# Safety of furosemide in preterm infants at risk of bronchopulmonary dysplasia: A randomized controlled trial

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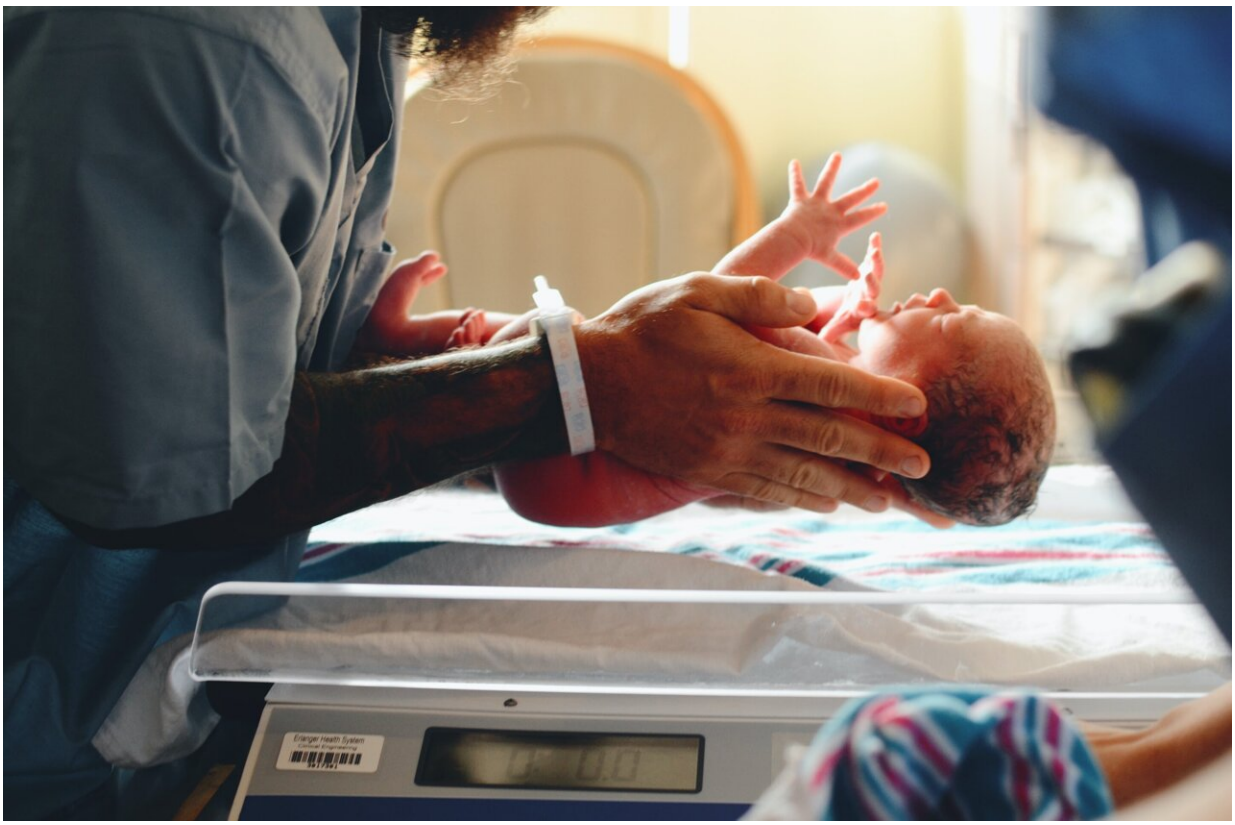

Credit: Unsplash/CC0 Public Domain

A randomized controlled trial evaluates the safety of furosemide in preterm infants at risk of bronchopulmonary dysplasia. Findings from

the study will be presented during the Pediatric Academic Societies (PAS) 2022 Meeting, taking place April 21-25 in Denver.

The objective of the study was to evaluate the safety and preliminary efficacy of furosemide in preterm infants at risk of developing bronchopulmonary dysplasia.

Researchers found that in preterm infants at high risk for bronchopulmonary dysplasia, adverse events occurred in nearly all infants regardless of treatment group. Furosemide increased the risk of electrolyte adverse events. There was no difference in hearing loss, nephrocalcinosis, or bronchopulmonary dysplasia/death.

