SHORT REPORT: Q FEVER PNEUMONIA: ARE CLARITHROMYCIN AND MOXIFLOXACIN ALTERNATIVE TREATMENTS ONLY?

MIRO MOROVIC*
Department for Infectious Diseases, Zadar General Hospital, Zadar, Croatia

Abstract. Medical records of 77 patients with Q fever pneumonia that was serologically confirmed by enzyme-linked immunosorbent assay were studied to compare the clinical efficacy of doxycycline, clarithromycin, and moxifloxacin. The mean times to defervescence were 2.4 days for those receiving doxycycline, 1.9 days for those receiving clarithromycin, and 2.2 days for those receiving moxifloxacin. There were no interruptions of the regimens in any groups because of side effects, and outcome was favorable in all patients with no complications or relapses during follow-up. This efficacy of clarithromycin and moxifloxacin, together with their safety profiles, suggest that these alternative agents in the treatment of Q fever pneumonia could also be used as the first-line therapy.

For more than two decades doxycycline has remained the preferred antibiotic in the treatment of Q fever pneumonia.1 Alternative treatments include macrolides or fluoroquinolones,2,3 agents often recommended in recent international guidelines for patients with community-acquired pneumonia.5,6 The bacteriostatic activity of these agents against Coxiella burnetii was demonstrated in studies in vitro.7–10 However, clinical responsiveness of C. burnetii to a newer macrolide, clarithromycin, was assessed in only one relevant study11; the efficacy of moxifloxacin, a new fluoroquinolone compound, was not clinically evaluated.

Adequate alternative treatment is of particular importance in areas where Q fever is endemic and when other causes of atypical pneumonia are expected. In this preliminary nonrandomized study, the comparative efficacy of clarithromycin, moxifloxacin, and doxycycline in the treatment of Q fever pneumonia has been evaluated.

Q fever is a well-known zoonosis in Dalmatia, in the coastal region of Croatia.12 In the Zadar region in northern Dalmatia, two outbreaks of serologically confirmed Q fever pneumonia involved 117 hospitalized patients from January to May in both 2003 and 2004.

Medical records for 77 of the 117 patients treated with monotherapy with doxycycline, clarithromycin, or moxifloxacin were analyzed (the other 40 patients were excluded because they received combined therapy, usually with β-lactams. Doxycycline was administered at a dose of 100 mg, twice a day, clarithromycin at a dose of 500 mg, twice a day, and moxifloxacin at a dose of 400 mg, once a day. The medical records were reviewed for clinical features, antibiotic regimens, and outcomes. All patients were given relevant information regarding their therapy before signing general consent required by law on hospitalization; institutional review is not needed for retrospective chart reviews.

The serologic diagnosis of Q fever was conducted at the University Hospital for Infectious Diseases in Zagreb using an enzyme-linked immunosorbent assay (Virion-Serion, Wurzburg, Germany). Phase 2 IgM antibodies and phase 1 IgG and IgA antibodies to C. burnetii were detected by comparing the absorbance value of unknown samples with that of the cut-off control value. The diagnosis of acute Q fever was confirmed by seroconversion and/or significant increases (more than double) in the antibody titer; borderline values for phase 2 IgG antibodies were 20–30 units/mL. The regimens were compared by a two-tailed independent samples t-test.

Sixty-six (85.7%) of the patients were men and 11 (14.3%) were women. Their mean age was 35.7 years (range = 11–66). Fifty (64.9%) worked in rural areas with high densities of sheep and during the main lambing season, i.e., January to May. The most common (71.4%) radiographic abnormalities were unilateral single opacities.

A comparison of the efficacy of doxycycline, clarithromycin, and moxifloxacin in 77 Q fever patients is shown in Table 1. The mean time to defervescence was 2.4 days for doxycycline, 1.9 days for clarithromycin and 2.2 days for moxifloxacin. There were no statistically significant differences between the regimens. The outcome was favorable in all patients, with no complications or relapses during the follow-up period.

In vitro studies have shown that doxycycline, various fluoroquinolones, macrolides, co-trimoxazole, rifampicin, and linezolid have bacteriostatic activity against C. burnetii.5–10,13 These agents inhibit bacterial multiplication and subsequently allow the immune system to control the infectious process. However, the clinical efficacy of a specific antibiotic is difficult to evaluate because acute Q fever is usually a self-limited disease, and the diagnosis could be confirmed almost exclusively by serologic tests. Therefore, some studies have shown different, even contradictory, results.14 Doxycycline has been the first-line therapy for Q fever pneumonia for many years, whereas fluoroquinolones and macrolides have been more recently used as alternative treatments.2,3,14

This appears to be the first study to assess the comparative efficacy of doxycycline and the newer members of the macrolide and fluoroquinolone families, clarithromycin and moxifloxacin. In this study, the clinical response to clarithromycin and moxifloxacin, in terms of days to apyrexia, was better than that to doxycycline, although the difference was not sta-

<table>
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<tr>
<th>Antibiotic</th>
<th>No. (%) of patients</th>
<th>Mean ± SD days to defervescence</th>
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<tbody>
<tr>
<td>Doxycycline</td>
<td>20 (26.0)</td>
<td>2.4 ± 1.1</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>32 (41.5)</td>
<td>1.9 ± 0.92</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>25 (32.5)</td>
<td>2.2 ± 0.92</td>
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</tbody>
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* Differences are not statistically significant.
tistically significant. A similar effect with doxycycline was previously reported, but the efficacy of clarithromycin was shown to be higher.\textsuperscript{11}

The efficacy of clarithromycin and moxifloxacin, together with their safety profiles, suggest that these alternative agents could be used as the first-line treatment for Q fever pneumonia, particularly in areas endemic for Q fever, such as Dalmatia, or when atypical agents could cause community-acquired pneumonia. Further prospective studies will clarify the usefulness of clarithromycin and moxifloxacin in the treatment of Q fever pneumonia.

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Author’s address: Miro Morovic, Department for Infectious Diseases, Zadar General Hospital, Boze Periciça 5, 23000 Zadar, Croatia, E-mail: miro.morovic@zd.t-com.hr.

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