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ARTICLE

Genital *Mycoplasma* infections and their resistance phenotypes in an African setting

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Abstract We investigated the antimicrobial susceptibilities of mycoplasmas in Gabonese men and women. A total of 1,332 men and women were included in the study. Sperm, urine, ureteral or vaginal swabs were collected from the subjects. Mycoplasmas identification and antimicrobial susceptibility to azithromycin, clarithromycin, erythromycin, josamycin, pristinamycin, doxycycline, tetracycline, ofloxacin and ciprofloxacin were tested using the *Mycoplasma* IST 2 kit. 794 subjects were positive for *Mycoplasma*. Respectively, 1.6 % and 82.24 % of subjects were singly infected with *M. hominis* and *Ureaplasma urealyticum* and 15.87 % had a mixed infection. *M. hominis* isolates were resistant to erythromycin and had an intermediate (I) to resistant (R) profile to azithromycin and clarithromycin. 84.6 % of *M. hominis* strains were sensitive (S) to josamycin and pristinamycin. 30.8 % and 92.3 % of *M. hominis* strains were sensitive to tetracycline and doxycycline, respectively. 76.9 and 84.6 % of *M. hominis* isolates were sensitive to ciprofloxacin and ofloxacin, respectively. The sensitivity rates of *U. urealyticum* strains were 45.23 %, 47.7 %, 63.84 %, 90.8 % and 92 % for azithromycin, erythromycin, clarithromycin, pristinamycin and josamycin, respectively. *U. urealyticum* strains showed 62.2 % and 79.7 % sensitivity to tetracycline and doxycycline, respectively. The resistance rates to azithromycin, clarithromycin and erythromycin for samples with mixed infection were 72.8 %, 84.7 % and 85.6 %, respectively. Josamycin and pristinamycin were 81.5 % effective on samples with mixed infection. The sensitivity rates of samples with mixed infection to tetracycline, doxycycline, ciprofloxacin and ofloxacin were 32 %, 69.6 %, 8.9 % and 18.5 %, respectively. Sub-Saharan Africa needs to use antibiotics rationally, as falling to do so would compromise the management of infectious diseases.

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Introduction

In developing countries, the spread of antimicrobial resistance is a matter for concern, as its compromises the management of infectious diseases [1]. The excessive use of antimicrobials causes selective pressure for resistance. Empirical treatment with ineffective antibiotics and poor patient adherence to antibiotic treatment regimens could potentially lead to drug resistance [1, 2].

M. hominis and *U. urealyticum* are commonly found in urogenital infections. The antibiotics of choice in the treatment of mycoplasmas include macrolides, tetracyclines and fluoroquinolones [3, 4]. *M. hominis* resists erythromycin, azithromycin and all macrolides with a 14- or 15-membered ring (e.g. clarithromycin). *U. urealyticum* are moderately susceptible to these macrolides. *M. hominis* is sensitive to josamycin and both *U. urealyticum* and *M. hominis* are known to be susceptible to pristinamycin.

This study is the first providing *Mycoplasma* resistance phenotypes for a range of antimicrobial classes (tetracyclines, macrolides and fluoroquinolones) in Central Africa (Gabon).

Methods

This study was carried out during the second semester of the year 2009 in the setting of the Gabonese National Laboratory of Public Health in Libreville. As part of our routine activity, 1,332 individuals (917 female and 414 males aged 13 to 76 years) were tested for mycoplasmas. Samples used were sperm, urine, ureteral or vaginal swabs collected from the subjects.

Mycoplasma identifications and sensibility tests to azithromycin, clarithromycin, erythromycin, josamycin, pristinamycin, doxycycline, tetracycline, ofloxacin and ciprofloxacin were done using *Mycoplasma* IST 2 test strips (bioMérieux, France). All tests were done following manufacturer's instructions and protocols. The National Laboratory of Public Health review board approved this study protocol.

Results

Of the 1,332 subjects tested, 794 (59.6 %) were positive for *Mycoplasma*. 126 (15.87 %) of the positive subjects had a mixed infection of *M. hominis* and *U. urealyticum*. *M. hominis* monoinfection was found in 13 (1.64 %) subjects, whereas *U. urealyticum* monoinfection was seen in 653 (82.24 %) subjects. The rate of infection was 68.5 % in females and 40.1 % in males.

