

## **Publication**

A prospective, open-label, randomized trial of doxycycline versus azithromycin for the treatment of uncomplicated murine typhus

## JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

**ID** 4499537

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Year 2019

**Title** A prospective, open-label, randomized trial of doxycycline versus azithromycin for the treatment of uncomplicated murine typhus

Journal Clinical Infectious Diseases

Volume 68 Number 5

Pages / Article-Number 738-747

Murine typhus, or infection with Rickettsia typhi, is a global but neglected disease without randomized clinical trials to guide antibiotic therapy.; A prospective, open, randomized trial was conducted in nonpregnant, consenting inpatient adults with rapid diagnostic test evidence of uncomplicated murine typhus at 2 hospitals in Vientiane, Laos. Patients were randomized to 7 days (D7) or 3 days (D3) of oral doxycycline or 3 days of oral azithromycin (A3). Primary outcome measures were fever clearance time and frequencies of treatment failure and relapse.; Between 2004 and 2009, the study enrolled 216 patients (72 per arm); 158 (73.2%) had serology/polymerase chain reaction (PCR)-confirmed murine typhus, and 52 (24.1%) were R. typhi PCR positive. The risk of treatment failure was greater for regimen A3 (22.5%; 16 of 71 patients) than for D3 (4.2%; 3 of 71) or D7 (1.4%; 1 of 71) (P <.001). Among R. typhi PCR-positive patients, the area under the time-temperature curve and the fever clearance time were significantly higher for A3 than for D3 (1.8- and 1.9-fold higher, respectively; P = .005) and D7 (1.5and 1.6-fold higher; P = .02). No patients returned with PCR-confirmed R. typhi relapse.; In Lao adults, azithromycin is inferior to doxycycline as oral therapy for uncomplicated murine typhus. For doxycycline, 3- and 7-day regimens have similar efficacy. Azithromycin use in murine typhus should be reconsidered. Investigation of genomic and phenotypic markers of R. typhi azithromycin resistance is needed.; ISRCTN47812566.

Publisher Oxford University Press ISSN/ISBN 1058-4838 ; 1537-6591 edoc-URL https://edoc.unibas.ch/69662/

Full Text on edoc Available;

Digital Object Identifier DOI 10.1093/cid/ciy563

PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/30020447

ISI-Number MEDLINE:30020447

Document type (ISI) Journal Article