Master Thesis

Multidrug-resistant tuberculosis in Manila, Philippines:
- Effect of treatment interruptions on treatment outcomes
- Factors leading to treatment interruptions and default

By Marianne Jost, August 2008

Dissertation submitted as partial fulfilment of the requirements for the degree of
Master in International Health (MIH)

Supervisor from Swiss Tropical Institute, University in Basel:
Bernadette Peterhans, RN, MPH

Advisor from the Tropical Disease Foundation:
Christian Auer, PhD

Abstract

Background

Adherence to and completion of the full course of MDR-TB treatment under direct observation are important to enhance successful treatment outcomes as well as to avoid amplification and spread of resistance to anti-TB drugs. However, frequent interruptions and discontinuation of treatment are common among MDR-TB patients enrolled in the DOTS-Plus programme in Manila, Philippines despite implementing various measures to facilitate adherence. The objectives of this study were: (1) to determine the prevalence and degree of treatment interruptions, (2) to assess the effect of treatment interruptions on adverse treatment outcomes, (3) to identify factors leading to repeated treatment interruptions and default (defined as prolonged treatment interruptions for more than 2 months) and (4) to make recommendations on interventions how to minimize treatment interruptions.

Methods

The first part of the study was quantitative. It included a retrospective review of clinical charts of patients enrolled in the DOTS-Plus programme in Manila from July 2003 until October 2005.
The second part of the study was qualitative. It consisted of 5 focus groups discussions (FGDs) with MDR-TB patients, 3 FGDs with well adherent patients and 2 FGDs with poorly adherent patients, and 4 in-depth interviews with defaulted MDR-TB patients.

Results

Of the 240 patients who were enrolled in the quantitative part of the study, 10.4% of patients were non-adherent to therapy (defined as ≥ 20% missed doses). 75.8% of patients were cured, 12.9% defaulted, 9.6% died and 1.7% failed treatment.
In the multivariate analysis on non-adherence to treatment, no conclusive results were obtained. Alcohol abuse in the past suggested an increased risk for non-adherence (although it did just not reach statistical significance), and treatment at the community-based DOTS centres during the continuation phase did not improve adherence.
In the multivariate analysis on adverse outcomes, high percentage of missed doses (OR=1.13; 95%CI 1.08-1.18; p=<0.001), body weight at baseline below the median (OR=2.82; 95%CI 1.02-7.81; p=0.046) and resistance to a second-line drug (OR=0.30; 95%CI 0.11-0.81; p=0.017) were associated with default. No association was found between adverse drug reactions and adverse

treatment outcome. The intensive phase proved to be most crucial for default; 61% of patients who defaulted discontinued treatment during this period.

In the focus group discussions and interviews, the main reported reasons for interruptions and discontinuation of treatment were: adverse drug reactions, difficult access to clinic, financial burden of TB treatment, lack of family support and dissatisfying patient-provider relationships. The main motivating factors for adherence to and completion of treatment were supportive relationships of patients to health staff, to fellow patients and to family members.

Conclusion

The relatively high cure rate in this study provided encouraging confirmation that successful MDR-TB treatment is possible in a resource-limited setting. However, because of the important public health implications, further efforts are required to improve adherence and facilitate completion of treatment despite the relatively low rate of non-adherence and default. Missed appointments need to be regarded as warning signal that patients might be at risk of defaulting, especially during the intensive phase. Prompt action of the health care team to retain patients on treatment is required.

Our study showed that a combination of factors is interrelated and influences patients' ability to adhere to and complete treatment. Before effective interventions can be developed, it is essential to understand the problems MDR-TB patients face. In this regard, it might be beneficial to assess encouraging and discouraging factors related to adherence through a standardized evaluation at treatment start and on a regular basis while on treatment, so that patients at risk for non-adherence and default could be identified and relevant support be provided. Possible interventions to facilitate adherence and minimize default may include: strengthening social support (including nutritional support), income generating activities, emotional support by health staff (including support for side effects), psychosocial support through patient group discussions, more convenient DOT and improving access to MDR-TB treatment.