

# Evaluation of 3-months isoniazid –rifapentine and 6-months isoniazid regimens for tuberculosis prevention in people living with HIV

Tinashe Mudzviti<sup>1,2</sup>, Bahati Kasimonje<sup>1</sup>, Takudzwa Chatindo<sup>1</sup>, Tinei Shamu<sup>1,3,4</sup>, Cleophas Chimbetete<sup>1</sup>, Samuel Makhaza<sup>2</sup>, Samuel Gavi<sup>5</sup>

<sup>1</sup>Newlands Clinic, Zimbabwe, <sup>2</sup>Department of Pharmacy and Pharmaceutical Sciences, University of Zimbabwe, Zimbabwe, <sup>3</sup>Institute of Social and Preventive Medicine, University of Bern, Switzerland, <sup>4</sup>Graduate School of Health Sciences, University of Bern, Switzerland, <sup>5</sup>Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, U.S.A

## Background

- Tuberculosis preventive treatment (TPT) can reduce the risk of individuals developing Tuberculosis (TB)
- Two treatment modalities are available for treating latent tuberculosis infection (LTBI)
- Isoniazid once daily for 6-months (6H)
- Rifapentine/Isoniazid once weekly for 3 months (3HP)
- 3HP has been shown to cause less adverse reactions and patients achieved higher adherence compared to 6H<sup>1</sup> in study settings
- This study was done to see if adherence to treatment of LTBI was different between 3HP and 6 in people living with HIV
- The study was also conducted to identify the causes of treatment discontinuation in either of the 2 regimens

## Methods

- This was a retrospective cohort study at Newlands Clinic, Zimbabwe<sup>2</sup>
- Data for patients receiving HIV and LTBI treatment were abstracted from an electronic medical record database
- Exposure variables were either 3HP or 6H use
- Demographic variables abstracted included:
  - Age
  - Gender
  - Education level attained
  - Employment status
  - Marital status
- Outcome variable was complete adherence to scheduled treatment regimen
- Patients lost to follow-up or with unknown outcomes were included as a weighted censored variable in the analysis
- Measured/unmeasured confounding was controlled in the marginal structural model
- All records of patients receiving LTBI treatment between 2020 to 2021 were included
- A marginal structural logistic regression model was used

## Results

- A total of 1,494 PLHIV received treatment for LTBI in the treatment programme
- 993 patients (66.5%) received 6H and 501 (33.5%) received 3HP

**Table 1: Demographic Characteristics of PLHIV treated**

Variable	6H, 993 (66.5%)	3HP, 501 (33.5%)
<b>Age Category</b>		
2-17 years	426 (42.9%)	42 (8.4%)
18-30 years	166 (16.7%)	177 (35.3%)
31-50 years	260 (26.2%)	182 (36.3%)
51+ years	141 (14.2%)	100 (20.0%)
<b>Gender</b>		
Male	471 (47.4%)	180 (35.9%)
Female	522 (52.6%)	321 (64.1%)
<b>Current Level of Education</b>		
No Formal School	367 (37.0%)	76 (15.2%)
Primary School	190 (19.1%)	128 (25.5%)
High School	299 (30.1%)	225 (44.9%)
University/College Graduate	137 (13.8%)	72 (14.4%)
<b>Employment Status</b>		
Child or Student	514 (54.0%)	193 (39.5%)
Unemployed	188 (19.7%)	105 (21.5%)
Employed	250 (26.3%)	191 (39.0%)
<b>Missing values (3.7%)</b>		
<b>Marital Status</b>		
Child	426 (43.0%)	42 (8.4%)
Single	207 (20.9%)	202 (40.3%)
Divorced/Widowed	108 (10.9%)	86 (17.2%)
Married	249 (25.2%)	171 (34.1%)

- There was a strong association between younger age and use of 6H in a Chi-square test (p<0.001)

**Table 3: Discontinuation Rates and Discontinuation Reasons**

Variable	6H, N = 993	3HP, N = 501
<b>Adverse Effects leading to discontinuation, n(%)</b>		
Liver toxicity	64 (6.4)	7 (1.4)
Developed TB	4 (0.4)	0 (0)
Rash	6 (0.6)	2 (0.4)
Other	11 (1.1)	5 (1.0)
Deceased/LTFU/Transfer Out	16 (1.6)	0 (0)
<b>Median Time to discontinuation, weeks(IQR)</b>	10 (4-15)	2 (0-6.3)

- Discontinuation rates were 3.4% for 3HP and 9.6% for 6H
- Of the discontinuations in the 3HP arm 7(1.4%) were caused by an adverse effect
  - 2 developed a rash
  - 2 developed nausea and vomiting
  - 1 developed facial oedema
  - 1 developed impaired renal function
  - 1 of the adverse effects was undocumented
  - 1 discontinued as a result of a drug interaction.
- Of the 95 discontinuations in the 6H arm, 64(6.4%) were as a result of an adverse effect or drug interaction.

**Table 2: Marginal Structural Model Logistic Regression Analysis**

Variable	Odds Ratio	95% CI	p-value
<b>Treatment</b>			
6H vs. 3HP	3.7	2.1 to 6.6	<0.0001
<b>Gender</b>			
Male vs. Female	1.15	0.8 to 1.6	0.4

- 3HP use was associated with statistically significant higher completion rates (OR = 3.7, CI: 2.1 – 6.6, p<0.0001) compared to 6H
- There was no statistically significant difference in completion rates of LTBI treatment between males and Females (OR = 1.15, CI: 0.8-1.6, p = 0.4)

## Conclusion

- Strong causal relationship between short term treatment regimens of 3HP and complete adherence to treatment
- 3HP was more tolerable compared to 6H
- Use of 3HP which has a shorter duration will have better retention in TPT
- 3HP has reduced discontinuation rates due to toxicities

## References

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Corresponding author:

Tinashe Mudzviti

E: [tinashem@newlandsclinic.org.zw](mailto:tinashem@newlandsclinic.org.zw)

C: +263772290511

