

EDITORIAL



# Selective digestive decontamination: We must make an international decision on this 40-year old controversy

Jean Carlet\*

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Selective digestive decontamination (SDD) has been proposed by Stoutenbeek, Van Saene, and Zanstra in critically ill patients under mechanical ventilation, to prevent infections acquired in the intensive care unit (ICU), particularly ventilator-associated pneumonia (VAP), and therefore, to reduce morbidity and mortality in those patients [1]. It was very inventive, and original, to propose using antibiotics for prevention rather than for therapy. Since 1984, a huge amount of peer-reviewed papers (n=1010), randomised controlled trials (RCTs) performed in the ICU (n=283), meta-analysis (n=72), and pro/con debates were published and the topic is still highly controversial. It was decided by the promoters of the technique that SDD “definition” would be the combination of topical and non-absorbable antibiotics in the oro-pharynx and in the stomach, with a “short course” of systemic antibiotics (SA) (third-generation cephalosporins in most studies). In fact, in the literature, we can see that this short course could go up to 6 days in several studies. I do not know if the pioneers of this technique considered that intravenous (IV) antibiotics were part of SDD, or not. Personally, I have never understood the rationale for the systematic and preventive usage of systemic antibiotics, within a cocktail supposed to be local, and not absorbable. The word “selective” was used because the topical antibiotics respect anaerobic flora. This is very true, but the use of systemic antibiotics modifies the concept. One of the most important issues has been, since 1984, that the usage of systematic SA was far from being intuitive and clear for clinicians, since the use of SA did not appear in the acronym “SDD”. The risk

of increasing antimicrobial resistance (AMR) was considered too high by many intensive care specialists, in particular those working in countries with already high levels of resistance. In addition, a sub-optimal quality of some studies has been emphasized by some intensivists, and by the Cochrane authors, explaining that they consider that the effect of this technique remains doubtful. Those two factors explain the reluctance to use SDD, the interminable controversy concerning this technique, and the heterogeneity of its usage between units and countries. I do think that it is not acceptable and unethical to continue like this.

Some RCTs and meta-analyses show discordant results. The National Institute for Health and Care Research (NIHR) published a very good, and balanced paper [2]. The participants thought, at least in 2014, that additional data were mandatory, in particular on the issue of mortality. Sixty-five RCTs and 11 meta-analyses have been published from 2007 to 2023 [3–14]. Indeed, all studies showed a clear-cut decrease in ICU-acquired bacteremia and VAP. Concerning mortality, the results were more discordant, since 6 studies showed that mortality was reduced only in patients receiving topical plus systemic antibiotics. This was the case in two excellent RCTs [7, 8] and 4 meta-analyses [3, 6, 9–14], including two Cochrane meta-analyses [3, 6]. This represents 54.5% of the 11 meta-analyses. This is very important data, since it confirms that it was a good idea to add SA to the topical ones. However, it is mandatory to consider the balance between positive and negative ones, including the risk of increasing AMR, but not only. The only meta-analysis gathering patients receiving only topical antibiotics, with the aim to decrease the rate of ICU acquired bloodstream infections and mortality, was negative [13]. In the study

\*Correspondence: [jeancarlet@gmail.com](mailto:jeancarlet@gmail.com)  
ESICM and Waaar (World Alliance Against Antibiotic Resistance), Créteil, France

from De Smet et al. [14], no decrease in crude mortality was found in the mono-variate analysis (27.5, 26.6 and 26.9% mortality in the 3 groups) and a small difference was found in the multi-variate one (0.74–0.99 for selective oropharyngeal decontamination (SOD), and 0.97 for SDD). The endpoint which has been chosen, in most studies performed in intensive care, is mortality. It is not always the best choice. It is important to remind that attributable mortality of VAP is minor [15], and therefore, an important decrease in mortality is likely to be due to other factors than the local effect of SDD. My last comment would be about side effects of this technique, which have been investigated in all studies but only partially, although those side effects could affect mortality [16].

A first pro/con debate was published in Intensive Care Medicine (ICM) in the past. A new, very interesting “pro/con/not sure” debate was published recently [17–19]. The letter from Wieringa [18] is the most inventive one, because the role of the microbiome and the effect of SDD, which has been poorly studied, is also discussed. However, it is likely that those 3 opinion leaders will not stop this passionate controversy, and the opposite behaviors of units and countries concerning this technique will persist. There are very few drugs or combinations of drugs which have been shown to reduce mortality in critically ill patients. If SDD is in fact one of them, we lost many years, and we should decide to use it immediately. Unfortunately, a study looking at the respective role of SDD and systemic antibiotics, which is a key issue, is still lacking. A large multi-centric, double-blind RCT is urgently needed to better understand this issue! Honestly, I do not think that a new meta-analysis, or pro-con debate will help to decide how to properly prevent ICU-acquired infections, and eventually decrease mortality. The main effect of what is called wrongly SDD, could be due, at least in part, to systemic antibiotics. Using the acronym SDD, which was logical to describe a local therapy has been misleading since the beginning of this technique. We should use an acronym like SDD-SA, where SA stands for systemic antibiotics. Obviously, SDD had no negative effects upon AMR in countries having a low level of resistance. This must be confirmed by studies performed in the many countries with moderate or high AMR levels. Continuing to live comfortably in our units with such an uncertainty concerning a potentially life-saving therapy, would be, in my opinion, unethical. Interestingly enough, the conclusion of the very good paper from the SUDDICU [9] group was: “Whether SDD reduces mortality in ICU patients remains uncertain”. The Cochrane paper, in 2021, by Minozzi et al. came to the same conclusion.

In conclusion, an international consensus conference, gathering informed people from all medical societies or

agencies involved in the therapy of critically ill patients, including physicians without extensive knowledge in the topic of SDD, patient and society representatives, is required to adjudicate whether SDD has been demonstrated to be both safe and effective in the ICU context. They will also have to answer the main question I raised in the title of this paper: considering the present scientific knowledge on SDD, is it ethical to continue this dichotomy between user and non-user countries of a potentially life-saving therapy?

#### Conflicts of interest

The Author declares no conflict of interests.

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