Comment on: Effects of selective digestive decontamination (SDD) on the gut resistome

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Sir,

We read with interest the report by Buelow et al.¹ entitled ‘Effects of selective digestive decontamination (SDD) on the gut resistome’. The authors undertook metagenomic analyses to highlight the effect of SDD on an individual’s gut resistome. The authors eloquently describe the limitations of conventional culture techniques, especially as no resistant organisms were cultured in parallel to the molecular methods. We would like to highlight the importance of phenotypic methods of identification of resistant organisms.

We report two recent cases of vancomycin-dependent enterococci (VDE) isolated from rectal swabs of patients receiving SDD in an intensive care unit (ICU). These were identified as Enterococcus faecium. In our institution, all patients expected to be intubated for >48 h receive SDD consisting of 6 hourly administration of 80 mg of tobramycin, 250 000 U of colistin and 1 million units of nystatin by mouth and nasogastric tube for the duration of intubation. Vancomycin (500 mg) is added to this oral and nasogastric administration due to concerns about methicillin-resistant Staphylococcus aureus (MRSA).

Patient 1 was admitted to an ICU for management of quadriplegia following an episode of meningitis. He had been an inpatient for several weeks prior to his ICU admission, during which he received several courses of intravenous vancomycin. Whilst in the ICU he continued to receive vancomycin as part of SDD. VDE was isolated from a rectal screening swab on day 145 of intubation.

Patient 2 was admitted for management of status epilepticus. She had not been treated with vancomycin other than as part of SDD. VDE was first isolated on day 7 of intubation. Bacterial growth occurred at vancomycin concentrations >1 mg/L, which gave the phenotypic characteristic of growth occurring only around the antibiotic disc or the MIC test strip.

To our knowledge, these are the first two isolates of VDE to be reported associated with SDD.

VDE were described in the UK in 1994 relating to two renal patients in separate hospitals.² Since then, numerous cases of VDE have been reported including nosocomial outbreaks.³,⁴ VDE grow in the presence of vancomycin and are mutants of vancomycin-resistant enterococci. This phenotype results from mutations in the ddl gene leading to an inactive host D-Ala-D-Ala ligase requiring vancomycin to induce the production of peptidoglycan precursors.⁵ Although an ability to cause nosocomial infection is recognized, the clinical significance of VDE is not entirely clear. With regard to our cases, VDE was isolated on routine screening swabs and did not appear to lead to clinically significant infection.

SDD is a controversial technique and is not employed in all UK ICUs. SDD regimens differ between units, often reflecting local microbiological epidemiology. Including enteral vancomycin has been shown to be effective at controlling MRSA in endemic settings.⁶ In 2013, a meta-analysis detected no relationship between the use of SDD or selective oral decontamination (SOD) and the development of antimicrobial resistance.⁷ However, the authors acknowledged the need for research over the longer term in ICUs.⁷ A recent 4 year ecological study published in JAC reported decreasing trends for resistance to third-generation cephalosporin and ciprofloxacin antibiotics.⁸ Conventional culture-based methods were used in both the aforementioned studies focusing on a small selection of resistant organisms.⁷,⁸ We welcome the study by Buelow et al.¹ for widening the scope of antimicrobial resistance detection, via molecular techniques, highlighting the importance of mobile genetic elements in cross-species transfer of genetic resistance.

Molecular techniques have limitations and our two cases demonstrate the continued need for rigorous phenotypic evaluation of organisms isolated in a diagnostic microbiology laboratory. The potential unintended consequence of SDD/SOD on antimicrobial resistance needs careful consideration. We believe that a whole gut microbiome approach is warranted rather than focusing on a narrow spectrum of politically worrisome organisms.

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Letters to the Editor

References


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Comment on: Measurement units for antibiotic consumption in outpatients

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Sir,

We are grateful for the interest of Čizman1 in our work2 on appropriate measurement units for outpatient antibiotic consumption.

Based on data for Slovenia and referring to the correlation between antibiotic consumption and resistance, he argues that for an international benchmarking of antibiotic use in outpatients, the number of defined daily doses (DDDs) per 1000 inhabitants per day (DID) is a better measurement unit than the number of packages per 1000 inhabitants per day (PID), and that if substantial changes in the number of DDDs per package occur over time, additional measurement units should be used, such as PID and the number of prescriptions per 1000 inhabitants per year, to identify trends in national prescribing. The latter statement is completely in line with our recommendation to use a similar combination of measurement units or to exercise caution when interpreting trends based only on DDDs when such changes occur or are unknown.

This recommendation was first based on the observation in Belgium that outpatient antibiotic consumption in terms of DID had not decreased since the start of the national public antibiotic awareness campaign, whereas we observed a substantial decrease in PID due to the less frequent treatment of fewer individuals. These contrasting trends coincided with a decrease in the proportion of pneumococci resistant to penicillins, tetracyclines and macrolides and are explained by a substantial increase in the number of DDDs per package for the most commonly used antibiotics. In Slovenia, the latter is not the case based on the data provided by Čizman. Meanwhile, we have shown that the number of DDDs per package increased for most commonly used antibiotics in Europe (31 countries), resulting in contrasting trends depending on whether DID or PID is used as the measurement unit and corroborating our recommendation to adopt PID to monitor outpatient antibiotic use in Europe. Based on that study, Figure 1 shows the estimated linear trends in the number of DDDs per package for total outpatient antibiotic consumption in Europe, Belgium and Slovenia. These data explain why consumption trends expressed in DID or PID are contrasting for Belgium and Europe, and similar for Slovenia.

Figure 1. Trends in the number of DDDs per package for total outpatient antibiotic consumption.