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Transient tachypnea of the newborn

Anne-Catherine Vanhove[a], Trudy Bekkering[a], Filip Cools[a]

[a] Cochrane Belgium, Belgian Centre for Evidence-Based Medicine (Cebam)

info@cochrane.be

Question

Are restricted fluid therapy or treatment with salbutamol effective and safe to treat transient tachypnea in neonates?

Context

Transient tachypnea of the newborn (TTN) is characterized by abnormally fast breathing and signs of respiratory distress starting shortly after birth. It is caused by delayed clearance of fluids in the lungs and typically occurs in term and late preterm newborns. Although TTN is usually self-limiting, it does result in many neonatal intensive care unit admissions for supportive care and sometimes even respiratory support. Several Cochrane reviews have already been published about possible treatments for this condition, such as diuretics, steroids and epinephrine, but at the moment the only treatment for TTN remains supportive care, primarily intravenous fluid and oxygen therapy. Recently two new Cochrane reviews were published investigating the effectiveness and safety of fluid restriction therapy and salbutamol treatment respectively (Gupta 2021, Moresco 2021). Both treatments may accelerate the clearance of fluids from the lungs, resulting in faster resolution of symptoms and decreased need for supportive care and/or hospitalization.

Criteria for study selection

The first review compared the use of restricted versus standard fluid therapy in term and preterm neonates with TTN. Restricted fluid therapy consisted of a total fluid intake that was 90% or less than the standard amount for at least 24 hours in the first week of life. The salbutamol review compared the use of salbutamol to placebo, no treatment or any other drugs in infants born at least 34 weeks' gestational age. The primary outcomes in both reviews were duration of supplemental oxygen therapy and the need for non-invasive or invasive ventilation.

Summary of the results

Fluid restriction

Four studies with 317 infants were included in the review. Three studies included late preterm and term neonates with TTN and the fourth trial included only term neonates. The infants were on different additional respiratory support methods (room air, oxygen, nasal continuous positive airway pressure). The neonates in the fluid restriction group received 15 to 20 mL/kg/day less fluid than those in the standard fluid therapy group. Typically, term infants would receive 40, 60 and 80 mL/kg/ day in the fluid restricted group, and 60, 80 and 100 mL/kg/day in the standard group on day 1, 2 and 3 of life. The duration of the intervention varied.

We are uncertain whether fluid restriction therapy, compared to standard fluid therapy, decreases or increases the duration of oxygen therapy (control: range 6-53 hours vs intervention: on average 13 hours less (95% CI*: 33 hours less to 7 hours more); 2 studies, 172 neonates, very low-certainty evidence), the need for invasive ventilation (control: 57 per 1000 vs intervention: 42 per 1000 (95% CI*: 13 to 128 per 1000); 3 studies, 242 neonates, very low-certainty evidence) or the need for non-invasive ventilation (control: 250 per 1000 vs intervention: 100 per 1000 (95% CI*: 35 to 292 per 1000); 2 studies, 150 neonates, very low-certainty evidence). Similarly, there is uncertainty for the incidence of hypernatremia and hypoglycemia, length of hospital stay and cumulative weight loss at 72 hours of age.

Salbutamol

Seven studies with 498 neonates compared a nebulized dose of salbutamol to normal saline. Either a single dose was administered (4 studies), 3 to 4 doses (2 studies) or additional doses were administered if needed (1 study). The duration of oxygen therapy was significantly reduced in the infants receiving salbutamol (control: range 26-77 hours vs intervention: on average 19 hours less (95% CI*: 24 to 15 hours less); 4 studies, 338 neonates), but the level of certainty about this effect was downgraded to very low because of risk of bias, inconsistency of results between studies, and small sample size. The use of salbutamol may also decrease the length of hospital stay by about 1.5 days (control: range 5-9 days vs intervention: on average 1.5 days less (95% CI*: 1.8 to 1.2 days less); 4 studies, 338 neonates, low-certainty evidence). We are uncertain about the effect of salbutamol on the need for continuous positive airway pressure (control: 533 per 1000 vs intervention: 389 per 1000 (95% CI*: 203 to 741 per 1000) 1 study, 46 neonates, very low-certainty evidence) or the need for mechanical ventilation (control: 25 per 1000 vs intervention: 15 per 1000 (95% CI*: 3 to 71 per 1000); 3 studies, 254 neonates, very low-certainty evidence). We are also uncertain about the effect on the duration of respiratory support and the occurrence of pneumothorax. Duration of mechanical ventilation was not reported in any of the studies.

Conclusion

Only limited evidence was available for both interventions. It is still uncertain whether fluid restriction therapy or salbutamol treatment have any positive effects on the duration of oxygen therapy and the need for invasive of non-invasive ventilation. Salbutamol may shorten the length of stay at the hospital. Five trials with salbutamol are still ongoing and given the simplicity of the fluid restriction intervention, a well-designed trial should be considered to evaluate its effectiveness and safety.

Implications for practice

As of now, it still remains unclear whether fluid restriction therapy or treatment with salbutamol are effective or safe.

REFERENCE:

Gupta N, Bruschettini M, Chawla D. Fluid restriction in the management of transient tachypnea of the newborn. Cochrane Database of Systematic Reviews 2021, Issue 2. Art. No.: CD011466. DOI: 10.1002/14651858.CD011466.pub2.

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Access the full text of these reviews via the Cebam Digital Library for Health (www.cebam.be/nl/cdlh or www.cebam.be/fr/cdlh)

* **CI:** confidence interval
^ **MD:** mean difference