Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial

Selective digestive decontamination and COVID-19: Uncertainty in a moving area

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In an interesting letter to the editor, Luque-Paz et al. suggested that selective digestive decontamination (SDD) in COVID-19 patients might be associated with a reduction in bacterial ventilator-associated pneumonia (VAP) and improved 28-day survival [1]. This is a supplemental study in favour of the use of SDD, which is recommended by our national guidelines on hospital-acquired pneumonia [2]. To our knowledge, this is the first comparative study assessing SDD in COVID-19 patients.

Selective digestive decontamination consisted of the administration of a short course of systemic antibiotic to fight against the occurrence of early-onset VAP and the application of topical antibiotics directed against digestive Gram-negative bacteria to fight against late-onset VAP (Fig. 1) [3]. A meta-analysis clearly showed that the combination of both systemic and topical antibiotics was associated with a reduced mortality rate, whereas the single use of topical antibiotics was only associated with a reduced incidence of VAP [4]. In this study, the incidence of VAP per 1000 ventilator days was 9.4 and 23.5 in the SDD group and the control group ($P < 0.001$), respectively. However, considering VAP as a clinical end-point to assess the efficiency of SDD may be misleading since SDD can make the bronchial sample negative. Thus, most studies on SDD stressed on the 90-day mortality rates. Hence, the authors showed a decrease of the 28-day mortality rate in the SDD group (adjusted hazard ratio 0.33, 95% confidence interval [0.12-0.87]; $P = 0.03$).

The concept of SDD may be interesting in patients with COVID-19 requiring invasive mechanical ventilation since the rate of bacterial VAP can reach up to 50% [4]. In the UK, Maes et al. showed that 48% of 81 patients with COVID-19 requiring invasive mechanical ventilation developed an episode of VAP [5]. Among 8 Italian centres including 774 patients with a > 24-h ICU stay, 50% developed an episode of hospital-acquired pneumonia due to Gram negative bacteria and *Staphylococcus aureus* in 64% and 28% of cases, respectively [6]. This high incidence makes the prevention of VAP a major step in the management of COVID-19 patients. This susceptibility to bacterial infection may be attributed to immune dysfunction and could be potentiated by the use of drugs like steroids or anti-interleukin-6.

Several results of the study of Luque-Paz et al. deserve to be elucidated. The rate of bloodstream infection was similar in both groups (13% *vs.* 17%, $P = 0.53$), whereas a decreased rate in the SDD group would have been expected if the intervention was efficient. In addition, while the information of VAP rates look extremely convincing; the fact that the duration of mechanical ventilation remains the same in the SDD and non-SDD groups makes the results difficult to understand. One could argue that VAP carries a high mortality burden, and the studies with attributable mortality have not been able to solve this problem [7]. However, it is difficult to understand in modern critical care that a therapy reduces by half the incidence of VAP with no influence in the time spent under mechanical ventilation.

Other limitations need to be underlined. The patients receiving SDD were younger and the severity scores at admission were lower than those of controls. This reflects differences in triage and management of patients between both centres. In addition, the diagnosis of bacterial VAP is challenging in COVID-19 patients. Indeed, the clinical and radiological signs may be confounding between a viral infection and a bacterial infection. A pneumonic change on chest radiograph, the re-increase of biomarkers like procalcitonin or a change in the ferritin-to-procalcitonin ratio may help for the diagnosis [8]. The study did not resolve the uncertainty in the diagnostic of bacterial VAP among the included patients.

The systematic use of antibiotics in COVID-19 ICU patients is still under debate. At the onset of pandemics, the strategy tended to cover the potential bacterial co-infections, based on historical data. Indeed, autopsy series of patients dying during the 1918 influenza pandemic showed that evidence of bacterial co-infection on Gram stain in 94% of cases [9]. However, a previous study compared a first period in which prophylactic antibiotics were given at ICU admission for 5 days with a second period in which antibiotics were given only based on clinical and biological symptoms. The strategy based on prophylactic antibiotics was associated with an increased use of antibiotics but no association was found with the patient outcomes [10]. The prophylactic use of antibiotics has thus been ruled out by several ICU teams.

An inherent risk associated with SDD is the emergence of multidrug-resistant bacteria. This risk was not clearly investigated by the authors, which represents a weakness of the study. However, if outbreaks of multidrug-resistant bacteria were reported in patients treated with SDD, several studies showed

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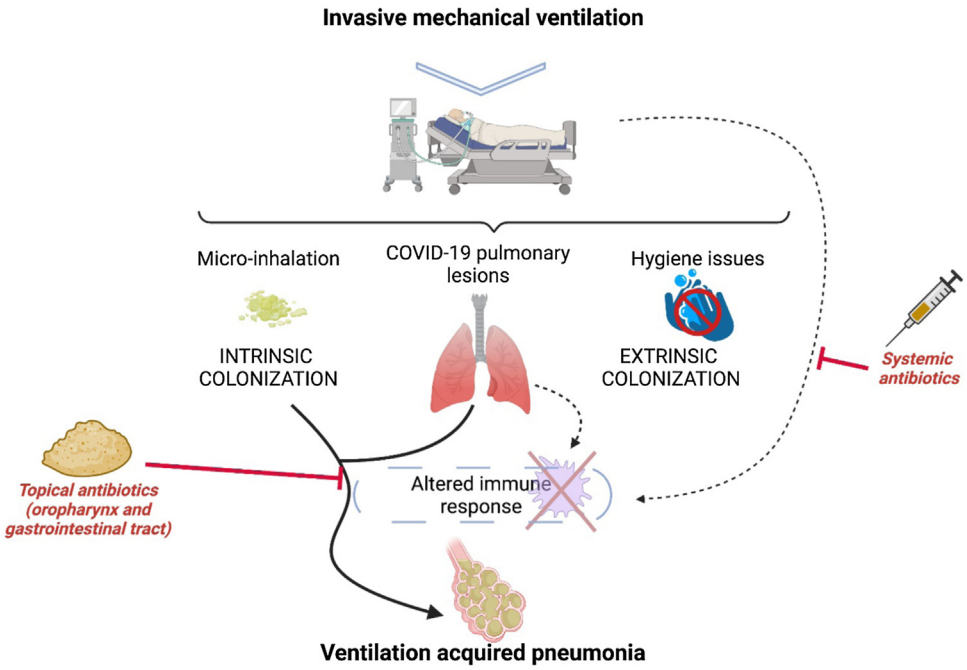

Fig. 1. Principle of selective digestive decontamination: is there a role in COVID-19?

that the incidence of resistance decreased after the implementation of SDD, mainly explained by a reduction in the global use of infections and consequently broad-spectrum antibiotics [11]. In COVID-19 patients, reducing the global exposure to antibiotics, especially in those developing long forms of the disease may be of interest.

Thus, to date, we still do not know either the true impact of SDD in patients with COVID-19, nor the effects of SDD on resistance level, which is still unclear in this population. The findings reported in this study are of major interest but several biases reflect an attitude of caution, like the imbalance between groups, the imprecision of diagnosis, different size effects between exposure to mechanical ventilation and VAP rate, and the lack of data on resistance emergence. Future studies are urgently needed in those patients.

Conflicts of interests

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