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CORRESPONDENCE

Ventilation-associated pneumonia and probiotics: many clues do not make evidence. Response to comments by Colombo and Codazzi

Juan Zeng and Chun-Ting Wang*

Dear Editor,

We thank Drs Jacopo Colombo and Daniela Codazzi for their interest in our article. Diagnosis of ventilator-associated pneumonia (VAP) is still a problem that is not yet fully solved [1]. Our study used the clinical diagnostic criteria of VAP as recommended by the American College of Chest Physicians (ACCP) and have also been used in a lot of randomized controlled clinical trials [2]. These criteria were also recommended by the Chinese Society of Critical Care Medicine and are widely used in China. Considering the histopathology of lung biopsies as a gold standard for VAP diagnosis, these criteria had reasonable diagnostic accuracy with a sensitivity of 69 % and a specificity of 75 % for VAP diagnosis [3]. The ACCP did not recommend the use of worsening oxygenation to diagnose VAP. In addition, the criteria of worsening oxygenation for VAP diagnosis varied considerably among different clinical criteria. Furthermore, the stricter clinical criteria used to diagnose VAP may lead to the poor outcome of critically ill patients. Vincent et al. reported that the delay before diagnosis of VAP increased from 4 to 8 days with increasingly stringent criteria and the mortality from 50 to 80 % [4]. The mortality was greatest in patients whose VAP was diagnosed using the most stringent set of criteria.

About the annual enrollment rate in our study; at first, the target amount was 20–22 patients per ICU. Some ICUs had to wait for the ethical approval in their own hospital and started the process of screening and enrollment late. Some ICUs achieved the target slowly and we had to change their target amount of enrollment. This led to further delays in the process of enrollment. So the amount of enrolled patients in every ICU per year was not the same.

Why did we choose a maximum study period of 14 days? A previous study reported that the administration of synbiotic for only 7 days resulted in a significantly lower incidence of potentially pathogenic bacteria and multiple organisms in nasogastric aspirates in critically ill patients than in controls [5]. The inhibition of potentially pathogenic bacteria in the upper gastrointestinal tract is the underlying mechanism of VAP prevention by probiotics. So chose the maximum study period of 14 days because it is a sufficient duration to allow the probiotics to exert their beneficial effects on the inhibition of potentially pathogenic bacteria in the stomach and VAP prevention.

The critically ill patients always had more than one site of infection at the same time. Probiotics have no beneficial effect on the incidence of clinically diagnosed VAP as our study reported. In general, the physicians started the initial antibiotics for VAP and stopped the antibiotic treatment according to the clinical signs but not microbiologic results. Consequently, although probiotics use was associated with the reduced incidence of VAP, the antibiotics consumption for VAP and antibiotic-free days did not decrease accordingly as our study reported. However, although probiotics are ineffective on outcomes including antibiotics use and our conclusion can not be generalized to ICUs with a lower VAP incidence as Drs. Colombo and Codazzi correctly stated, probiotics are

*Correspondence: wcteicu@126.com
Department of Intensive Care Unit, Shandong Provincial Hospital Affiliated to Shandong University, Jingwu Road 324#, Jinan, Shandong, People's Republic of China

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still considered as a promising alternative for VAP prevention by reducing bacterial colonization in the upper digestive tract via a combination of local and systemic effects in critically ill patients [6].

We agree with Drs. Colombo and Codazzi that the results with probiotics for VAP prevention are far from conclusive until now because the current clinical trials have different study populations, different sample sizes and designs, different definitions of VAP, and different probiotic strains, dosings, and routes of administration [7]. However, the positive results from these trials justify further double-blind placebo-controlled clinical trials with large sample sizes to evaluate the preventive effect of probiotics on VAP.

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Compliance with ethical standards

Conflicts of interest
There is no conflict of interest of any authors in relation to the submission and the future publication.

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