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Treatment of MDR/XDR-TB. Where do we stand?

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Principles for treatment of MDR-TB

The generally accepted principles for treatment of MDR-TB patients is: 1) use any first-line agents showing susceptibility; 2) use injectable and quinolones if susceptible; 3) add second-line bacteriostatic agents as needed to make up the five-drug regimen; and 4) treat for two years after culture conversion.¹ Suggested regimens in patients with MDR-TB caused by *M. tuberculosis* resistant to isoniazid, rifampicin, (and streptomycin) are summarized in table 1.

Table 1. Suggested regimens in patients with MDR-TB caused by *M. tuberculosis* resistant to isoniazid, rifampicin, (and streptomycin)

	Year	Regimen	Duration	References/ comments
World Health Organization	2006	<ul style="list-style-type: none"> • Pyrazinamide • Ethambutol • Injectables* • Fluoroquinolones • One or two of group 4 agents[†] 	<ul style="list-style-type: none"> • at least 6 months with injectables (at least 4 months of culture conversion), • At least 18 months after culture conversion 	<ul style="list-style-type: none"> • ²
ATS/CDC/IDSA	2004	<ul style="list-style-type: none"> • Fluoroquinolones • Pyrazinamide • Ethambutol • Injectables* (Alternative agents) 	<ul style="list-style-type: none"> • 18-24 months 	<ul style="list-style-type: none"> • ³, • Consider surgery

Abbreviations: ATS; American Thoracic Society, CDC; Centers for Diseases Control and Prevention

Treatment outcomes of patients with MDR-TB

Treatment outcomes for patients with MDR-TB vary between studies. In a Korean study involving 1011 patients, the cure rate was as low as 48% with a 39% default rate.⁴ However, a 75% long-term success rate was reported for 205 patients in the USA.⁵ Treatment outcomes from recent reports were summarized in table 2. Treatment outcomes from recent reports are summarized in Table 2. Differences in outcomes arise from the varying baseline characteristics of patients, including drug susceptibility patterns, whether the treatment was based on DOT, the presence of comorbidities including HIV status, and so on. Given the different definitions of “cure” and “failure” in the treatment of MDR-TB, the adoption of a common set of definitions is critical, as suggested recently.⁶

Table 2. Treatment outcomes in patients with MDR-TB

Author	Year	Country	Number of patients	Treatment outcomes	Reference
Tahaoglu K et al	2001	Turkey	158	75% of long term success	⁷
Mitnick C et al	2003	Peru	66	83% of probable cure	⁸
Kim HJ et al	2004	South Korea	1011	44% of cure rate	⁴
Chan ED et al	2004	USA	205	85% of initial response 75% of long term success	⁵

The role of surgery in treatment for MDR-TB

After the successful introduction of surgical resection of the diseased lung in patients with refractory MDR-TB, favourable results among patients with MDR-TB ensued. The rates of sputum conversion or of patients who remained negative after surgical resection are as high as 80%–98%. Recently, surgical resection along with drug therapy using new quinolones has been accepted widely as improving the results of treatment for patients with MDR-TB.⁵ However, clinicians should be very cautious when selecting candidates for surgical resection, because it carries considerable complication rates and costs. We recently reported that low body mass index, primary resistance, resistance to ofloxacin, and cavitory lesions beyond the range of resection are possible poor prognostic factors for surgical lung resection in MDR-TB patients.⁹

Extensively drug resistant TB

Because the efficacies of quinolones and injectables in treatment of MDR-TB are well defined, concerns about extensively drug-resistant tuberculosis (XDR-TB), showing resistance to quinolones and injectables in addition to isoniazid and rifampicin, have recently been raised.¹⁰⁻¹² According to the recent survey, including 25 reference laboratories on six continents, 10% of multidrug-resistant tuberculosis (MDR-TB) strains were XDR.¹⁰ In Latvia, 115 patients (19%) had XDR-TB among 605 individuals with MDR-TB who initiated therapy during 2000–2002. Expectedly, treatment outcomes in patients with XDR-TB were poorer than in patients with MDR-TB.¹² Although international attention has been drawn to the emergence of XDR-TB, the data on clinical features including treatment outcomes, especially in non-HIV-infected patients with XDR-TB, is scarce.

Unresolved issues on MDR-TB/ XDR-TB

Although some progress has been made, there are many unresolved and controversial issues in the management of patients with MDR/XDR-TB. How many drugs are needed? For how long should we use injectables? How long should we treat patients after culture conversion? In which patients should we perform surgical resection? Is linezolid helpful for patients with MDR-TB? Could interferon-gamma or *Mycobacterium vaccae* treatments be tried for patients with refractory MDR-TB? How should we treat patients with XDR-TB? To answer these questions, well-designed studies enrolling large number of patients are needed urgently.

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