The results from the antimicrobial sensitivity testing are shown in Table 1.

Macrolides

All *M. hominis* isolates obtained from singly infected subjects were resistant to erythromycin and had an intermediate (I) to resistant (R) profile to azithromycin and clarithromycin (details in Table 1). 84.6 % of *M. hominis* strains were sensitive (S) to josamycin and pristinamycin.

The antibiogram of mix infection samples showed a resistance rate to erythromycin of 85.6 % (S: 2.4 %; I: 11.2 %). The resistance rate to azithromycin of samples with mixed infection was 72.8 % (S: 2.4 %; I: 23.2 %). The resistance rate to clarithromycin was 84.7 % (S: 6.4 %; I: 8.9 %). The sensitivity rates to josamycin and pristinamycin were 81.5 % (R: 13.7 %; I: 4.8 %) and 81.5 % (R: 16.9 %; I: 1.6 %), respectively.

Looking at *U. urealyticum* strains isolated from singly infected subjects, the resistance rates to erythromycin, azithromycin and clarithromycin were 34 % (S: 47.7 %; I: 18.3 %), 29.54 % (S: 45.23 %; I: 25.23 %) and 32.78 % (S: 63.84 %; I: 3.38 %), respectively. The sensitivity rates to josamycin and pristinamycin were 92 % (R: 5.7 %; I: 2.3 %) and 90.8 % (R: 8.6 %; I: 0.6 %), respectively.

Tetracyclines (drug family)

The sensitivity rates to tetracycline and doxycycline of *M. hominis* strains obtained from singly infected subjects were 30.8 % (R: 46.1 %; I: 23.1 %) and 92.3 % (I: 7.7 %), respectively.

The sensitivity rates to tetracycline and doxycycline of samples with mixed infection were 32 % (R: 52 %; I: 16 %) and 69.6 % (R: 22.4 %; I: 7.2 %), respectively. *U. urealyticum* strains isolated from singly infected subjects showed, respectively, 62.2 % sensitivity (R: 29.2 %; I: 8.6 %) and 79.7 % sensitivity (R: 14 %; I: 6.3 %) to tetracycline and doxycycline

Fluoroquinolones

Of the *M. hominis* strains obtained from singly infected subjects, 76.9 % (R: 7.7 %; I: 15.4 %) and 84.6 % (I: 15.4 %) were sensitive to ciprofloxacin and ofloxacin, respectively.

The sensitivity rates to ciprofloxacin and ofloxacin of samples with mixed infection were 8.9 % (R: 61.3 %; I: 29.8 %) and 18.5 % (R: 11.3 %; I: 70.2 %), respectively.

U. urealyticum strains isolated from singly infected subjects showed resistance rates of 45.4 % (S: 11.1 %; I: 43.5 %) and 5.7 % (S: 32.6 %; I: 61.7 %) to ciprofloxacin and ofloxacin, respectively.

Discussion

Because the National Laboratory of Public Health is the principal laboratory in the country equipped to carry out bacteriological tests, we believe that the data presented here represents the situation in Libreville. The rates of *Mycoplasma* infections in females and males suspected to have urogenital infection were 68.5 % and 40.1 %, respectively. Like what was observed in China by Zhu et al. [5], *U. urealyticum* single infection was the most common infection (82.24 %), followed by *M. hominis* and *U. urealyticum* mixed infection (15.87 %) and *M. hominis* monoinfection (1.67 %).

Selected macrolides, tetracyclines and fluoroquinolones are drugs used for *Mycoplasma* infections therapy. *M. hominis* is known to be naturally resistant to C14 macrolides (erythromycin, clarithromycin, azithromycin etc.), whereas *U. urealyticum* is moderately sensitive to these. Our results were in agreement with these facts. Among the macrolides, josamycin and pristinamycin showed the highest activity against both *M. hominis* (81.5 %) and *U. urealyticum* (92 % for josamycin; 90.8 % for pristinamycin).

In our setting, doxycycline proved to be more active against *M. hominis* and *U. urealyticum* (92.3 and 79.7 %, respectively) than tetracycline (30.8 and 62.2 %, respectively).

