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Scientific letters

Ciprofloxacin resistance in nontypable *Haemophilus influenzae* clinical isolates



Resistencia a la ciprofloxacina en aislados clínicos de *Haemophilus influenzae* no tipificables

Haemophilus influenzae is responsible of community-acquired respiratory tract and otolaryngology infections. First line treatment is based on betalactam antibiotics (aminopenicillins and cephalosporins), although fluoroquinolones (FQ) are widely used among adults. Resistance to these compounds remains relatively rare among *H. influenzae* strains. Chromosomal point mutations in the quinolone resistance-determining regions of the genes encoding DNA gyrase (*gyr A* and *gyr B*) and topoisomerase IV (*parC* and *parE*) constitute the main FQ resistance mechanisms in *H. influenzae*.¹ Other mechanisms such as efflux pumps and porin loss have been suggested to be involved in the resistance of these compounds.²

Between January 2014 and March 2017, a total of 895 clinical strains of *H. influenzae* were isolated from various clinical specimens at the Microbiology Laboratory of the University Hospital of Álava (Vitoria-Gasteiz, Spain). Ciprofloxacin (CIP) susceptibility data for all these strains was recorded and is currently being analysed in order to determine the CIP-resistant rates among *H. influenzae* and its relationship with the patients age. For this evaluation, one isolate per patient was considered.

Minimum inhibitory concentration (MIC) of CIP was determined by the microdilution method with *Haemophilus* test medium (HTM) and commercial panels (STRHAE2, Sensititre, West Sussex, England). *H. influenzae* ATCC 49247 was used as a susceptible control strain. MIC distribution of CIP is displayed in Fig. 1.

Following Clinical and Laboratory Standards Institute (CLSI) interpretative criteria,³ which defines the CIP susceptibility breakpoint at ≤ 1 mg/L, 65 (7.3%) of the strains evaluated were CIP non-susceptible. All CIP-resistant strains following CLSI were isolated from patients that were over 36 years old (mean age of 70.1); none were isolated in children (Table 1). This could be explained by the avoidance of FQ use among paediatric population due to toxicity concerns.

Major differences between the European Committee on Antimicrobial Susceptibility Testing⁴ (EUCAST) and the CLSI in terms of culture media (Mueller-Hinton agar + 5% defibrinated horse blood and 20 mg/L β -NAD (MH-F), compared to HTM) and breakpoints for susceptibility testing of *H. influenzae* make it almost impossible to come to a harmonized conclusion when comparing studies following recommendations by either committee.

Thus, if EUCAST criteria in terms of CIP susceptibility breakpoint (≤ 0.06 mg/L) and irrespective of the medium were applied,

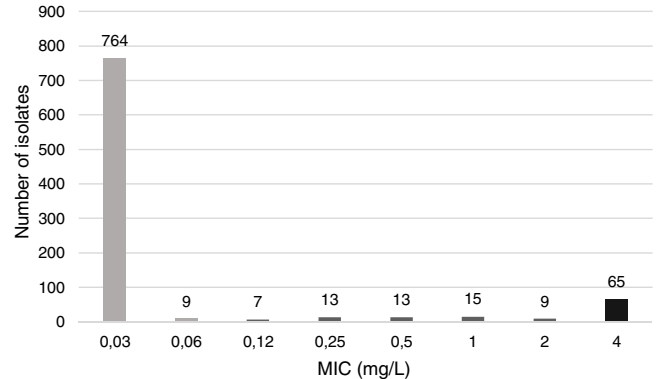


Fig. 1. Minimum inhibitory concentration (MIC) distribution of ciprofloxacin (CIP) for *H. influenzae*.

Table 1

Prevalence of fluoroquinolone-resistant *H. influenzae* and patient age.

Patient age group	No. of strains	No. of resistant strains (CLSI)
0–9	188	0
10–19	9	0
20–29	11	0
30–39	37	2
40–49	43	5
50–59	84	9
60–69	146	10
70–79	198	21
≥ 80	179	18

122 (13.6%) strains would be considered resistant. These results suggest that the adoption of CLSI CIP susceptibility breakpoint of ≤ 1 mg/L might lead to under recognition of low-level CIP-resistance *H. influenzae* strains.

In our analysis, a high percentage of FQ-resistant *H. influenzae* were found compared to previous studies.⁵ This could be due to the extended use of these compounds in Spain. Our results are intended to rise the concern about the increase of FQ-resistance among *H. influenzae* and to highlight the importance of surveillance programmes to control the emergence of this type of strains in order to avoid therapeutic failures. Harmonized criteria for susceptibility testing and interpretation are needed to provide accurate advice to clinicians as well as to obtain reliable epidemiological information at local, regional or national levels.

