Comment on: Daily 300 mg dose of linezolid for the treatment of intractable multidrug-resistant and extensively drug-resistant tuberculosis

Wing Wai Yew1, Kwok Chiu Chang2 and Chi Hung Chau1*
1Tuberculosis & Chest Unit, Grantham Hospital, 125 Wong Chuk Hang Road, Aberdeen, Hong Kong, China; 2Tuberculosis & Chest Service, Department of Health, Hong Kong, China

Keywords: dosage, TB, oxazolidinones

*Corresponding author. Tel: +852 2518-2648; E-mail: chau_ch@hotmail.com

Sir,

Koh et al.1 reported the use of 300 mg of linezolid daily for the treatment of intractable drug-resistant tuberculosis. While it is certainly beneficial to reduce the dosage of linezolid and minimize undesirable adverse drug reactions, there are a number of concomitant concerns.

Although the proportion of reported patients with consecutive negative sputum culture taken at least 4 weeks apart appeared high (92%), the actual cure rate would be likely to be much lower,1 as suggested by a previous report.2 Even if there were cures, it might be difficult to attribute them to treatment with 300 mg of linezolid daily. Important confounders included accompanying drugs used, alongside their dosages and scheduling (especially for moxifloxacin/levofloxacin), as well as recourse to surgical resection. Furthermore, the peak serum levels of linezolid did not appear to correlate well with the reported outcomes.1 While linezolid can achieve a good concentration in epithelial lining fluid in human volunteers,3 this might not be so in the presence of sequestered pulmonary tuberculosis with sizeable thick-walled cavities.

Resistances to linezolid among Mycobacterium tuberculosis isolates is emerging in various parts of the world.4,5 It is indeed a pressing issue to delineate the optimal dosage and scheduling of linezolid in the treatment of difficult drug-resistant tuberculosis, through balancing efficacy, suppression of drug resistance, tolerance and toxicity of the oxazolidinone.6 It would be very important to follow-up on the susceptibility of the M. tuberculosis isolates harboured by those patients reported by Koh et al.1 who failed to achieve cure after antituberculosis chemotherapy.

Transparency declarations

None to declare.

References


Sir,

The valuable comments of Yew et al.1 on our article2 are appreciated. We agree with their views on many points. There were possible confounders, such as accompanying drugs used. However, our cases were very ‘difficult’ drug-resistant tuberculosis (TB) cases as they had many aspects, such as previous treatment history and extent of drug resistance. As of June 2009, among the 24 patients, treatment was completed with a ‘cure’ outcome in 6 more patients.2 In addition, in previous studies on various doses of linezolid,3–6 linezolid was used in combination with other drugs. Its clinical efficacy therefore was not directly demonstrable. Thus, further prospective randomized studies may be needed to address this issue.