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Treatment of chronic Q fever: data from a nationwide cohort study

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Background: It is advised to treat chronic Q fever patients with tetracyclines and hydroxychloroquine for at least 18 months, but evidence on effectivity is scarce and side effects occur frequently. We compared outcomes of different antibiotic strategies.

Material/methods: We used data from the Dutch national chronic Q fever database and performed a time-dependent Cox proportional hazards analysis, to compare efficacy of tetracycline (TET) plus quinolones (QNL) with or without hydroxychloroquine (HCQ), QNL alone and TET alone in patients with proven or probable chronic Q fever. Treatment with TET plus HCQ (without QNL) was the reference category. Outcomes were overall mortality and therapy failure (defined as a new complication >6 weeks after initiation of treatment, new positive PCR after having been negative for >3 months, PCR-positivity persisting >6 months during treatment or chronic Q fever-related mortality). To account for delay in the effect of antibiotics, we used a lagtime of four weeks.

Results: We evaluated 276 patients that received antibiotic treatment for proven (n = 227, 82%) or probable (n = 49, 18%) chronic Q fever. Mean treatment duration was 2.0 (SD1.4) years. TET plus HCQ was most frequently prescribed (n=254, 92%), while 160 patients (58%) used multiple regimens consecutively (*figure 1*). Events occurring during the studied treatment strategies are described in *table 1*. Compared to TET plus HCQ, treatment with TET plus QNL (n=71, 26%) was associated with a lower hazard for overall mortality (HR0.27, 95%CI 0.13–0.58, p<0.001) and therapy failure (HR0.40, 95%CI 0.22–0.71, p<0.01). Treatment with QNL alone (n=93, 34%) was associated with a lower hazard for therapy failure (HR0.36, 95%CI 0.21–0.62, p=<0.001) but not for overall mortality (HR0.53, 95%CI 0.27–1.07, p=0.09). QNL alone and TET alone were frequently discontinued due to subjective insufficient clinical response. (n=27, 29% and n=32, 59%). TET plus QNL and TET plus HCQ were most frequently discontinued due to side effects (n = 24, 34% and n=110, 43%).

Conclusions: Treatment of chronic Q fever with TET plus QNL appears to be a safe alternative for TET plus HCQ. Definite conclusions on safety of QNL alone and TET alone cannot be drawn due to potential confounding by indication. However, frequent alterations of these treatment strategies because of insufficient clinical response, suggest insufficient effectivity.

Table 1. Treatment strategy at moment of occurrence of events

	TET/HCQ	TET/QNL	TET	QNL
N (%)	254(92)	71(26)	54(20)	93(34)
Overall mortality (%)	27(11)	8(11)	3(6)	13(14)
Chronic Q fever-related mortality (%)	22(9)	5(7)	3(6)	10(11)
Complications (%)	34(13)	11(15)	5(9)	12(13)
Therapy failure (%)	61(24)	12(17)	9(17)	21(23)

Figure 1. Individual treatment timelines for proven or probable chronic Q fever patients

