

LETTERS

Risk of tuberculosis in close contacts of patients with multidrug resistant tuberculosis: a nationwide cohort

Data on the efficacy of drugs for preventing multiple drug resistant tuberculosis (MDR-TB) in people at risk after close contact with patients is lacking. In a systematic review, we found only two small cohort studies that addressed this question.¹ The aim of the present study was to describe the incidence of MDR-TB disease in people who were in close contact with patients with pulmonary MDR-TB, and to compare the incidence in people that were offered prophylaxis to those that were not (see online appendix).

Patients with MDR-TB were identified by inspecting the records of patients that were referred to the nine designated TB centres in Israel; records of the national referral laboratory and the central registry held by the Ministry of Health from 1998 to the end of 2006. Patients with MDR-TB diagnosed from 1998 to 2003 were defined as cases (patients). For each patient, we extracted demographic and clinical data, and data on close contacts. For each contact, demographic and clinical data, and whether they were advised to take prophylaxis, were recorded. Israel has no guidelines for prophylaxis in close contacts of patients with MDR-TB, and the decision is at the discretion of the treating physician.

The list of close contacts was matched to the list of MDR-TB patients (years 1998–2006) according to the Israeli national ID number, and by family name. Follow-up for contacts was defined as the interval from the initial interview to the end of 2006. The study was approved by the research ethics committee of Rabin Medical Centre.

During 1998–2003, 78 patients with pulmonary MDR-TB were newly diagnosed in

Israel (table 1). A total number of 476 close contacts were identified (mean of 6 contacts per patients, median 4, range 1–47; median age of contacts 29 years, range 2–87). The median values of their tuberculin skin reaction was 10 mm (range 0–36) and 245 had a skin reaction ≥ 10 mm. Median follow-up for contacts was 6 years (range 3–8), a total of 2666 person-years. Twelve contacts were offered treatment with a tailored regimen (mainly ciprofloxacin and pyrazinamide), all of them with a positive tuberculin skin reaction; 71 were given isoniazid, six other treatments and 387 were not offered treatment.

No cases of MDR-TB were detected in the contacts during the follow-up period (0% of 476 patients, 95% confidence interval (CI) 0.0% to 0.7%; in incidence density terms, 0 cases during 2666 person years, 95% CI 0.0 to 1.0 cases per 1000 person years).

These low values are compatible with the observation that resistant strains are less likely to result in secondary cases.² However, the data were obtained in a location with an overall low prevalence and incidence of TB, and where an effective (and resource consuming) national programme for detection of patients and contacts, directly observed treatment, follow-up and isolation of culture positive patients is in place. In locations with a high prevalence of TB and no such programme, rates as high as 8% were described in contacts of MDR-TB patients.³

Regimens recommended for treating latent TB in contacts of MDR-TB patients are associated with toxicity.⁴ Our results support a policy of no treatment, close observation of MDR-TB close contacts in settings similar to the one we describe.

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Aminoglycoside ototoxicity susceptibility in cystic fibrosis

Ototoxicity is a recognised dose-related complication of aminoglycoside antibiotics.

Predisposition to these ototoxic effects, even when levels are within the therapeutic range, is associated with an inherited mitochondrial DNA mutation known as m.1555A>G.^{1,2}

We report a case of a 22-year-old woman with cystic fibrosis (CF), genotype delta F508 homozygous, with bilateral high frequency hearing loss. This was discovered when an audiogram (not previously performed) was requested for routine screening by our centre before commencement of nebulised TOBI (preservative-free pH-adjusted preparation of tobramycin for inhalation).

She had a history of diabetes mellitus, exocrine pancreatic insufficiency and developed chronic *Pseudomonas aeruginosa* infection when aged 5 years. She had received regular intravenous antibiotics at both paediatric and adult CF centres, which usually included a β -lactam and an aminoglycoside. Since transfer to the adult centre at the age of 18, she had received an average of three courses of antibiotics per year, predominantly tobramycin and ceftazidime. There were no risk factors for noise-induced hearing loss. Current medication included oral azithromycin, nebulised dornase alfa and TOBI.

Although the patient did not complain of hearing loss, the audiogram showed that the hearing threshold was reduced 3–8 kHz (fig 1) with normal middle ear pressures. This is consistent with hearing loss associated with aminoglycoside toxicity.

As a consequence of this result, she underwent DNA testing for the deafness mutation m.1555A>G and was found to be positive heteroplasmic (intermediate 30–70%). There is no family history of hearing impairment although, as far as we are aware, her relatives have not received intravenous aminoglycosides. The genetic report did comment that her surname was known and that she may belong to a family known to have m.1555A>G.

We now plan to avoid intravenous aminoglycosides in this patient and perform surveillance audiograms while she continues on nebulised TOBI.

To our knowledge, this is the first report of a patient with CF with this mitochondrial

Table 1 Characteristics of 78 patients with MDR-TB

Characteristic	
Women	25 (32)
Age (years)	39 (15–93)
Place of birth	
Former USSR	58 (74)
Ethiopia	9 (12)
Israel	2 (3)
Other	9 (12)
Years since emigrated to Israel	3.5 (0–65)
TB in the past*	36 (46)
Treated for TB in the past*	27 (35)
IV drug abuse	9 (12)
HIV positive	6 (8)
No of contacts	4 (1–47)

Categorical values are given as number (%) and continuous data as median (range).

MDR-TB, multiple drug resistant tuberculosis.