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 mono-resistant TB at diagnosis; 29 patients (8.7%) had isoniazid mono-resistant TB and 10 patients (3.0%) had rifampicin mono-resistant 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 mono-resistant and 50% of rifampicin mono-resistant TB patients achieved long-term cure with the standard regimens. In addition to poorer treatment outcome, patients with isoniazid mono-resistant TB and rifampicin mono-resistant 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 mono-resistant TB are treated with standard first line anti-TB regimens. TB therapy should be augmented for patients with isoniazid and rifampicin mono-resistant TB.