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Ventilator-associated pneumonia or bacterial colonization of the airway, what do probiotics decrease?

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Dear Editor,

Originating from a resource-limited country, the paper by Banupriya et al. [1] proposes an affordable and novel therapy for ventilator-associated pneumonia (VAP) reduction. However, there are a few concerns that need clarifications:

Banupriya et al. have cited VAP criteria used by Kollef MH et al. [2]. However, in contrast to the criteria used by Kollef to define VAP, as "new or 'progressive' radiographic infiltrates", Banupriya et al. have used "new or 'persisting' radiographic infiltrates (persisting beyond 72 h)" [1]. CDC/NHSN surveillance definition (2008) has also used the term 'new' or 'progressive and persistent' radiographic infiltrates. Persistence of radiographic infiltrates for 72 h or more is not uncommon in severe pneumonia; time to radiographic resolution may vary from 2 weeks (RSV or para-influenza) to 8 weeks (Pneumococcus). Around 51–60 % of children with severe pneumonia continue to be febrile on day 5 of treatment. Therefore, the authors may have significantly overdiagnosed VAP in children who were recovering from the primary pneumonia.

Tracheal cultures are sensitive (around 90 %) for diagnosis of VAP, but they have poor specificity (40 %). Though non-bronchoscopic techniques provide etiological clues, quantitative cultures alone ($>10^4$ CFU/ml) can differentiate between colonization and true infection [3]. Without quantitative cultures, the significant reduction in prevalence of airway colonization with *Klebsiella* and *Pseudomonas* in the probiotic group may not be a true reflection of a reduction in VAP. Data presented by Banupriya et al. show that probiotics reduced tracheal colonization; whether it reduced VAP is questionable. Also, a complete microbiological profile of the VAP and colonization should be presented to help readers assess applicability of these results in their work environment (external validity).

In studies on VAP, especially in open-label trials, it is important to record the degree of compliance to established 'VAP prevention bundles' as well as other standard care practices (hand hygiene, oral care, tracheal suctioning protocols, sedo-analgesia protocols, etc.). Increased emphasis on VAP prevention in the intervention group may have led to unintentional, better quality of care.

Banupriya et al. [1] have stratified patients by age for randomization, but have not used these strata while presenting the results. There is overwhelming evidence that variables used in the process of randomization should be accounted for in the analysis [4]. Also, Banupriya et al. have presented several continuous variables as mean and standard deviations (Tables 1, 3). Data of many of these variables appear skewed. Were these variables tested for normality using Kolmogrov–Smirnov or Shapiro–Wilk tests and non-parametric tests applied for these variables? Presentation of these variables as median and interquartile range could have been more meaningful.

Multiple logistic regression analysis was used to overcome the effect of confounding variables. It showed that probiotics decreased the risk of acquiring VAP by 77 %. However, two aspects are unclear: what were the variables entered into the regression analysis and why other proven risk factors of VAP such as genetic syndromes, transport-out-of-PICU, use of steroids, etc. [5] were not included in the analysis.

Clarifying the above issues would help the readers appreciate the work better.

Conflicts of interest On behalf of all the authors, the corresponding author states that there is no conflict of interest.

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