Some Healthy Skepticism about Inhaled Therapy for Tuberculosis

Str—We certainly are far from determining optimal management of pulmonary tuberculosis. Multidrug treatment of 6 months’ duration is required to achieve predictable cures for drug-susceptible disease [1], and re-treatment regimens of 18–24 months’ duration, perhaps accompanied by resectional surgery, are required to control multidrug-resistant disease [2]. Therefore, the report by Sacks et al. [3] on the use of adjunctive treatment with inhaled aminoglycosides for patients who have pulmonary tuberculosis and sputum smear results and cultures that are persistently positive for Mycobacterium tuberculosis is of potentially great importance.

However, the article by Sacks et al. [3] left several critical issues unanswered and potentially may be profoundly misleading. The article addressed 2 groups of patients: patients with drug-susceptible disease who had delayed conversion of positive sputum smear and culture results to negative status, and a separate group of patients with drug-resistant tuberculosis who had sputum smear and culture results that remained positive “despite ≥2 months of optimal systemic therapy.”

Regarding the first group of patients with drug-susceptible disease, it is well recognized that a small proportion of patients with extensive pulmonary disease are slow to achieve negative culture results while they are receiving chemotherapy. The most important implication of this finding is the requirement for an extended duration of treatment [1]. There is no evidence to suggest that slow conversion is associated with an increased risk for transmission, treatment failure, or acquired drug resistance so long as appropriate chemotherapy is maintained. Therefore, it is difficult to justify the disruption of patients’ lives and the expenses that are associated with treatment with inhaled aminoglycosides. In addition, although it is interesting that inhaled therapy seemed to result in rapid conversion, one cannot determine whether this therapy “simply” helped sterilize the secretions in the Airways or whether it actually affected the populations of mycobacteria in the walls of the cavity (or cavities). If such therapy achieves the former (but not the latter) effect, patients would have an increased risk for reactivation of disease if treatment were abandoned prematurely.

More confusing is the role of inhaled aminoglycoside therapy in patients with drug-resistant tuberculosis. It is not clear from this article whether inhaled therapy was the only variable that was associated with the reported improvement in these patients. Sacks et al. [3] described standard protocols for the treatment of patients with drug-resistant tuberculosis, but they did not stipulate which or how many active drugs the patients were receiving. Frankly, it is counterintuitive to think that inhaling gentamicin, a drug with very marginal activity against M. tuberculosis, would have a substantial effect against chronic cavitary tuberculosis.

We have cared for a substantial number of patients with multidrug-resistant tuberculosis during the past 20 years. We have performed ventilation-perfusion lung scans on several hundred such individuals while evaluating them for potential resectional surgery. A striking and consistent finding is the absence of ventilation (as marked by the failure of inhaled xenon to reach the area) in regions with chronic cavitary tuberculosis involvement. Therefore, it is quite implausible that inhaled aminoglycosides would be deposited in such lesions in concentrations that would be sufficient enough to exert real killing of mycobacteria.

I believe that the critical question is whether the inhaled therapy truly resulted in long-term, durable improvement for these patients or, rather, transient, “cosmetic” improvement in their sputum status. The authors imply that the former is true, but without clearer evidence, one must remain quite skeptical.

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References


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