Letter to the Editor

Pulmonary surfactant combined with budesonide in the treatment of neonatal respiratory distress syndrome

Hongxing Guo[1], Xinyang Chen[2#], Haizhen Hui[3#], Qingbo Feng[1], Yuanxiang He[1]

[1]Department of General Surgery, Kweichow Moutai Hospital, Renhuai, China; [2]West China School of Medicine, West China Hospital, Sichuan University, Chengdu, China; [3]Department of Dermatology, Chongqing Hospital of Traditional Chinese Medicine (Chongqing Key Laboratory of Integrative Dermatology Research/Chongqing Clinical Research Center for Dermatology), Chongqing, China

[#]These authors contributed equally to this work.

Correspondence to: Yuanxiang He, MD. Department of General Surgery, Kweichow Moutai Hospital, Renhuai, China. Email: heyx-navy@sohu.com.

Comment on: Yi Z, Tan Y, Liu Y, *et al.* A systematic review and meta-analysis of pulmonary surfactant combined with budesonide in the treatment of neonatal respiratory distress syndrome. Transl Pediatr 2022;11:526-36.

Keywords: Pulmonary surfactant (PS); budesonide; neonatal respiratory distress syndrome (NRDS)

Submitted Jan 13, 2023. Accepted for publication Apr 30, 2023. Published online May 08, 2023.
doi: 10.21037/tp-23-30
View this article at: https://dx.doi.org/10.21037/tp-23-30

Newborn respiratory distress syndrome (RDS) is a disease that is unique to newborn infants and caused by a shortage of pulmonary surfactant (PS). Since hyaline membranes were observed in the alveoli of animal models of RDS, research has been conducted to supplement PS deficiency (1). It has been 30 years since PS replacement therapy was first offered for neonatal RDS (NRDS) in China. A recent article entitled "*A systematic review and meta-analysis of pulmonary surfactant combined with budesonide in the treatment of neonatal respiratory distress syndrome*" published in *Translational Pediatrics* caught our attention (2).

The authors have provided us with a meta-analysis evaluating PS in combination with budesonide in treating NRDS. The meta-analysis revealed that for infants with NRDS, the use of budesonide in combination with animal-derived PS can successfully shorten hospital stays, decrease the need for invasive mechanical ventilation, and lower the incidence of bronchopulmonary dysplasia, but it does not raise the incidence of fatal complications or other connected outcomes. Although the authors have discussed some shortcomings of this study, several limitations should be noticed.

To begin with, while the authors stated that they presented the article in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting checklist (3), it was discovered that this review was not International Prospective Register of Systematic Reviews (PROSPERO) registered nor had a Centre for Reviews and Dissemination (CRD) number after careful examination. In addition, there is a small error in the article. The authors stated there are 10 articles in this study involving 527 children, but it can be seen from the data in *Tab. 1* that the total number of patients in 10 articles have reached 1,177, which is clearly a contradiction.

Secondly, we found some subtle differences in the definition of outcome indicators in the articles included by the authors. In *Fig. 3*, the authors analyzed the effect of PS combined with budesonide on invasive mechanical ventilation time in infants with NRDS. However, Pan *et al.* defined the duration of ventilator use as the study outcome, and Wang *et al.* defined the duration of assisted ventilation as the study outcome (4,5). Both definitions include not only invasive mechanical ventilation, but also non-invasive mechanical ventilation, which may affect the results of the meta-analysis. Similarly, in *Fig. 6*, the outcome indicator discussed by the authors was the mortality rate of infants with NRDS, while in the study of Pan *et al.*, the outcome was limited to the case fatality rate at 36 weeks of corrected gestational age, which may lead to the accuracy of the results (4,5). More than that, the authors did not specify the severity of bronchopulmonary dysplasia. Most studies defined neonates requiring oxygen dependence for more

than 28 days, while bronchopulmonary dysplasia is defined as requiring more than 21% oxygen in Wang *et al.* and Yeh *et al.*'s studies (5,6). These differences may also affect the conclusion of this meta-analysis.

Thirdly, interventions are often different in different studies, and the authors considered that different administration methods might affect the results of the meta-analysis, so a subgroup analysis was conducted to exclude the influence of the mode of administration on the results. Therefore, it is suggested that the authors should also conduct a subgroup analysis for different drug dosages, which would make the results more accurate and reliable.

In the end, most of the articles included by the authors are in Chinese, which may have a certain publication bias. The authors did not use funnel plots for qualitative assessment of publication bias nor statistical tests (e.g., Begg's or Egger's tests) for quantitative assessment. In addition, sensitivity analysis is necessary for meta-analysis, yet the authors did not conduct sensitivity analysis to make the results more convincing. These are some of the details we think the authors should add.

In summary, Yi *et al.* carried out a good-quality meta-analysis to analyze the effect of PS combined with budesonide in the treatment of NRDS. We appreciate the contribution of the authors and believe that this is a valuable study. There is a generational change taking place in the era of PS, rather than just improving infant survival, this will likely lead to better outcomes and a lower complication rate.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was a standard submission to *Translational Pediatrics*. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-23-30/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Bae CW, Kim CY, Chung SH, et al. History of Pulmonary Surfactant Replacement Therapy for Neonatal Respiratory Distress Syndrome in Korea. J Korean Med Sci 2019;34:e175.
2. Yi Z, Tan Y, Liu Y, et al. A systematic review and meta-analysis of pulmonary surfactant combined with budesonide in the treatment of neonatal respiratory distress syndrome. Transl Pediatr 2022;11:526-36.
3. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2535.
4. Pan J, Chen MW, Ni WQ, et al. Clinical efficacy of pulmonary surfactant combined with budesonide for preventing bronchopulmonary dysplasia in very low birth weight infants. Chinese Journal of Contemporary Pediatrics 2017;19:137-41.
5. Wang YZ, Zhang DF. Effect of budesonide inhalation combined with pulmonary surfactant on newborns with RDS. Modern Medical Journal 2018;46:1243-6.
6. Yeh TF, Chen CM, Wu SY, et al. Intratracheal administration of budesonide/surfactant to prevent bronchopulmonary dysplasia. Am J Respir Crit Care Med 2016;193:86-95.

Cite this article as: Guo H, Chen X, Hui H, Feng Q, He Y. Pulmonary surfactant combined with budesonide in the treatment of neonatal respiratory distress syndrome. Transl Pediatr 2023;12(6):1288-1289. doi: 10.21037/tp-23-30