

ALCOHOL USE AND SUBOPTIMAL ADHERENCE TO ISONIAZID IN PERSONS WITH HIV AND LATENT TB

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BACKGROUND

- The World Health Organization (WHO) recommends Isoniazid preventive therapy (IPT) as a key strategy to decrease tuberculosis (TB) disease development in persons with HIV (PWH)^(1,2)
- Unhealthy alcohol use is associated with increased risk of progression to TB disease^(3,4)
- Most current alcohol use in PWH in Uganda is unhealthy use⁽⁵⁾
- Unhealthy alcohol use is associated with reduced adherence to antiretroviral therapy (ART)⁽⁶⁾ but its effect on IPT adherence is not well known.

AIMS

Among PWH on ART in south-western Uganda, we sought to:

- Determine the level of adherence to IPT, overall and by drinking status
- Evaluate the association between alcohol use and IPT adherence

METHODS

Setting and Study Population:

Adult PWH attending the Mbarara Regional Hospital HIV clinic

Key inclusion/exclusion criteria:

Inclusion:

- Current alcohol consumption (prior 3 months) or alcohol abstaining (prior year) (via self-report), recruited in a ratio of 2:1
- All on ART for ≥ 6 months

Exclusion:

- ALT/AST >2x upper limit of normal; taking Nevirapine
- History of active TB or prior TB treatment or history of prior IPT

Latent TB status determined by:

A positive Tuberculin Skin Test (TST) marked by ≥ 5mm induration.

All received IPT using Isoniazid (INH) 300mg once daily (a 6 months course taken in less than 9 months marked a full course)

Adherence Measurement was monitored using Medication Event Monitoring System (MEMS) caps.

Our Primary Outcome:- Sub-optimal INH adherence

Defined as less than 90% of days with any MEMs opening in the prior 90 days

Main Independent Variable:- Alcohol use

Captured by a composite measure of the Alcohol Use Disorders Identification Test – Consumption (AUDIT-C) & phosphatidylethanol (PEth), an alcohol biomarker and categorized as:

- None:** no self-report, and PEth < 8ng/mL
- Moderate:** AUDIT-C 1-2 (women) or 1-3 (men), and/or PEth 8- <50 ng/mL
- Unhealthy:** AUDIT-C ≥3 (women) or ≥4 (men), and/or PEth ≥50 ng/mL

Covariates: Age, gender, ART adherence, study time on INH, symptoms of depression, Grade 2+ liver enzyme elevations (LEEs) or symptoms and social support.

Analyses:

We used generalized estimating equations logistic regression to assess the association between alcohol use and sub-optimal INH adherence, adjusting for the covariates

RESULTS

Key Findings:

- The overall prevalence of sub-optimal INH adherence was 31.3% at 3 months and 43.9% at 6 months.
- The odds of sub-optimal INH adherence increased with level of alcohol consumption; the adjusted odds for those in the unhealthy consumption group were 2.78 (95% CI: 1.62-4.76) and 1.59 (95% CI: 0.94-2.71) in the moderate consumption group, compared to those abstaining.

Table 1. Participant Characteristics by INH Adherence at 3 and 6 months

	3 months (n=275)		6 months (n=264)	
	≥ 90% N (%) (n=189)	< 90% N (%) (n=86)	≥ 90% N (%) (n=148)	< 90% N (%) (n=116)
Alcohol use, prior 3 months				
None	79 (82.3)	17 (19.8)	73 (70.2)	31 (29.8)
Moderate	43 (72.9)	16 (27.1)	26 (61.9)	16 (38.1)
Unhealthy	67 (55.8)	53 (44.2)	49 (41.5)	69 (58.5)
Age (median [IQR])	40 [35-49]	38 [32-44]	41 [35-49]	38 [32-44]
Gender				
Female	102 (72.9)	38 (27.1)	83 (61.9)	51 (38.1)
Male	87 (64.4)	48 (35.6)	65 (50.0)	65 (50.0)
Grade 2+ LEEs or symptoms				
No	160 (70.2)	68 (29.8)	135 (58.2)	97 (41.8)
Yes	29 (61.7)	18 (38.3)	13 (40.6)	19 (59.4)
ART adherence, prior 30 days				
Good/fair/poor/very poor	13 (39.4)	20 (60.6)	15 (42.9)	20 (57.1)
Excellent/very good	176 (72.7)	66 (27.3)	133 (58.1)	96 (41.9)
Social desirability				
Low/moderate	89 (64.0)	50 (36.0)	67 (50.8)	65 (49.2)
High	100 (73.5)	36 (26.5)	81 (61.4)	51 (38.6)
Years since HIV diagnosis at baseline (median [IQR])	8 [5-12]	7 [4-10]	8 [5-12]	7 [4-10]

- Of the 302 enrolled persons, 279 were on INH for three or more months.
- Reasons for non-completion included disenrollment due to ineligibility (n=1), discontinuation prior to 3 months because of liver or other toxicities (n=19), and loss to follow up (n=3).
- Of the 279 persons at baseline:
 - Half (50.9%) were female
 - 80.7% reported very good to excellent adherence to ART in prior 30 days at baseline
 - 21.9% and 50.5% were in the moderate and unhealthy alcohol groups, respectively, while 27.6% had no alcohol use, confirmed by PEth.

LIMITATIONS

- MEMs does not inform us about the actual ingestion of the pill hence may not provide perfect information on adherence to medications.
- MEMs device manipulation, repeated opening or failure to return the bottles at the set follow-up visits may affect its accuracy.

Table 2. Unadjusted and Adjusted Odds Ratios (OR)* and 95% Confidence Intervals (CI) for INH adherence <90% in the prior 3 months among PWH with latent TB (n = 539 observations; n = 279 participants).

	Unadjusted OR (95% CI)	p-value	Adjusted OR** (95% CI)	p-value
Alcohol use, prior 3 month (ref = None)	1.00		1.00	
Moderate	1.56 (0.95, 2.55)	0.08	1.59 (0.94, 2.71)	0.09
Unhealthy	2.70 (1.68, 4.36)	<0.01	2.78 (1.62, 4.76)	<0.01
Age (per 1 year decrease)	1.05 (1.02, 1.07)	<0.01	1.05 (1.02, 1.08)	<0.01
Gender (ref = Female)	1.00		1.00	
Male	1.54 (1.01, 2.34)	0.04	1.25 (0.76, 2.05)	0.38
ART adherence, prior 30 days (ref = Excellent/very good)	1.00		1.00	
Good/fair/poor/very poor	2.17 (1.35, 3.48)	<0.01	2.45 (1.46, 4.14)	<0.01
Study visit (ref = 3 months)	1.00		1.00	
6 months	1.72 (1.34, 2.21)	<0.01	1.86 (1.39, 2.49)	<0.01

*GEE logistic regression models

**Multivariable model also adjusted for symptoms of depression, Grade 2+ liver enzyme elevations or other symptoms, and social support.

CONCLUSIONS

- Sub-optimal adherence to INH at 3- and 6-months was high among PWH and was it was associated with unhealthy alcohol use.
- Adherence support and/or alcohol reduction strategies are needed for this group at high risk for active TB.

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