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O0495 Can minocycline add activity to treatment regimens for non-tuberculous mycobacterial disease?

Jasper Sangen*[1], Mike Marvin Ruth[1], Sanne Zweijpfenning[2], Wouter Hoefsloot[2], Lian Pennings[1], Heiman Wertheim[1], Jakko Van Ingen[1]

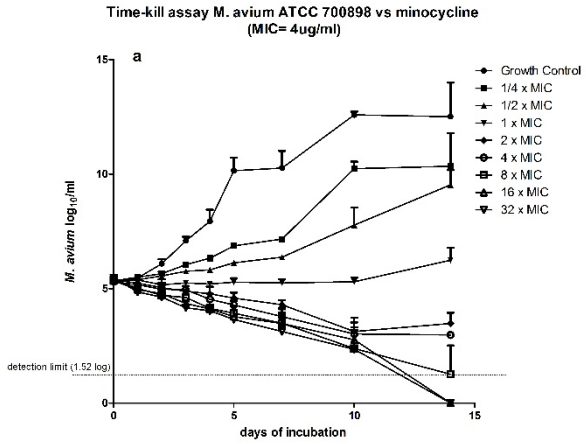
[1]Radboud university medical center, Medical Microbiology, Nijmegen, Netherlands, *[2]Radboud university medical center, Pulmonary Diseases, Nijmegen, Netherlands*

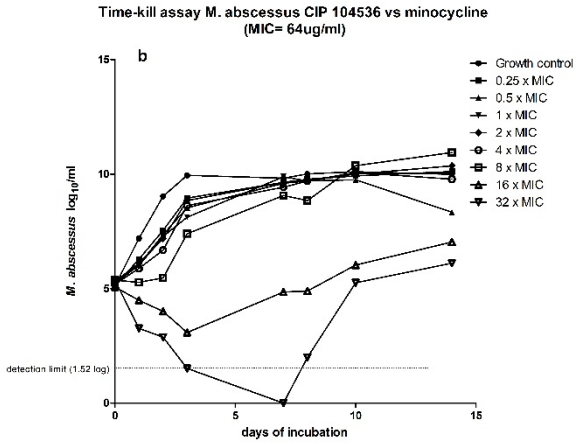
Background: Nontuberculous mycobacteria cause difficult to treat opportunistic infections in humans. New antibiotic treatment regimens are urgently needed. Therefore, we aim to explore the potential role of minocycline in the treatment of infections caused by *Mycobacterium abscessus* or Mycobacterium avium complex (MAC).

Materials/methods: The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of minocycline against clinical and reference strains of *M. abscessus* and *Mycobacterium avium* were determined by broth microdilution according to CLSI guidelines. Synergistic activities with established anti-mycobacterial drugs were determined using checkerboard titrations. To study pharmacodynamics, minocycline time-kill assays were performed against *M. abscessus* and *M. avium*.

Results: *M. abscessus* is less susceptible to minocycline (median MIC 64 mg/L) than MAC bacteria (median MIC 4 mg/L). Minocycline is bacteriostatic against both *M. abscessus* (MBC/MIC ratio >8) and *M. avium* (MBC/MIC = 8). Minocycline showed no synergy with established anti-mycobacterial drugs against *M. abscessus*. Synergy was found between minocycline and ethambutol against *M. avium*. Minocycline displayed significant concentration-dependent activity against *M. avium*; its activity against *M. abscessus* was rapidly abrogated by the emergence of resistance (Figure).

Conclusions: Minocycline alone is inactive against *M. abscessus* but moderately active against MAC. No synergy is seen between minocycline and established anti-mycobacterial drugs against *M. abscessus.* Therefore, the place of minocycline in currently recommended regimens for *M. abscessus* treatment needs to be reconsidered. In contrast, the MIC results and synergy seen between minocycline and established anti *M. avium* drugs warrants new studies investigating the potential role of minocycline in the treatment of MAC disease. A hollow-fiber model to confirm these findings is ongoing.


Time-kill assay M. avium ATCC 700898 vs minocycline
(MIC= 4ug/ml)
a
Growth Control
1/4 x MIC
1/2 x MIC
1 x MIC
2 x MIC
4 x MIC
8 x MIC
16 x MIC
32 x MIC
M. avium log10/ml
detection limit (1.52 log)
days of incubation


Time-kill assay M. abscessus CIP 104536 vs minocycline
(MIC= 64ug/ml)
b
Growth control
0.25 x MIC
0.5 x MIC
1 x MIC
2 x MIC
4 x MIC
8 x MIC
16 x MIC
32 x MIC
M. abscessus log10/ml
detection limit (1.52 log)
days of incubation