"The drug furosemide is commonly used in premature infants hospitalized in the neonatal intensive care unit to prevent bronchopulmonary dysplasia, a type of chronic lung disease," said Rachel G. Greenberg, MD, MB, MHS, associate professor of pediatrics with the division of neonatal-perinatal medicine at Duke University Medical Center, and program director with Duke Neonatal-Perinatal Medicine Fellowship. "Unfortunately, very little data is available to help neonatologists understand whether furosemide is safe and effective. Our study, which was performed at 17 centers within the NICHD Pediatric Trials Network, was the first randomized controlled trial to evaluate the safety and preliminary efficacy of furosemide in premature infants at risk for developing bronchopulmonary dysplasia."

| | Cohort 1 Furosemide (N=31) | Cohort 2 Furosemide (N=30) | Placebo (N=19) |
|---|---|---|---|
| **Gestational age (weeks)** | 26.7 (25.1, 27.4) | 25.9 (24.7, 26.6) | 25.3 (24.6, 27.9) |
| **Birth weight (g)** | 840 (700, 960) | 743 (630, 900) | 800 (650, 1020) |
| **Baseline weight (g)** | 923 (735, 1108) | 908 (810, 1030) | 1020 (800, 1200) |
| **Postnatal age at randomization (days)** | 14 (10, 24) | 25 (19, 27) | 22 (18, 27) |
| **Male** | 14 (45) | 14 (47) | 11 (58) |
| **Race** | | | |
| **White** | 18 (58) | 16 (53) | 8 (42) |
| **Black** | 10 (32) | 9 (30) | 10 (53) |
| **Other** | 0 (0) | 1 (3) | 1 (5) |
| **Not reported** | 3 (10) | 4 (13) | 0 (0) |
| **Hispanic ethnicity**[a] | 3 (10) | 7 (23) | 2 (11) |
| **Respiratory status at randomization** | | | |
| **High frequency ventilator** | 5 (16) | 5 (17) | 3 (16) |
| **Conventional mechanical ventilator** | 6 (19) | 12 (40) | 8 (42) |
| **Non-invasive support**[b] | 20 (65) | 13 (43) | 8 (42) |

Categorical values are shown as n (%). Continuous values are shown as median (25th, 75th percentiles).

[a]No ethnicity reported in 1 infant Cohort 2 Furosemide group and 1 infant in Placebo group

[b]Non-invasive support includes non-invasive positive pressure ventilation, high flow nasal cannula >1 liter per minute, continuous positive airway pressure

Demographics and clinical characteristics. Credit: Duke Clinical Research Institute

| | Cohort 1 Furosemide (N=31) | Cohort 2 Furosemide (N=30) | Placebo (N=19) |
|---|---|---|---|
| **Number of AEs** | 123 | 100 | 70 |
| **Infants with at least one AE** | 28 (90) | 28 (93) | 18 (95) |
| **Number of SAEs** | 8 | 6 | 2 |
| **Infants with at least one SAE** | 7 (23) | 5 (17) | 2 (11) |
| **Number of related SAEs** | 1 | 1 | 0 |
| **Participants with at least one related SAE** | 1 (3) | 1 (3) | 0 |
| **AE severity** | | | |
| **Mild** | 54 | 53 | 47 |
| **Moderate** | 61 | 35 | 20 |
| **Severe** | 8 | 12 | 3 |
| **Highest AE severity per participant** | | | |
| **Mild** | 11 (36) | 8 (27) | 9 (47) |
| **Moderate** | 10 (32) | 13 (43) | 7 (37) |
| **Severe** | 7 (23) | 7 (23) | 2 (11) |
| **Relationship (all AEs)** | | | |
| **Not related** | 82 | 66 | 62 |
| **Related** | 41 | 34 | 8 |
| **Strongest relationship per participant** | | | |
| **Not related** | 12 (39) | 10 (33) | 13 (68) |
| **Related** | 16 (52) | 18 (60) | 5 (26) |
| **Severity (all SAEs)** | | | |
| **Moderate** | 2 | 2 | 1 |
| **Severe** | 6 | 4 | 1 |
| **Relationship (all SAEs)** | | | |
| **Moderate** | 7 | 5 | 2 |
| **Severe** | 1 | 1 | 0 |
| **Severity (all related SAEs)** | | | |
| **Severe** | 1 | 1 | 0 |

Values are given as either n or n(%). AE=adverse event; SAE=serious adverse event

Adverse events. Credit: Duke Clinical Research Institute

| | Cohort 1 Furosemide (N=31) | Cohort 2 Furosemide (N=30) | Placebo (N=19) |
|---|---|---|---|
| **Moderate or Severe BPD or death*** | 17/27 (63) | 22/26 (85) | 12/18 (67) |
| **Nephrocalcinosis** | | | |
| **Negative** | 22 (71) | 21/25 (84) | 12/17 (71) |
| **Positive** | 9 (29) | 4/25 (16) | 5/17 (29) |
| **No ultrasound available** | 0 | 5 | 2 |
| **Hearing loss** | 4/31 (13) | 4/25 (16) | 4/18 (22) |
| **Serum electrolyte adverse event** | 26/31 (84%) | 28/30 (93%) | 12/19 (63%) |

*This outcome was missing in 9 infants who did not complete BPD assessment. BPD=bronchopulmonary dysplasia

Secondary end points. Credit: Duke Clinical Research Institute

Dr. Greenberg added that they "found that infants exposed to furosemide had more electrolyte problems but no greater risk of overall safety events, including kidney stones and hearing problems. The results of this study will help the practicing neonatal provider and help to design future trials."

**More information:** Conference: www.pas-meeting.org/

Provided by American Pediatric Society