



Association of Fluid Balance With Short- and Long-term Respiratory Outcomes in Extremely Premature Neonates

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Background

Mounting evidence shows that BPD may be due to a systemic insult on top of susceptible, premature lungs—especially when timed during critical periods of lung development.

- One common co-morbidity in premature infants is acute kidney injury (AKI) which occurs in 40% of extremely premature infants.
- AKI was initially thought to be an isolated organ dysfunction, but recent work suggests AKI is an inflammatory condition that contributes to the dysfunction of other organs, including the lung.
- The author and others have previously reported that infants with AKI had a higher likelihood of BPD (x4 and 70% more)
- The mechanism of this association is unknown but Altered angiogenesis is observed in animal models and in premature infants after kidney injury.

Questions

Is fluid balance associated with respiratory outcomes in extremely premature neonates?

Study design/inclusion criteria/exclusion criteria

This study is a secondary analysis of the Preterm Erythropoietin Neuroprotection Trial (PENUT), conducted in 30 neonatal intensive care units in the US from 2013 to 2016. This analysis included 874 extremely premature neonates born at 24 to 27 weeks gestation. Secondary analysis was performed in November 2021.

The inclusion criteria were (1) infants born between 24 0/7 and 27 6/7 weeks of gestation in participating NICUs, (2) enrollment at less than 24 h of age, and (3) available arterial or venous access.

Exclusion criteria included: (1) major life-threatening brain, cardiac, and chromosomal anomalies; (2) hematologic crises such as disseminated intravascular coagulation or hemolysis (3) hematocrit >65%; (4) hydrops fetalis; (5) known congenital infection (6) neonates who died in the first 14 days

Results

A total of 874 neonates were included in this analysis. 458 (52.4%) received mechanical ventilation on postnatal day 14, and 291 (33.3%) had severe BPD or had died. Median peak positive FB was 11%, occurring on postnatal day 13 (IQR, 9-14). A total of 93 (10.6%) never decreased below their BW. Neonates requiring mechanical ventilation at postnatal day 14 had a higher peak FB compared with those who did not require mechanical ventilation. On postnatal day 3, neonates requiring mechanical ventilation were more likely to have a higher FB (5%below BW vs 8%below BW, $P < .001$). The median time to return to BW was shorter in neonates who received mechanical ventilation (7 vs 8 days, $P < .001$) and those with severe BPD (7 vs 8 days, $P < .001$). After adjusting for confounding variables, for every 10% increase in peak FB during the first 14 postnatal days, there was 103%increased odds of receiving mechanical ventilation at postnatal day 14.

Primary outcome

invasive mechanical ventilation (high-frequency or conventional ventilation) on postnatal day 14.

Secondary outcome

severe BPD or death according to Neonatal Research Network definitions by Jensen criteria

Conclusion

In this secondary analysis of a placebo-controlled randomized clinical trial in 874 premature neonates, fluid balance during the first 2 postnatal weeks was associated with mechanical ventilation and bronchopulmonary dysplasia. The time to return to birth weight was shorter in neonates who continued to receive mechanical ventilation, and every 5%increase in fluid balance was associated with an increase in the odds of mechanical ventilation.