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Commentary

Aminoglycoside resistance mechanism inference algorithm: Implication for underlying resistance mechanisms to aminoglycosides

Abdelaziz Touati *

Laboratoire d'Ecologie Microbienne, Université de Bejaia, 06000, Algeria

The discovery of antibiotics in 1928 and their subsequent large-scale production are considered to be one of the most important achievements in the history of medicine [1]. One of the most important discoveries after that of β-lactams was streptomycin, the first aminoglycoside discovered. The history of aminoglycosides was then marked by the successive introduction of a series of compounds (kanamycin, gentamicin, and tobramycin) for the treatment of infections due to Gram-negative bacilli [2].

The recent expansion of extensively drug-resistant (XDR) pathogens and particularly that of carbapenem-producing *Enterobacteriaceae* (CRE) has brought into light aminoglycosides, which may retain activity even in XDR isolates [3]. Specific indications for aminoglycoside therapy include amikacin and gentamicin administered intravenously for infections caused by MDR Gram-negative organisms [4].

Interpretative reading of antimicrobial susceptibility test results allows to analyze the susceptibility pattern and to predict the underlying resistance mechanisms [5]. Contrary to β-lactams antibiotics, correlations between resistance to aminoglycosides inferred based on the European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints and expert rules are generally poor [6]. Therefore, the need for improvement of detection of aminoglycosides resistance mechanisms in routine is of great importance.

Recently in *EBioMedicine*, Mancini and colleagues presented an Aminoglycoside Resistance Mechanism Inference Algorithm (ARMIA) for the inference of resistance mechanisms from inhibition zone diameters [7]. This algorithm uses ECOFFs for gentamicin, tobramycin and kanamycin as well as a working separator cut-off for amikacin. They compared the performance of ARMIA and EUCAST CBPs/expert rules with that of whole-genome sequencing (WGS) in predicting aminoglycoside resistance. The results of this study showed that ARMIA-based inference of resistance mechanisms and WGS data were congruent in 96·3%. In contrast, there was a poor correlation between resistance mechanisms inferred using EUCAST CBPs/expert rules and WGS data (85·6%) [7].

When assessing the accuracy of various susceptibility testing methods as compared to standard reference methods, the terms very major errors (vME) have been used to describe false susceptible [8]. Thus, in the comparison made by Mancini and colleagues, they reported that EUCAST produced 63 (12·9%) vME, compared to only 2 (0·4%) vME with ARMIA [7].

In vitro susceptibility rates may vary significantly, depending on the aminoglycoside resistance mechanisms, which are frequently co-transferred along with other resistance genes on mobile genetic elements [3]. It is reported that aminoglycoside resistance mechanisms, such as 16S rRNA methylase, coexist with other resistance mechanisms including extended-spectrum β-lactamase, carbapenemase, and plasmid-mediated quinolone resistance determinants [9]. Thus, it is important to detect the underlying aminoglycosides resistance mechanisms to prevent co-selection of these resistance mechanisms. The ARMIA developed by Mancini and colleagues would be useful for this purpose to avoid misidentification of the aminoglycoside resistance mechanisms.

Declaration of Competing Interest

None to declare.

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* Corresponding author.
E-mail address: ziz1999@yahoo.fr.

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