Treatment Outcomes in Low Level Isoniazid Resistant Tuberculosis

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BACKGROUND

- Isoniazid (INH) is an important drug in the treatment of *Mycobacterium tuberculosis* (TB).[1,2]
- Resistance to INH is classified as either high-level (MIC > 2 µg/mL) or low-level (MIC 0.2 – 1 µg/mL) resistance.[3]
- Treatment of high-level resistant TB usually requires discontinuation of INH and, either a more prolonged treatment course, or a greater number of drugs in the continuation phase.
- Some evidence suggests that including INH in the treatment regimens of low-level resistant strains may be acceptable, as resistance can be overcome when high serum concentrations of INH are achieved.[4,5]

METHODS

A retrospective study was conducted on all cases of low-level INH resistant TB in Alberta, Canada. The purpose was to determine whether treatment with conventional INH-containing regimens was associated with a higher rate of treatment failure.

- All cases of low-level INH resistant TB in Alberta between 1992 and 2012 were identified using a provincial TB surveillance database.
- Cases were stratified into two groups based on whether the treatment regimen included INH for the entire duration of therapy or an alternative non-INH containing regimen was used.
- Data on baseline characteristics of the two groups were obtained, including site of disease, sex, age, country of origin, HIV status and previous TB treatment.
- The mean duration of therapy in the two groups was determined.
- Rates of treatment failure were determined for both groups (INH treated vs. non-INH treated). Treatment failure was defined as relapse at one year through passive surveillance.
- Statistical analysis was performed using Chi-square goodness of fit test, or Fisher's exact test.

RESULTS

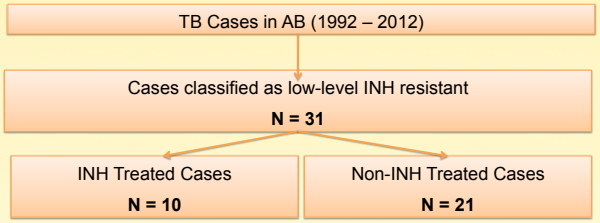

Fig. 1: Stratification of cases of low-level INH resistance based on treatment approach.

Table 1: Baseline Characteristics of Patients with Low-level INH Resistance

	INH Treated	Non-INH Treated	P-value
Site of Disease:			
Respiratory	8	16	
Non-respiratory	2	5	1.00
Sex:			
Male	5	15	
Female	5	6	0.423
Age, mean (range)	40 (26-57)	48 (15-87)	0.251
Country of Origin:			
Canada	2	1	
Aboriginal	1	0	
Foreign Born	7	20	0.087
HIV Positive	2	1	0.237
Previous TB Treatment	2	6	1.00

Table 2: Duration and Outcomes of Treatment in Patients with Low-level INH Resistance

	INH Treated	Non-INH Treated	P-value
Mean duration of therapy, months (SD)	8.5 (2.5)	12.9 (3.9)	0.004
Disease Relapse @ 1 year*	0**	0**	-

*Disease relapse within one year was determined by passive surveillance through the provincial TB services program, which is informed of any positive *M. tuberculosis* culture results in Alberta.
**Minimum one year follow up after completion of TB therapy could not be confirmed for two patients (one in each group) as it could not definitively be determined if they continued to reside in Alberta for that time.

RESULTS CONT'D

DATA COLLECTION:

- 31 total cases of low level INH resistant tuberculosis were identified through the provincial database.
- 10 cases were treated with INH for the entire duration of therapy, and 21 were treated with alternative regimens.

BASELINE CHARACTERISTICS:

- The majority of TB cases identified were classified as pulmonary diseases (80% in INH group and 76% in non-INH group).
- There was no statistically significantly difference between the two groups with respect to sex, age, country of origin (or ethnicity), HIV status and history of previous TB treatment.

STATISTICAL ANALYSIS:

- Mean duration of therapy in the INH group was significantly lower than in the non-INH group ($p = 0.004$).
- No cases of disease relapse were identified through passive surveillance in either group at one year post treatment.

CONCLUSIONS

- First line INH-containing regimens may be used in cases of low-level INH resistant TB.
- Patients who receive INH-containing regimens may be treated with shorter courses of therapy.
- There is no apparent increase in risk of early disease relapse in those receiving INH.
- The study is limited by low numbers and it's retrospective design. Larger prospecitve studies are required to corroborate these findings.

ACKNOWLEDGMENTS

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