Low prevalence of mcr-1 positive Enterobacteriaceae isolates in a health area*

Baja prevalencia de aislados mcr-1 positivos en enterobacterias en nuestra área

Dear Editor,

A new, plasmid-encoded colistin resistance determinant (mcr-1) has recently been described in Enterobacteriaceae in China. The mcr-1 gene was detected in *Escherichia coli* and *Klebsiella pneumoniae* isolates from pigs, chicken and pork meat, and even in clinical isolates. Subsequently, this gene has been detected in Europe, Africa and South America, also including isolates of *Salmonella enterica ser. Typhimurium*. In an epidemiological context where an infection emergency caused by carbapenemase-producing Enterobacteriaceae and multidrug-resistant Gram-negative bacilli is unfolding, the presence of a colistin resistance determinant capable of horizontal transfer poses a threat to global health, as this antibiotic is one of the few therapeutic options available. The objective of this study was to find out the prevalence of this new determinant in our catchment area.

In April–May 2016, a total of 1260 Enterobacteriaceae isolates were studied at the Microbiology Department of the Hospital Virgen Macarena (a catchment area comprising 481,263 inhabitants).
The susceptibility study was conducted by broth microdilution using commercial MicroScan® panels (Beckman Coulter, USA) and employing the EUCAST 2016 criteria for interpreting the MICs of colistin (resistance >2 μg/ml) (The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 6.0, 2016. http://www.eucast.org). The isolates that presented a colistin MIC >2 mg/l, ruling out isolates belonging to the *Proteus*, *Morganella* and *Providencia* genera (*n* = 19) (there were no *Serratia marcescens* isolates in this period), were studied using Etest® (BioMérieux).

In 24 isolates (1.5%), a colistin MIC of >2 mg/l was observed with MicroScan® technology, and they included 18 *E. coli* isolates (2%), three *K. pneumoniae* isolates (1.6%), three *S. enterica* isolates (9%) and one *Enterobacter aerogenes* isolate (4%). The colistin CMI value observed using Etest® was less than 0.5 mg/l in 22 isolates (92%) and two *E. coli* isolates (0.2% of the total *E. coli* studied) presented values of 4 mg/l. Mcr-1 detection by means of a PCR was positive in one of the two isolates, using the aforementioned primers1 and subsequent sequencing. The isolate came from a primary care urine sample from a 56-year-old woman with no previous urinary disease and no history of colistin treatment. This isolate matched a strain of *E. coli* ST38 by means of MLST (http://mlst.warwick.ac.uk/mlst/dbs/Ecoli/) of phylogroup B1, which was also resistant to ampicillin, pipercillin, tetracycline, nalidixic acid and co-trimoxazole. Plasmid extraction was performed using the Kieser method and subsequent electroporation in selected *E. coli* DH10 with Müller–Hinton agar, supplemented with 2 mg/l of colistin. The plasmid was characterised as IncX4 through IncX replicon subtyping.1 It is worth highlighting the discrepancy observed between the results obtained with MicroScan® panels and the Etest® method (22 isolates), which has also been commented upon recently in various studies where the correlation between the automated MicroScan® system and reference method (broth microdilution) was lower than that of the Etest®.3,7 On this basis, in case of discrepancies, we took the Etest® values as a reference.

In our area, the prevalence of this determinant in clinical isolates during the study period was very low (0.2% of the total *E. coli* isolates and 0.08% of the total Enterobacteriaceae, excluding those that are naturally resistant to colistin); this is similar to what has been observed in the United Kingdom (0.05%) and is lower than what has been described in China (1.1%).1 Likewise, the prevalence in animal isolates in Europe is low (1.2% in Spain,6 1.5% in the Netherlands3) compared to China (20.6%).1 The presence of the mcr-1 gene has also been described in extended-spectrum beta-lactamase–producing Enterobacteriaceae and carbapenemase–producing Enterobacteriaceae, although there are no data on its prevalence. The presence of this resistance determinant has previously been detected in plasmids of different incompatibility groups (IncI2, X4, H12 and P),1 which did not encode additional plasmid mechanisms of resistance to other families of antibiotics, thus coinciding with the lack of multidrug resistance in our positive mcr-1 isolate (sensitive to cephalosporins, aminoglycosides and fluoroquinolones). In order to understand the extent to which this determinant has spread in Spain and its promotion factors, it would be interesting to perform monitoring studies on clinical isolates.

In conclusion, colistin is one of the active alternatives against multidrug-resistant Enterobacteriaceae and Gram-negative pathogens such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, in which the prevalence of plasmid-mediated resistance is very low in our field. Nevertheless, we do feel it is important to monitor the frequency of this determinant.

**References**


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