

536 Completion rate and safety of twelve weekly doses of directly observed isoniazid and rifapentine for latent tuberculosis infection

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1. Introduction

- Treatment of latent tuberculosis infection (LTBI) is a cornerstone of TB control.
- The standard of care for LTBI is 9 months of self-administered isoniazid (9H).
- In 2011, the CDC recommended 12-dose isoniazid and rifapentine once-weekly and directly observed (3HP) based on a clinical trial demonstrating equal efficacy and a higher completion rate than 9H.
- The Infectious Disease clinic at the University of Vermont Medical Center (UVMCC) began using 3HP in 2012.
- The anecdotal experience was that completion rates were not as high as previously reported but our predominantly refugee population may account for this.
- Our primary objective was to compare the completion rates and safety of 3HP and 9H in a real world setting.

2. Methods

- Retrospective, matched cohort study comparing all 82 adult patients who received 3HP therapy for LTBI with 82 patients who received 9H.
- Pre-specified matching criteria for the 9H cohort was based on age, sex, refugee, foreign birth, birth in Bhutan and hospital employee.
- Demographic, clinical, laboratory, and dosage data were collected from chart review.

3. Statistical Analysis

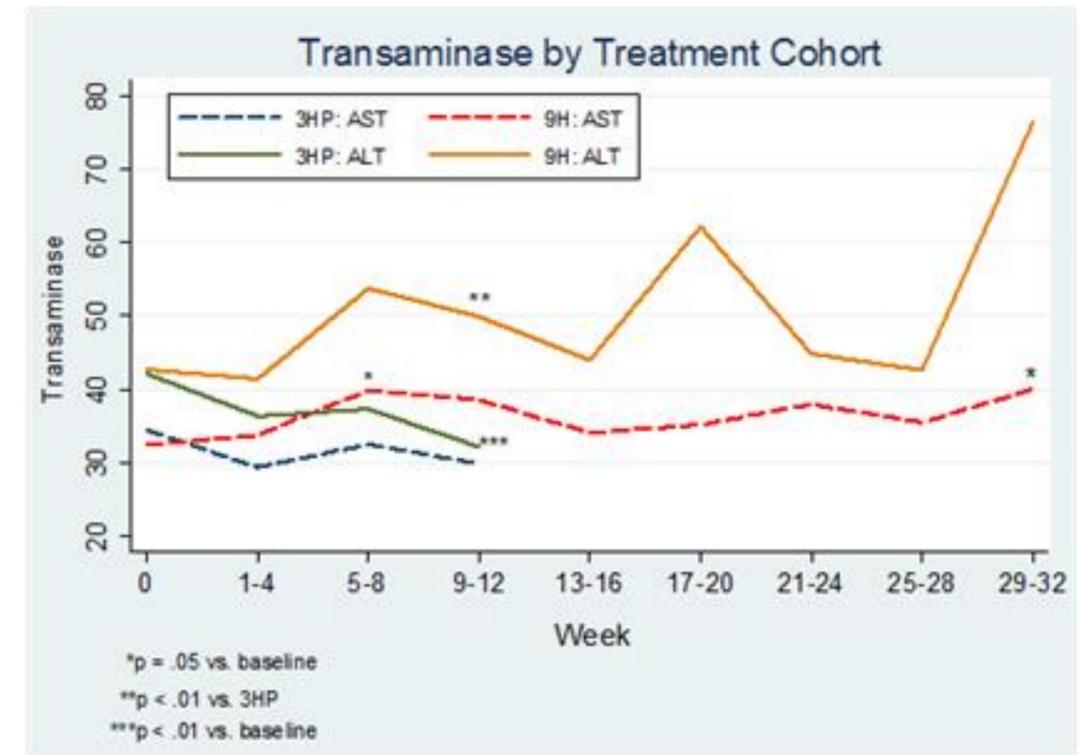
- Summary statistics for clinical and demographic variables were calculated for both cohorts.
- Categorical variables were compared using χ^2 or Fisher's exact test.
- Continuous variables were analyzed using the Student's t-test or Wilcoxon Rank sum test as appropriate.
- Stata 10 was used for data analysis and a two-sided p-value of ≤ 0.05 was considered statistically significant.

4. Results

Summary of baseline characteristics, safety and completion rates between 3HP and 9H

| n (%) | 3HP (n=82) | 9H (n=82) | p-value |
|---|-------------|-------------------------|---------|
| Demographic/Clinical Characteristics | | | |
| Age*, years | 36.7 ± 14.0 | 42 ± 15.7 | .03 |
| Sex*, male | 50 (61.0) | 49 (60.0) | .87 |
| Foreign-born* | 75 (91.5) | 77 (93.9) | .77 |
| Refugee* | 61 (74.4) | 62 (75.6) | .86 |
| Bhutanese/Nepali* | 40 (48.8) | 45 (54.9) | .44 |
| UVMCC employee* | 18 (22.0) | 9 (11.0) | .06 |
| Cardiac | 1 (1.2) | 16 (19.5) | <.01 |
| Pulmonary | 1 (1.2) | 4 (4.9) | .37 |
| Diabetes mellitus | 1 (1.2) | 6 (7.3) | .12 |
| Hepatitis | - | 3 (3.7) | .25 |
| Cirrhosis | - | - | - |
| Seizure history | - | - | - |
| Cancer | 1 (1.2) | 3 (3.7) | .62 |
| HIV | - | 2 (2.4) | .50 |
| Alcohol use | 5 (6.2) | 14 (20.6) | .01 |
| Baseline weight | 65.4 ± 15 | 65.9 ± 17 | .76 |
| BMI ^b | 25.7 ± 5.3 | 25.8 ± 4.7 | .62 |
| Adverse Drug Reactions | | | |
| Total ^b | 145 | 100 | |
| Rate ^c | 1.8 | 1.2 | |
| Completion | 58/82 (71) | 61/81 (75) ^d | 0.51 |
| Permanent discontinuation | 19/82 (23) | 12/81 (15) ^d | 0.17 |

NOTE: Data are no. (%) of patients or mean value + SD unless otherwise indicated
 *matched variable
^adata available for 3HP (n=42) and 9H (n=50)
^bnumber of occurrences in each group
^crate based on n of 145 in 3HP and 100 in 9H
^d9H cohort completion status unknown for 1 patient (n=81)



5. Conclusions

- Completion rates with 3HP were not as high as previously published and were similar to 9H despite higher 9H cardiac comorbidity and alcohol use.
- A higher rate of adverse drug reactions and a higher frequency of severe reactions were experienced in 3HP.
- The rate of permanent discontinuation due to an adverse event was higher in 3HP and overall, discontinuation rates were higher than previously reported.
- Potential explanation for the lower 3HP completion rates may be related to ethnicity differences as the majority of the study population was foreign-born with roughly half Bhutanese.
- In this setting of primarily refugees, 3HP offered a safe and faster treatment of LTBI but not a greater likelihood of completion.