

## EDITORIAL

## Is SDD really without any risks?

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Application of the selective decontamination of the digestive tract (SDD) strategy in ICU patients is largely a Dutch invention. Predominantly, but not exclusively, Dutch intensivists both conceived the SDD concept<sup>[1]</sup> and performed the studies that show that application of SDD improves survival of the critically ill, with a number needed to treat of approximately 23 patients.<sup>[2-4]</sup> Thereby, SDD is a highly effective intervention in the critically ill, with a low risk of adverse events. Also, SDD is cost-effective. Consequently, SDD is part of the Dutch guidelines and applied in the majority of Dutch ICUs. But is the use of SDD really without any drawbacks?

Prompted by a case in which the application of SDD led to toxic serum levels of tobramycin, our colleagues at the Martini Hospital in Groningen set out to explore the incidence of detectable systemic levels of tobramycin in patients receiving SDD.<sup>[5]</sup> The motivation to perform this study was to determine whether therapeutic drug monitoring should be performed in order to avoid tobramycin levels >1 mg/l, which is a level associated with nephrotoxicity. They found that 13% of patients receiving SDD had detectable systemic tobramycin levels. In all patients who tested positive, tobramycin levels remained detectable throughout the course of their ICU stay.

The authors also tried to determine specific risk factors. The number of patients included in the study was small, which limited multivariate modelling. Nevertheless, their data suggest that in particular an impaired renal function may be a risk factor for detectable tobramycin levels during SDD, suggesting impaired elimination of the drug. The authors note that this is in line with previous findings.<sup>[6,7]</sup> Whether disruption of the gastrointestinal barrier due to surgery is a specific risk factor associated with absorption of topically applied tobramycin into the blood stream could not be dissected from their study with certainty, due to low patient numbers. This however seems a

likely explanation for the authors' findings and has also been suggested by others.<sup>[7]</sup>

As none of the patients reached toxic tobramycin levels, in terms of the risk of nephrotoxicity, this study may suggest that SDD is safe and that therapeutic drug monitoring of tobramycin is not needed. However, another conclusion is that the use of topical antibiotics leads to absorption into the blood stream in a subset of patients, resulting in sub-therapeutic levels. This poses another problem, which we may need to consider. It is a well-known phenomenon that in the presence of sub-therapeutic levels of antibiotics, bacteria are able to acquire resistance to these antibiotics. Should we then worry about tobramycin resistance due to SDD? A number of studies have addressed this question, suggesting that in a setting of low resistance rates, SDD does not increase antibiotic resistance in general. However, a gradual increase in aminoglycoside-resistant gram-negative bacteria was observed.<sup>[3,4]</sup>

Whether these findings are definitely reassuring can be questioned. It should be noted that these studies did not specifically address the incidence of resistance in patients with potential risk factors for absorption of topically applied antibiotics, such as patients undergoing gastrointestinal surgery in the presence of decreased renal function. In these patients, SDD-related increase in tobramycin resistance may be more prevalent. Another issue of concern is the overall increase in resistance rates in our country.<sup>[8]</sup> Of note, resistance to tobramycin in ICUs does not show an increasing trend. Thereby, one may argue that patients have acquired these resistant bacteria outside the ICU and that SDD has nothing to do with the rise in antibiotic resistance. However, as the use of systemic antibiotics and resistance rates go hand in hand, the phenomenon of detectable systemic levels of topically applied agents may be worrisome. In particular in patients who

have acquired an infection with bacteria that are intrinsically resistant to colistin, such as *Serratia* or *Proteus* species, increasing resistance to tobramycin is a potential problem. The risk of antibiotic resistance in at-risk patients receiving SDD requires further study.

### Disclosures

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