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Poster Session IV

Molecular epidemiology of Haemophilus, Moraxella, and Neisseria

MOLECULAR EPIDEMIOLOGY OF QUINOLONE RESISTANCE IN NEISSERIA GONORRHOEAE IN FRANCE

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Objectives: *Neisseria gonorrhoeae* (NG) infections are a major public health problem and the incidence of gonorrhoea is increasing with global emergence of multidrug-resistant strains. In France, resistance rate to quinolones was 43 % in 2011. The aim of the study was to characterize the molecular patterns of quinolone resistance among multidrug-resistant strains.

Methods: Eighty-five clinical isolates of NG with a reduced susceptibility to 3rd generation cephalosporins (C3G) and 20 additional clinical isolates with low level of resistance to ciprofloxacin (MICs < 4 mg/L) were investigated for resistance mechanisms to quinolones. Strains were screened by pyrosequencing for the presence of mutations in the quinolone resistance-determining regions (QRDR) in the DNA gyrase *gyrA* and Topoisomerase IV *parC* genes. The *gyrB* and *parE* genes and plasmid mediated resistance to quinolones determinants [*aac(6')Ib-cr*, *qepA* and *qnr* genes] were sought using real-time PCR and HRM. Molecular epidemiology typing was performed by the reference Multi-Antigen Sequence Typing (NG-MAST) method.

Results: All 85 isolates with a reduced sensitivity to 3rd generation cephalosporin were resistant to fluoroquinolones with MICs of ciprofloxacin ranging from 1.5 to ≥ 32 mg/L. Resistance was associated to at least two mutations in the QRDRs of *gyrA* and *parC*. A predominant genotype (80%) was observed with the substitution of Ser91Phe and Asp95Gly in GyrA and Ser87Arg in ParC. Ten isolates harboured a novel genotype with a novel substitution in ParC (Ser88Pro). Mutation in the QRDR of ParE (Pro439Ser) was found for two strains. Detections of *qnr*, *aac6'Ibcr*, *qepA* genes remained negative. Genotyping analysis found 17 different STs. The ST1407, known as a multiresistant clone currently circulating in Europe, was predominant (34.7 %) followed by the ST3168 (11%) previously described in isolates from India. For the 20 isolates with a low level resistance to ciprofloxacin, the increase in MIC was related to the number of mutations in the QRDRs: CIP MIC was 0.094 mg/L for the strain with one *gyrA* mutation; MIC ranged from 0.19 to 1.5 mg/L for 10 strains with two mutations; MIC ranged from 1 to 4 mg/L for 3 strains harbouring three mutations.

Conclusions: Our study shows that resistance of *N. gonorrhoeae* to quinolones in France is based not only on the dissemination of two clones ST 1407 and ST 3168 (in 45.7% cases) but also on unique isolates selected under treatment in 54.3% cases.