Should We Do Lung Recruitment Maneuvers When Giving Surfactant?

Commentary on the article by Krause *et al.* on page 34

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In the beginning of the surfactant era, various more or less elaborate procedures were performed at the time of surfactant instillation, including chest-positioning, manual ventilation, and changes in ventilator settings (1, 2). These procedures were thought to facilitate surfactant spreading but were largely undocumented and have gradually come out of fashion. Surfactant is now often given as one or two rapid boluses in the trachea during a short disconnection from the ventilator, and it is generally thought that the different techniques are probably similar in terms of outcome (3).

However, the poor documentation does not necessarily mean that these techniques are ineffective. In adults with acute lung injury or collapsed lungs during anesthesia, lung recruitment maneuvers can very effectively remove atelectasis and improve lung function (4, 5). Surfactant deficient preterm infants have a decreased stability of air spaces in expiration. During mechanical ventilation, this may lead to lung collapse if PEEP is set too low and if expiration time is unduly long. Such collapsed air spaces would, at least in theory, be recruitable if a sufficiently high end-inspiratory pressure is applied. If this is done before and during surfactant instillation, surfactant would be expected to spread into a larger part of the lung. Air spaces, temporarily stabilized by the recruitment maneuver, could be more permanently stabilized by surfactant, and the net result would be an improved effect of treatment. Krause and coworkers should be commended for exploring this possibility in a series of animal studies.

In young rabbits, surfactant depleted by lung lavage, a volume recruitment maneuver consisting of an increase in tidal volumes from 10 to 17.5 mL/kg during and after airway infusion of bovine surfactant (Survanta) resulted in an increase in FRC, dynamic compliance, and alveolar ventilation; these effects were not seen in rabbits receiving surfactant alone (6). However, these animals were ventilated with a PEEP of only 1 cm H_2O. When the study was repeated using a clinically more realistic PEEP of 3 cm H_2O, there was no effect of volume recruitment (7).

In this issue of *Pediatric Research*, Krause *et al.* (8) report the effects of three different lung recruitment maneuvers *versus* no recruitment on lung function, surfactant distribution, and lung morphology in lung-lavaged piglets treated with porcine surfactant (Curosurf). An increase in peak inspiratory pressure from 22 to 29 cm H_2O, causing an increase in tidal volume from 8 to 16 mL/kg, over a 12-min period before and after surfactant instillation gave the best response in terms of gas exchange and lung mechanics. Lung recruitment also resulted in a more homogenous surfactant distribution. Are these findings in animals with acquired surfactant deficiency applicable to preterm infants with RDS?

Lung lavage of previously healthy mature animals will induce a severe surfactant deficiency, decreased stability of air spaces, and widespread alveolar collapse. Such animals have a markedly reduced FRC, while inspiratory capacity (the volume change of the lungs from 0 to 30 cm H_2O, *i.e.* the equivalent of vital capacity as measured in spontaneously breathing subjects) initially remains unchanged (9). The atelectatic lung parts are relatively easy to open and are less unstable than in other models (10). The good effect of the recruitment maneuvers is therefore not surprising.

The pathophysiology of human RDS is often described in similar terms, *i.e.* alveolar collapse and low FRC, but the true situation is probably more complicated. Krause *et al.* state that the lack of improvement in dynamic compliance immediately after surfactant treatment of human infants with RDS suggests that a substantial compartment of unventilated air spaces still exists (8). This may be true, but it does not necessarily follow that these air spaces would be recruitable before surfactant administration. An unventilated compartment could be explained by atelectasis, which might be opened by a recruitment maneuver. Such maneuvers are certainly often used with good effect, *e.g.* after disconnections from the ventilator and endotracheal suctioning. However, in severe RDS, an unventilated compartment could also be caused by *e.g.* edema, hyaline membranes, or inflammatory infiltrates, which may not be eliminated by pressure alone.

In preterm monkeys, the major cause for the loss of lung capacity is the presence of proteinaceous alveolar edema rather than alveolar collapse (11). This results in a proportionally greater reduction in inspiratory capacity than in FRC (12). Similar lung mechanical findings have been reported in human infants with severe RDS (13), suggesting that a substantial portion of the unventilated lung compartment is probably not recruitable.

Krause *et al.* suggest that the RDS lung consists of populations of alveoli with varying degrees of instability and collapse (8). An alternative model would be that a large part of the lung is fluid-filled and does not take part in gas exchange, while some of the ventilated lung parts may have relatively normal mechanical properties. If the latter model is true, large tidal volumes may lead to overdistension of the aerated lung parts, while the fluid-filled parts cannot be recruited.

It is thought that lung injury may occur if end-inspiratory volume exceeds TLC (14). In ventilated neonates with healthy lungs, the maximal tidal volume range, *i.e.* the difference between FRC and TLC, was 23–38 (median 26) mL/kg, while in infants with severe RDS, it was only 5–19 (median 9) mL/kg (13). If large tidal volumes are used for recruitment, the safety margin may therefore be small.

Krause *et al.* end by stating that further trials of recruitment should be done in a "true" RDS model (8). We did a small study in five pairs of preterm twin lambs (15), where one twin in each pair was given five sustained lung inflations of 20 mL/kg just before rescue surfactant at 30 min of age. Peak Pa_{O_2} at 10 min after surfactant was significantly higher in the recruited lambs, suggesting a transient beneficial effect. However, inspiratory capacity, static compliance, and *postmortem* intrapulmonary air volume at 4 h was not significantly different between groups.

Surfactant is now often given shortly after birth as prophylaxis against RDS. At birth, the lung is fluid-filled rather than atelectatic, and experimental studies do not support the use of lung recruitment. In preterm lambs, surfactant spreads less homogeneously in a ventilated lung than when given before the first breath (16), and preliminary results from our laboratory indicate that this inhomogeneity is particularly pronounced following a recruitment maneuver at birth (17). Moreover, several studies in the lamb model have shown that hyperinflation of the lungs early in life may cause a blunted response to surfactant and signs of lung injury (18–20).

At present, we would advise against any attempt to recruit lung volume in the surfactant deficient preterm infant by large lung inflations at birth. As regards the situation when surfactant is given later, as rescue treatment for established RDS, the evidence for a clinically beneficial effect is so far insufficient. Hopefully, the study by Krause *et al.* will stimulate others to gather more data on this aspect.

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