

Statin Adjunctive Therapy for Tuberculosis Treatment

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With great interest we read the recently published article of Hennessy and colleagues on the effects of statins, which may be beneficial in the treatment of infectious diseases by reducing inflammation, modulating the immune system, and having antimicrobial effects (1). Hennessy et al. included the effect of statins on the intracellular growth of *Mycobacterium tuberculosis*. This is of great importance because one of the main problems in ending the tuberculosis (TB) epidemic is the long duration of treatment. It takes at least 6 months to treat drug-sensitive TB, and treatment duration for multidrug-resistant TB takes from 9 months to 2 years. Therefore, research focuses on strategies that offer a solution for eradication of dormant *Mycobacterium tuberculosis* bacilli that do not respond to most of the anti-TB drugs (2). Studies have shown that statins are able to reduce bacterial growth (3) and, moreover, to shorten TB treatment in mice (4). Results showed that simvastatin on top of isoniazid, rifampin, and pyrazinamide reduces the time to culture conversion in lung tissue. Dutta and coworkers concluded that, as with any other host-directed therapy, a prospective clinical trial is needed to show the beneficial effects of simvastatin (4).

Hennessy and colleagues pointed out that rifampin may interact with statins by inducing cytochrome P450 enzymes (1). Therefore, the translation of the effect observed in mice to humans may be difficult and would require additional studies. However, the drug-drug interaction between rifampin and simvastatin is already known (5). Perhaps it would have been better initially to select a statin that has no drug-drug interaction with rifampin. Statins like pravastatin and rosuvastatin show no drug-drug interaction, but more important is the drug-drug interaction with isoniazid, which was not mentioned. The combination of isoniazid and simvastatin may increase the risk of myopathy and rhabdomyolysis. Although TB treatment in combination with simvastatin may be shorter than 6 months, the duration of coadministration of these two drugs may increase the risk of these adverse events considerably. To avoid adverse drug events in patients with TB is of particular importance, as it is related to nonadherence and unsuccessful treatment (6, 7). We therefore suggest including not only efficacy parameters but also creatine kinase levels to monitor effects on muscle tissue in both clinical and preclinical studies. Moreover, we suggest in future experiments including statins that lack drug-drug interactions with the current first-line drugs. This enables an easier translation to human studies, reduces costs (as additional experiments are not needed), and eventually may help

to make the new host-directed adjunctive TB therapy available earlier for daily practice.

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