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First case of renal abscess by *Parvimonas micra*[☆]



Primer caso de absceso renal por *Parvimonas micra*

Perirenal abscesses usually present as an infrequent complication of urinary tract infections,¹ and may be secondary to bacteraemia. In the past, the erroneous and late diagnosis produced high mortality, reaching up to 20–50%. Currently, with the use of modern imaging techniques, an earlier diagnosis is achieved and, together with the optimal drainage of the abscess and antibiotic treatment, mortality is very low.²

We present the case of a 65-year-old man who went to the emergency department for fever of up to 39 °C which had been ongoing for four weeks, chills, weight loss of 5 kg and abdominal pain in the lower left flank, with a history of a tooth extraction which was performed three weeks prior to the onset of symptoms. The patient did not have urinary symptoms. Among the lab results, the following stood out: CRP (100.5 mg/l), procalcitonin (6.88 ng/ml) and neutrophilia. Renal ultrasound showed the presence of bilateral simple renal cysts with no other pathological findings. Urine and blood cultures were taken, empirical intravenous antibiotic therapy was started with meropenem and vancomycin and the patient was admitted. Renal CT scan showed left perirenal abscess (6 × 5 cm) with extension to spleen, posterior pararenal space and fascias, but the drainage of the renal lesion was not possible due to the lack of organised collections suitable for puncture. The echocardiogram showed no images compatible with valvular endocardial vegetation, ruling out endocarditis. The urine culture was negative. At 41.27 h the anaerobic blood culture bottle was positive, gram-positive cocci were observed in chains and a blood agar was taken in anaerobiosis, in which whitish and dwarf colonies grew at 96 h and were identified as *Parvimonas micra* by MALDI-TOF (*Vitek MS*[®]). The antibiogram (ATB ANA EU, *bioMérieux*) showed susceptibility to amoxicillin, amoxicillin-clavulanic acid, clindamycin, imipenem, metronidazole, penicillin, piperacillin, piperacillin/tazobactam, ticarcillin, ticarcillin/clavulanate and vancomycin, so the treatment was modified to ertapenem and clindamycin. The renal CT scan performed 10 days after admission showed a modest decrease in size (3.7 × 2.6 × 4.9 cm) and abscess density and the patient was discharged 25 days after admis-

sion. He completed the intravenous treatment for seven more weeks and then took oral clindamycin for six weeks until he was cured.

Parvimonas micra is an anaerobic gram-positive coccus, which is part of the normal flora of the mouth, respiratory and upper digestive tract, genitourinary system and skin. Its pathogenic potential has been discussed for years, although it is now known to cause opportunistic infections: brain and epidural abscesses, bacteraemia, endocarditis, necrotising pneumonia and septic abortion, among others.^{3–5} After searching in PubMed with the words *Parvimonas micra*/*Peptostreptococcus micros* and renal abscess we have not found any documented case, hence the relevance of this case report. Perirenal abscess is characterised by the presence of nonspecific signs and symptoms such as: fever, lumbar pain, vomiting, abdominal pain with tenderness to palpation and flank mass with irradiation to the leg, coinciding with the symptoms presented by our patient.⁶ The main route of infection is ascending, which is why it is associated with late complications of a urinary infection, especially urolithiasis. For this reason, the bacteria involved most frequently are *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus* spp., although cases of renal abscess due to *Staphylococcus aureus* have been documented.⁷ Occasionally, the symptoms may be suggestive of acute pyelonephritis with febrile syndrome and unilateral flank pain that does not improve with the treatment of acute pyelonephritis.⁸ Pyuria and proteinuria may be associated, but urine analysis is normal in up to 30% of cases with negative urine cultures in up to 40%, as occurred in our case. In the patient, the abscess appeared as a consequence of a bacteraemia of oral origin, since he had undergone a tooth extraction, which secondarily gave rise to the septic metastatic implant in the retroperitoneal, renal and splenic region, possibly favoured by the presence of previous renal cysts. The risk factors associated with this condition are: diabetes mellitus, urethral obstruction, vesicoureteral reflux, immunosuppression or parenteral drug use,⁹ none was present in our case, which makes us assess the opportunistic potential of *Parvimonas micra*. With all this, we can conclude that an early diagnosis and optimal treatment is essential to achieve a favourable evolution.

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