Table 1 *Mycoplasma* antibacterial sensitivity testing results

Antibiotics	*U. urealyticum* (*N*=650)			*M. hominis*/*U. urealyticum* mixed infection (*N*=124)			*M. hominis* (*N*=13)		
	S	I	R	S	I	R	S	I	R
Azithromycin	294 (45.23 %)	164 (25.23 %)	192 (29. 54 %)	3 (2.4 %)	29 (23.2 %)	91 (72.8 %)	1 (7.7 %)	5 (38. 5 %)	7 (53.8 %)
Clarithromycin	415 (63.84 %)	22 (3.38 %)	213 (32.78 %)	8 (6.4 %)	11 (8.9 %)	105 (84.7 %)	0 (0 %)	2 (15.4 %)	11 (84.6 %)
Erythromycin	310 (47.7 %)	119 (18.3 %)	221 (34 %)	3 (2.4 %)	14 (11.2 %)	107 (85.6 %)	1 (7.7 %)	0 (0 %)	12 (92.3 %)
Josamycin	598 (92 %)	15 (2.3 %)	37 (5.7 %)	101 (81.5 %)	6 (4.8 %)	17 (13.7 %)	11 (84.6 %)	1 (7.7 %)	1 (7.7 %)
Pristinamycin	590 (90.8 %)	4 (0.6 %)	56 (8.6 %)	101 (81.5 %)	2 (1.6 %)	21 (16.9 %)	11 (84.6 %)	2 (15.4 %)	0 (0 %)
Doxycycline	518 (79.7 %)	41 (6.3 %)	91 (14 %)	87 (69.6 %)	9 (7.2 %)	28 (22.4 %)	12 (92.3 %)	1 (7.7 %)	0 (0 %)
Tetracycline	404 (62.2 %)	56 (8.6 %)	190 (29.2 %)	40 (32 %)	20 (16 %)	65 (52 %)	4 (30.8 %)	3 (23.1 %)	6 (46.1 %)
Ofloxacin	212 (32.6 %)	401 (61.7 %)	37 (5.7 %)	23 (18.5 %)	87 (70.2 %)	14 (11.3 %)	11 (84.6 %)	2 (15.4 %)	0 (0 %)
Ciprofloxacin	72 (11.1 %)	283 (43. 5 %)	295 (45.4 %)	11 (8.9 %)	37 (29.8 %)	76 (61.3 %)	10 (76.9 %)	2 (15.4 %)	1 (7.7 %)

M. hominis was less sensitive to tetracycline than *U. urealyticum*. The emergence of tetracyclines resistance (the drugs of choice in the treatment of *Mycoplasma* infections) seen in our study should raise concerns. In other countries, tetracyclines resistance has increased over the years [6, 7]. In our setting, tetracycline has poor activity against mycoplasmas. If we don't want doxycycline to suffer the same fate, we need to start using antibiotics more rationally.

Ciprofloxacin and ofloxacin proved to be ineffective against the majority of *U. urealyticum*, with a substantial number of the strains having an intermediate (I) to resistant (R) profile. Only 11.1 % of *U. urealyticum* isolates were sensitive to ciprofloxacin and 32.6 % of *U. urealyticum* isolates were sensitive to ofloxacin. Both quinolones had a better activity on our few collection of *M. hominis* strains (13 strains). Respectively, 76.9 and 84.6 % of isolated *M. hominis* strains were sensitive to ciprofloxacin and ofloxacin. Others have reported the activity of fluoroquinolones on urogenital mycoplasmas, and like most of them, we found ciprofloxacin to be ineffective against the majority of *U. urealyticum* and ofloxacin to be active on the majority of *M. hominis* [8, 9]. However, contrary to these reports [8, 9], ofloxacin proved to be relatively ineffective against *U. urealyticum*. This is not surprising, as Nys et al. [10] showed us that, in some aspects, antibiotics resistance profiles are different from one country to another, this is probably due to the differences in the prescribing practice of clinicians.

Conclusion

It is, therefore, crucial to be aware of the local epidemiology of antimicrobial resistance to properly design antimicrobial stewardship [2] and limit bacteria drug resistance development. This is very important, particularly in the African setting, where the availability and accessibility of drugs are limited.

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Ethics The Laboratoire National de Santé Publique board and ethics committee approved this study.

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