Antibiotic treatment for 6 days versus 12 days in patients with severe cellulitis: a multicentre randomised, double-blind, placebo-controlled, non-inferiority trial

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Background: The recommended antibiotic treatment duration for patients hospitalized with cellulitis is 10-14 days, but this is mainly based on expert recommendation. We investigated whether 6 days of antibiotic treatment is non-inferior to 12 days in patients hospitalized with cellulitis.

Materials/methods: In this randomised, double-blind, placebo-controlled non-inferiority trial, we enrolled in 11 Dutch hospitals adult patients admitted with cellulitis and treated with intravenous flucloxacillin, with optional oral step-down. At day 6 participants who had improved substantially (defined as being afebrile, and having a lower cellulitis severity score) were randomised between additional 6 days of oral flucloxacillin or placebo. Randomisation was stratified by diabetes status and hospital. The primary outcome was cure by day 14 without relapse by day 28. Secondary outcomes included a modified cure assessment and the relapse rate by day 90. The trial was stopped early because of slow recruitment. This trial is registered on ClinicalTrials.gov (NCT02032654).

Results: Between August 26, 2014, and June 29, 2017, 151 of 248 included participants had sufficiently improved at day 6 to be randomised: 77 were allocated to receive 12 days of flucloxacillin, and 74 to receive 6 days of flucloxacillin. In the intention-to-treat analysis 71 and 69 participants, respectively, who took at least one dose of study drug were analyzed. Mean age was 63, 66% was male, 24% had diabetes. After 28 days, 35/71 (49.3%) of participants in the 12-day group and 35/69 (50.7%) in the 6-day group were cured without relapse by day 28 (absolute risk reduction 1.4 percentage points, 95% CI: -14.8 to 17.5). With the modified cure assessment, 53/71 (74.6%) and 49/69 (71.0%) participants in the 12-day and 6-day groups, respectively, were cured without relapse after 28 days (absolute risk reduction of -3.6, 95% CI: -18.1 to 11). After initial cure without relapse, day 90 relapse rates are higher in the 6-day group than in the 12-day group (Figure).
Conclusions: Six days of antibiotic treatment appeared on the short term to be as effective as 12 days of antibiotic treatment. However, patients with a short course of therapy showed significantly faster and more frequent relapses by day 90.

Log rank test
\( p = 0.04 \)