



Macrolides or fluoroquinolones as enteral antibiotic therapy for non-ICU legionellosis

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While legionellosis incidence has increased in Europe, up to 21% from 2012 to 2016 [1], the choice between fluoroquinolones or macrolides as first-line antibiotic therapy remains controversial. Indeed, a meta-analysis of 2014 [2] included 12 studies with some favoring fluoroquinolones and some macrolides, with a 0.5 mortality odds ratio for fluoroquinolones, but it was not significant. Length of stay (LOS) was shorter. In a recent study [3], which is the biggest series (446 legionellosis), no difference was found for mortality, LOS, and duration of fever. Herein we report the results of our cohort of patients presenting with legionellosis treated according to our internal guideline advising enteral macrolide since April 2008. Roxithromycin was selected among macrolide, for which there is no parenteral form (Table 1).

Data of all patients hospitalized in our infectious diseases department are incorporated since July 2005 in a medical dashboard integrating 28 parameters including the diagnosis, pneumonia severity index (PSI), the length of stay and the outcome [4]. The diagnosis of legionellosis was made based on the ECDC's criteria [5]. Exclusion criteria were prior care in intensive care unit (ICU) and nosocomial cases. Patients were separated into three groups according to their antibiotic therapy: single treatment by macrolides, single treatment by fluoroquinolones, and by other means (combination therapy and/or successive courses). We defined the failure of treatment by ICU requirement or death.

From July 2005 to June 2018, out of the 118 cases of legionellosis which fulfilled the inclusion criteria: 55 (47%) were treated by enteral macrolides (40 roxithromycin, 12 clarithromycin), 39 (33%) by enteral fluoroquinolones (22 ofloxacin, 8 ciprofloxacin, 5 levofloxacin) and 24 (20%) were treated by other means. Mean PSI was 83 ± 33 , 80 ± 30 and 88 ± 29 , respectively (p not significant). According to

PSI ≥ 4 , 44 (37%) patients presented with a severe form of legionellosis, among which 21 were treated by macrolides, 12 were treated by fluoroquinolone and 11 by other means.

The length of stay in our department, after exclusion or treatment failure, was shorter in the macrolide group compared to the fluoroquinolone ones: 6.8 days vs 9.1 days, respectively, $p=0,047$. Regarding the outcome, we had 12 (10.1%) failures of treatment: eight transfers in ICU and four deaths; 4/55 (7.1%) failures among which one death occurred using macrolides, 4/39 (10.3%) among which one death occurred using fluoroquinolones and 4/11 (16.6%) among which two deaths occurred using other means (p not significant). In the subgroup of severe forms, we had three failures (14%) in the macrolide group and four (33%) in the fluoroquinolone group.

This cohort study showed a similar rate of favorable outcome between macrolide and fluoroquinolone enteral therapy for legionellosis outside ICU. This result agrees with the recent Garcia-Vidal et al.'s study [3] which examined azithromycin vs levofloxacin administered parenterally, for 3–6 days. In our study, all the drugs were administrated orally. As the current antimicrobial stewardship policy is to limit both fluoroquinolone use and unnecessary parenteral therapy, our results argue about the use of enteral macrolide for legionellosis outside ICU. Oral doxycycline is also mentioned by some authors in the second intention.

In France, no ethical approval is required for a non-interventional study categorized “hors loi Jardé”. The medical dashboard of the Infectious Diseases Department of Nice university hospital is authorized by the French National Commission on Informatics and Liberty (number of registration: 1430722). A written signed consent form was used for each patient to allow the use of the clinical data recorded during current care in our university hospital.

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Table 1 Comparison of patients according to antibiotic treatment for legionellosis

	Macrolides <i>n</i> = 55 (47%)	Fluoroquinolones <i>n</i> = 39 (33%)	<i>p</i>	Other antibiotic therapies <i>n</i> = 24 (20%)
Mean age (years)	60	62	0.71	61
Men (%)	41 (75)	25 (64)	0.55	17 (70)
Comorbidity				
Cardiovascular	15 (27)	11 (28)	0.29	13 (54)
Respiratory	21 (38)	8 (21)	0.12	10 (42)
Neurologic	5 (9)	5 (13)	0.52	1 (4)
Cancer	1 (2)	1 (3)	0.32	2 (8)
Hepatobiliary	9 (16)	11 (28)	0.36	6 (25)
Diabetes	8 (14)	2 (5)	0.16	5 (21)
Renal	8 (14)	1 (3)	0.09	1 (4)
Mean PSI	83	80	0.69	88
Failure of treatment	4 (7.1%)	4 (10.3%)	0.46	4 (16.6%)
Length of stay (days)	6.8	9.1	<u>0.047</u>	8.9
Death	1 (1.8%)	1 (2.5%)	ns	2 (8.3%)

Compliance with ethical standards

Conflict of interest None.

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