O092

2-hour Oral Session

Trends in antimicrobial resistance

Molecular epidemiology of azithromycin resistance in *Neisseria gonorrhoeae* in France

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Objectives: In 2012, European guidelines recommend to use dual antimicrobial therapy, with extended-spectrum cephalosporins (ESCs) combined to azithromycin, for treatment of gonorrhea and of potentially concurrent chlamydial infection. In France, resistance rate of *Neisseria gonorrhoeae* (NG) to azithromycin was not known. The aims of this study were to determine the prevalence of azithromycin-resistance NG isolates in France and to characterize their molecular patterns.

Methods: From April 2013 to March 2014, 970 isolates of NG French isolates were tested for their susceptibility to azithromycin by determination of the MICs using E-test method (bioMérieux). Nine azithromycin-resistant, 45 azithromycin-intermediate susceptible and 18 azithromycin-susceptible NG isolates were investigated for resistance mechanisms to azithromycin. DNA of these isolates was extracted, amplified and sequenced for the major azithromycin resistance determinants (*mtrR, rrl, mefA*, *rplD*, *rplV*, *erm*, *ere* and *mphA* genes). Molecular epidemiology typing was performed by the reference NG Multi-Antigen Sequence Typing (NGMAST).

Results: Among the 970 NG isolates, 45 (4.6%) were intermediate susceptible to azithromycin (0.25 mg/L0.5 mg/L) with MICs to azithromycin ranging from 0.75 to 96 mg/L. All these 54 examined isolates were susceptible to ceftriaxone and to spectinomycin but two were resistant to cefixime (MIC=0.19 mg/L). Azithromycin-resistance was associated to C2599T mutations (NG numbering) in the peptidyltransferase loop of domain V of the *rrl* gene encoding the 23S rRNA allele for 3 isolates. For the 6 remaining azithromycin-resistant NG isolates, resistance could be due to (i) mutations in the *mtrR* promoter (A deletion for 3 isolates or Aà C substitution for 2 isolates), (ii) mutation in the *rplD* gene encoding the ribosomal protein L4 (G70D for 2 isolates and V125A, A147G and R157Q) and (iii) modifications in the amino acids sequence of the repressor MtrR especially in position A39T, 44RH and H105Y. No mutation was detected in the *rplV* genes and none of the *ermA*, *ermB*, *ermC, ermF*, *ereA*, *ereB*, *mefA/E*, *mphA* genes was found. Genotype analysis found 30 different ST types among the azithromycin-resistant and intermediate susceptible NG isolates. The ST type ST21 was predominant (18.5%) followed by the ST1407 (9.2%), known as a multiresistant clone circulating in Europe, and by the ST2400 (11.1%).

Conclusions: Our study shows that resistance of NG to azithromycin in France is based not only to the dissemination of three clones (38.8%) but also on unique isolates presumably selected under treatment in 61.2% of cases.