Contemporary PEDIATRICS

Ibuprofen not linked to lower mortality, bronchopulmonary dysplasia risk in infants

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News *Article*

There are reports that prophylaxis with ibuprofen in the first 12 to 24 hours of life can reduce the risk of severe intraventricular hemorrhage and pulmonary hemorrhage. However, it has not been found to increase survival without neurosensory impairment at 18 months.

Ibuprofen not linked to lower mortality, bronchopulmonary dysplasia risk in infants | *Image Credit: © appledesign - © appledesign - stock.adobe.com.*

Takeaways:

- A study published in The New England Journal of Medicine found no evidence that early treatment with ibuprofen reduced the incidence of death or moderate or severe bronchopulmonary dysplasia in extremely preterm infants with a large patent ductus arteriosus (PDA).
- The research focused on extremely preterm infants born between 23 weeks 0 days' and 28 weeks 6 days' gestation with a PDA of 1.5 mm or larger. The investigators conducted a randomized, double-blind, placebo-controlled trial involving 318 infants receiving ibuprofen and 318 receiving a placebo.
- The primary outcome, a composite of death or moderate or severe bronchopulmonary dysplasia evaluated at 36 weeks of postmenstrual age, showed no significant difference between the ibuprofen and placebo groups (adjusted RR, 1.09; P = 0.10).
- The incidence of death in the ibuprofen group was 13.6% compared to 10.3% in the placebo group, and the occurrence of moderate or severe

bronchopulmonary dysplasia was 64.2% in the ibuprofen group and 59.3% in the placebo group.
- The study concluded that early treatment with ibuprofen in extremely preterm infants with a large PDA did not show a lower incidence of death or moderate or severe bronchopulmonary dysplasia compared to the placebo.

There was no evidence that early treatment with ibuprofen was linked to a lower incidence of death or moderate or severe bronchopulmonary dysplasia in extremely preterm infants with a large patent dictus arteriosus (PDA), according to a recently published study in *The New England Journal of Medicine*.

In the last 20 years, the incidence of bronchopulmonary dysplasia has increased among extremely preterm infants. A higher mortality and morbidity, along with a higher risk of bronchopulmonary dysplasia is associated with a large PDA in this gestation group (≥1.5 mm in diameter).

According to the investigative team, the incidence of PDA is "inversely proportional to gestational age at birth: more than 40% of infants born at less than 28 weeks' gestation have persistent PDA by 4 months of age."

PDA beyond 1 to 2 weeks of age is also associated with increased risk of bronchopulmonary dysplasia or death in extremely preterm infants.

There are reports that prophylaxis with ibuprofen in the first 12 to 24 hours of life can reduce the risk of severe intraventricular hemorrhage and pulmonary hemorrhage. However, it has not been found to increase survival without neurosensory impairment at 18 months, the investigators stated.

Since PDAs can close spontaneously, many infants will receive unnecessary prophylactic treatment. Data on the treatment of infants with a symptomatic PDA are limited and there are lacking reports of clinical improvement outcomes.

The investigators hypothesized that patients with a PDA of 1.5 mm or larger (diameter)—with unrestricted flow that has been identified with bedside echocardiography—would see reductions in mortality and improvements in short-term outcomes, such as bronchopulmonary dysplasia, with early selective treatment (≤72 hours after birth) using ibuprofen compared to placebo.

The investigative team conducted a randomized, multicenter, double-blind, and placebo-controlled trial to evaluate early treatment with ibuprofen in extremely preterm infants (born

between 23 weeks 0 days' and 28 weeks 6 days' gestation) with a large PDA.

A composite of death or moderate or severe bronchopulmonary dysplasia evaluated at 36 weeks of postmenstrual age was the primary outcome of the trial.

Transthoracic echocardiography was performed for eligibility within 72 hours after birth and at 3 weeks of age (18 to 24 days) to assess the patency of the PDA. For the primary analysis, a physiological challenge of supplemental oxygen reduction was used to test oxygen need at 36 weeks. This differentiated mild and moderate bronchopulmonary dysplasia.

In all, 318 infants with data for outcome analysis were assigned to receive ibuprofen and 318, respectfully, received placebo.

A primary outcome event occurred in 220 of 318 infants in the ibuprofen group (69.2%) while an event occurred in 202 of 318 infants in the placebo group (63%) (adjusted RR, 1.09; 95% CI, 0.98-1.20 [*P* = 0.10]).

Forty-four of 323 infants in the ibuprofen group died (13.6%) compared to 33 of 321 infants (10.3%) in the placebo group (adjusted RR, 1.32; 95% CI, 0.92-1.90).

Moderate or severe bronchopulmonary dysplasia occurred in 176 of 274 infants in the ibuprofen group (64.2%) vs in 169 of 285 (59.3%) in the placebo group (adjusted RR, 1.09; 95% CI, 0.96-1.23), and 2 unforeseeable serious adverse events potentially related to ibuprofen occurred.

The study authors concluded that in the trial "involving extremely preterm infants with a large PDA, we found no evidence that early treatment with ibuprofen was associated with a lower incidence of death or moderate or severe bronchopulmonary dysplasia at 36 weeks of postmenstrual age than placebo. There was no significant between-group difference in either the risk of death or the risk of moderate or severe bronchopulmonary dysplasia."

Reference:

Gupta S, Subhedar NV, Bell JL, et al. Trial of selective early treatment of patent ductus arteriosus with ibuprofen. *N Engl J Med*. 2024;390(4):314-325. doi:10.1056/NEJMoa2305582

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