

TREATING ISONIAZID MONORESISTANT TB WITH STANDARD FIRST-LINE REGIMENS RESULTS IN HIGH RATES OF TREATMENT FAILURE, TB RECURRENCE AND TB-RELATED DEATH

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Optimal management of tuberculosis resistant to either isoniazid or rifampicin that is not multi-drug resistant (MDR) is poorly defined. In resource-poor settings, patients with isoniazid or rifampicin mono-resistant TB are usually treated with standard first line TB-treatment regimens. Little is known about the long term efficacy of such management. 356 patients from a community hospital in a peri-urban shanty town in Lima, Peru were enrolled after diagnosis of pulmonary TB disease; 309 were new TB cases and 47 were cases of retreatment. Patients were tested for resistance to rifampicin and isoniazid, and those resistant to both drugs (MDR-TB, 21 patients) were excluded. All other patients were followed prospectively throughout treatment and interviewed a median of 5 years after treatment completion for determination of the relationship between isoniazid and rifampicin resistance and failure, recurrence after cure, and long term TB-related death. Overall, 39 of 335 (12%) patients had laboratory-confirmed monoresistant TB at diagnosis; 29 patients (8.7%) had isoniazid monoresistant TB and 10 patients (3.0%) had rifampicin monoresistant TB. Among patients with first episodes of TB disease, 28 (10%) and 5 (1.7%) had isoniazid and rifampicin monoresistance, respectively. All new TB patients received six months of standard short-course chemotherapy and all patients with recurrent TB received nine months of first line drugs under the standard national retreatment scheme. At follow-up, only 55% of isoniazid monoresistant and 50% of rifampicin monoresistant TB patients achieved long-term cure with the standard regimens. In addition to poorer treatment outcome, patients with isoniazid monoresistant TB and rifampicin monoresistant TB at diagnosis suffered significantly higher rates of recurrence after cure and long-term TB-related death compared to patients with sensitive strains ($p < 0.01$ in all cases). In conclusion, monoresistance to rifampicin and particularly isoniazid are relatively common amongst non-MDR TB patients. Long-term morbidity and mortality is high when patients with isoniazid and rifampicin monoresistant TB are treated with standard first line anti-TB regimens. TB therapy should be augmented for patients with isoniazid and rifampicin