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A pilot, randomized, controlled clinical trial of lucinactant, a peptide-containing synthetic surfactant, in infants with acute hypoxemic respiratory failure.

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Abstract

OBJECTIVE: Inhibition of surfactant function and abnormal surfactant synthesis lead to surfactant dysfunction in children with acute hypoxemic respiratory failure. We evaluated whether intratracheal lucinactant, a synthetic, peptide-containing surfactant, was safe and well-tolerated in infants with acute hypoxemic respiratory failure, and assessed its effects on clinical outcomes.

METHODS AND MAIN RESULTS: Infants ≤ 2 yrs of age with acute hypoxemic respiratory failure were enrolled in a phase II, double-blind, multinational, placebo-controlled randomized trial across 36 pediatric intensive care units. Infants requiring mechanical ventilation with persistent hypoxemia meeting acute lung injury criteria were randomized to receive intratracheal lucinactant (175 mg/kg) or air placebo. One retreatment was allowed 12-24 hrs after initial dosing if hypoxemia persisted. Peri-dosing tolerability of intratracheal lucinactant and adverse experiences were assessed. Mechanical ventilation duration was analyzed using analysis of variance. The Cochran-Mantel-Haenszel test was used for categorical variables.We enrolled 165 infants (84 lucinactant; 81 placebo) with acute hypoxemic respiratory failure. There were no significant differences in baseline subject characteristics, with the exception of a lower positive end-expiratory pressure and higher tidal volume in placebo subjects. The incidence of transient peri-dosing bradycardia and desaturation was significantly higher in the lucinactant treatment group. There were no statistical differences between groups for other adverse events or mortality. Oxygenation improved in infants randomized to receive lucinactant as indicated by fewer second treatments (67% lucinactant vs. 81% placebo, p = .02) and a trend in improvement in partial pressure of oxygen in arterial blood to fraction of inspired oxygen from eligibility to 48 hrs after dose (p = .06). There was no significant reduction in duration of mechanical ventilation with lucinactant (geometric least square means: 4.0 days lucinactant vs. 4.5 days placebo; p = .254). In a subset of infants (n = 22), the duration of mechanical ventilation in children with acute lung injury (partial pressure of oxygen in arterial blood to fraction of inspired oxygen >200) was significantly shorter with lucinactant (least square means: 2.4 days lucinactant vs. 4.3 days placebo; p = .006).

CONCLUSIONS: In mechanically ventilated infants with acute hypoxemic respiratory failure, treatment with intratracheal lucinactant appeared to be generally safe. An improvement in oxygenation and a significantly reduced requirement for retreatment suggests that lucinactant might improve lung function in infants with acute hypoxemic respiratory failure.