Co-occurrence of extended spectrum β-lactamase and MCR-1 encoding genes on plasmids

Findings reported by Yi-Yun Liu and colleagues¹ identified the plasmid-borne gene mcr-1 encoding resistance to colistin with a high prevalence in Escherichia coli isolates from animals, foodstuff, and human beings in China. The same gene was then reported in Europe (Denmark) among extended-spectrum β-lactamase (ESBL) and AmpC-producing E coli isolates from chicken meat and human infections, but at a very low prevalence.²

We screened ESBL-positive E coli isolates collected in France for colistin resistance. Isolates were collected between 2005 and mid-2014 from faeces of diarrhoeic veal calves at farms, as part of a survey in the context of the French antimicrobial resistance Resapath surveillance network for animal pathogens. We screened these isolates for colistin resistance using disk diffusion and minimum inhibitory concentration determination by broth microdilution. We analysed plasmids bearing the mcr-1 gene by conjugation, S1-pulsed-field gel electrophoresis, PCR-based replicon typing, and Southern blot. We analysed clonal relationship of all isolates by enterobacterial repetitive intergenic consensus PCR and pulsed-field gel electrophoresis.

Of 517 ESBL-producing E coli isolates collected, 106 (21%) were mcr-1 positive. Notably, the oldest mcr-1-positive E coli isolate had been collected in 2005. The 106 mcr-1-positive E coli isolates originated from different individuals located in 94 widely distant farms, and they were donally unrelated.

Sequencing of the whole mcr-1 gene in 75 mcr-1-positive isolates revealed a 100% identity compared with the original sequence. Co-occurrence of the mcr-1 and ESBL genes was identified in a subset of seven isolates, with mcr-1 and blab_(TEM) being found on a large and conjugative IncHI2-type plasmid together with genes conferring resistance to sulfonamides and tetracyclines, two antibiotics widely used in veterinary medicine. These findings demonstrate a colocation of the mcr-1 gene along with an ESBL gene on a single plasmid, and additional studies are needed to clarify the diversity of the plasmid backbones spreading these two genes within our collection. Noticeably, the prevalence of the mcr-1 gene among ESBL producers in veal calves was much higher than that found in ESBL-positive E coli isolates in human beings and chicken meat reported in Denmark.³ This difference may reflect a major spread of the mcr-1 gene in European live animals. We showed that the dissemination of mcr-1, at least in France, had already occurred more than a decade ago, with one E coli isolate collected in 2005 identified as mcr-1 positive.

Altogether, available data reveal the occurrence of mcr-1 among different animals and human contexts over time.⁴ Worryingly, we show that selection pressure with broad-spectrum cephalosporins may select for colistin resistance and vice-versa, further highlighting the likelihood of a pandemic spread of mcr-1. Of note, the substantial use of tetracyclines and sulfonamides in animals might also substantially contribute to the dissemination of mcr-1 plasmids.

In a one-health perspective, and considering the renewed importance of colistin in human medicine, our data and those from others underscore the urgent need to limit the spread of mcr-1-positive plasmids by reconsidering the massive use of colistin in veterinary medicine worldwide.

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jean-yves.madec@anses.fr

Unité Antibiorésistance et Virulence Bactériennes, ANSES Site de Lyon, F-69364 Lyon, France (MH, PC, VM, RD, J-YM); Emerging Antibiotic Resistance Unit, Medical and Molecular Microbiology, Department of Medicine, Faculty of Science, University of Fribourg, Fribourg, Switzerland (LP, NK, PN); and HFR-Hôpital Cantonal, Fribourg, Switzerland (PN)

