



## EDITORIAL

## Pulmonary Drug Delivery by Surfactant



Exogenous surfactant and early use of nasal continuous positive airway pressure significantly decreased the incidence and severity of respiratory distress syndrome (RDS) and improved the survival of preterm infants. However, the incidence of RDS-related complication-chronic lung disease (CLD) is still high.<sup>1,2</sup> This may be due to the multifactorial etiology of CLD. Recently, Huang et al<sup>3</sup> reported that combined administration of surfactant and budesonide further increased the fluorescent intensity in the lungs of mice compared with the control condition. This study may give us an alternative therapeutic strategy for not only treating RDS but also for preventing the subsequent development of CLD in preterm infants.

The causes of bronchopulmonary dysplasia (BPD) include immaturity, genetic susceptibility, prolonged oxygen therapy, barotrauma, inflammation, and nutritional deficiency.<sup>4</sup> Among these factors, inflammation induced by oxygen therapy or sepsis plays an important role in the pathogenesis of CLD in preterm infants, especially for those with RDS. Therefore, systemic glucocorticoids have been used to prevent or treat CLD in preterm infants who required prolonged mechanical ventilation by suppressing the lung inflammation. However, because of the systemic glucocorticoids are not recommended for routine use now.<sup>5</sup> So far, no effective therapy has been proven useful in preventing CLD in preterm infants.

Because preterm infants complicated with RDS require oxygen therapy or ventilator support right after birth, the CLD-related inflammatory process may also start as early as the first breath. Thus, intratracheal delivery steroid with surfactant for preterm infants with RDS may have the advantages of early prevention of inflammation and of decreasing the side effects of the steroid due to local treatment rather than systemic therapy. Previously Yeh et al<sup>6</sup> demonstrated that early postnatal intratracheal instillation of budesonide using surfactant as a vehicle significantly improved the combined outcome of death or chronic lung disease, and also increased the number of survivors without CLD. However, the pulmonary distribution of budesonide is not clear. By using the *in vivo* image system, Huang et al<sup>3</sup> demonstrated that mice treated with both surfactant and budesonide showed a significant increase in fluorescent intensity compared with mice treated with either surfactant or budesonide alone. These data show that surfactant is not only powerful for treating RDS, but also that surfactant alone or with budesonide can be used as an effective vehicle for pulmonary drug delivery.

## **Conflicts of interest**

The author declares no conflicts of interest.

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## References

- Nakhshab M, Tajbakhsh M, Khani S, Farhadi R. Comparison of the effect of surfactant administration during nasal continuous positive airway pressure with that of nasal continuous positive airway pressure alone on complications of respiratory distress syndrome: a randomized controlled study. *Pediatr Neonatol* 2015;56:19–24.
- 2. Dunn MS, Kaempf J, de Klerk A, de Klerk R, Reilly M, Howard D, et al. Randomized trial comparing three approaches to the initial respiratory management of preterm neonates. *Pediatrics* 2011;**128**:e1069–76.
- Huang LT, Yeh TF, Kuo YL, Chen PC, Chen CM. Effect of surfactant and budesonide on the pulmonary distribution of fluorescent dye in mice. *Pediatr Neonatol* 2014. http://dx. doi.org/10.1016/j.pedneo.2014.04.009. pii:S1875-9572(14) 00128-4, [Epub ahead of print].

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- 4. Martin RJ, Fanaroff AA. The preterm lung and airway: past, present, and future. *Pediatr Neonatol* 2013;54:228-34.
- Yeh TF, Lin YJ, Lin HC, Huang CC, Hsieh WS, Lin CH, et al. Outcome at school age after postnatal dexamethasone therapy for lung disease of prematurity. N Engl J Med 2004;350:1304–13.
- 6. Yeh TF, Lin HC, Chang CH, Wu TS, Su BH, Li TC, et al. Early intratracheal instillation of budesonide using surfactant as a vehicle to prevent chronic lung disease in preterm infants: a pilot study. *Pediatrics* 2008;121:e1310–8.