due to the cost of DOT and rifapentine [11]. Two correctional setting factors may increase 3HP cost-effectiveness. First, patients in correctional settings already receive medications via DOT; therefore, no additional visit or staffing costs are incurred. Second, progression to active TB among incarcerated patients may result in higher societal costs compared with cases occurring in the community due to increased potential for outbreaks and large contact investigations in a congregate setting. The 3HP cost-effectiveness analyses in correctional settings are needed to determine whether preventing progression to active TB in high-risk groups may offset the additional cost of 3HP.

Our study had several limitations. The retrospective 9H design potentially impacted data collection quality for this cohort. Because we used medical administration records and not medical charts for the 9H cohort, we may have underestimated 9H treatment completion rates. Patients who transferred before treatment was completed were considered to be noncompleters, although they may have completed treatment elsewhere, which may have disproportionately underestimated the treatment completion of the 9H cohort because the treatment duration is shorter for 3HP therapy. Moreover, the side-effect profile among the 3HP cohort who transferred before treatment completion was also incomplete. The inclusion criteria between 9H and 3HP were different, which may have influenced characteristics and completion rate differences. Although the 3HP cohort was older, we were not able to evaluate age effect on completion rate given the limited data collected on the historical 9H cohort. In addition, we were unable to compare differences in ADRs between groups because we did not have medical charts for the 9H cohort. We were also unable to identify factors associated with the higher 3HP treatment completion rate; however, a shorter treatment duration and once-weekly versus twice-weekly dosing may have been contributing factors.

CONCLUSIONS

In summary, LTBI treatment completion increased with implementation of the 3HP regimen in this urban county jail. Adverse drug reactions with 3HP were mild with low rates of treatment discontinuation. Despite high rates of substance abuse and hepatitis, only 1 case of transient hepatotoxicity was reported in the 3H group. Because correctional settings are important LTBI reservoirs for community TB cases, 3HP may be an effective strategy in decreasing correctional and possibly subsequent community TB cases [12].

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