Statins Increase Rifampin Mycobactericidal Effect.

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Introduction: Mycobacterium leprae and Mycobacterium tuberculosis antimicrobial resistance has been followed with great concern during the last years, while the need for new drugs able to control leprosy and tuberculosis, mainly due to XDR-TB, is pressing. Our group has recently described that M. leprae is able to induce lipid body biogenesis and cholesterol accumulation in macrophages and Schwann cells, facilitating its viability and replication. Considering these previous results, we investigated the efficacy of two statins on the intracellular viability of mycobacteria within the macrophage, and atorvastatin effect on BALB/c mice during M. leprae infection. Material and Methods: Macrophage cultures infected with viable M. leprae, M. bovis (BCG) or M. tuberculosis were treated with atorvastatin or simvastatin during 72 h or one week. Analysis of the viability of mycobacteria was carried out by real-time PCR (M. leprae) and CFU counting (M. tuberculosis and M. bovis). BalbC mice were infected with M. leprae following Sheppard’s model and treated with atorvastatin during 5 months before footpad harvest to determine the bacillary count. Furthermore, the cytotoxicity of different statins doses and rifampin associations were checked by MTT assays and seric transaminase activity in cells and mice, respectively. Results and Discussion: We observed that intracellular mycobacteria viability markedly decreased after incubation with both statins, but atorvastatin showed the best inhibitory effect when combined with rifampin. Using Shepard’s model we observed atorvastatin efficacy in control M. leprae and inflammatory infiltrate in the BALB/c footpad, in a serum cholesterol level dependent way. Conclusions: Statins contribute to macrophage-bactericidal activity against M. bovis, M. leprae and M. tuberculosis. It is likely that statins association with the actual multidrug therapy could effectively reduce mycobacteria viability and tissue lesion in leprosy and tuberculosis patients, although epidemiological studies are still needed for confirmation.

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