

PULMONARY HAEMORRHAGE

Supporting information

Can pulmonary haemorrhage be caused by excessive fluids, coagulation abnormalities, or surfactant therapy?

Massive pulmonary haemorrhage may result from severe pulmonary oedema, one of the causes of which is reduced intravascular oncotic pressure associated with fluid overload (Bland, 1982).

The role of coagulation abnormalities is "unclear", although secondary disseminated intravascular coagulation is not uncommon (Greenough, 1999).

A Cochrane systematic review of RCTs infants (Soll, 2010) concluded that prophylactic treatment with synthetic surfactant increased the risk of pulmonary haemorrhage, metaanalysis showing a RR of 3.28 (95% CI 1.50 to 7.16).

Paradoxically, there is some suggestion that surfactant may be used to successfully treat pulmonary haemorrhage, although a Cochrane review (Aziz, 2012) found no randomised or quasi-randomised trials that would allow a firm conclusion to be reached.

A case-control study in 787 VLBW neonates treated with surfactant (Pandit, 1999) found that 94 (11.9%) developed pulmonary haemorrhage. In these infants, this was associated with increased risk of death (OR 7.8, 95% CI 2.6-28) and short term morbidity (OR 4.4, 95% CI 1.3-15.7) if moderate or severe.

Aziz A, Ohlsson A. Surfactant for pulmonary hemorrhage in neonates. Cochrane Database of Systematic Reviews 2012, Issue 7. Art. No.: CD005254

<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005254.pub3/full>

Bland RD. Edema formation in the newborn lung. Clin Perinatol, 1982;9:593-611

Greenough A, Robertson NR. Acute respiratory disease in the newborn. In: Rennie JM, Robertson NR (eds). Textbook of neonatology, 3rd ed. Edinburgh: Churchill Livingstone, 1999. p552

Pandit PB, O'Brien K, Asztalos E, et al. Outcome following pulmonary haemorrhage in very low birthweight neonates treated with surfactant. Arch Dis Child Fetal Neonatal Ed 1999;81:F40-4

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1720955/pdf/v081p00F40.pdf>

Soll RF, Ozek E. Prophylactic synthetic surfactant for preventing morbidity and mortality in preterm infants. Cochrane Database of Systematic Reviews 2010, Issue 2. Art. No.: CD001079

<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001079.pub2/full>

Evidence Level: V (fluids, coagulopathy); I (synthetic surfactant)

What is the most effective treatment for pulmonary haemorrhage?

A 2021 systematic review found that surfactant therapy and high-frequency oscillatory ventilation (HFOV) are the most successful evidence-based treatment methods (Barnes, 2021). Surfactant administration was found to be an effective method for the treatment of pulmonary haemorrhage in reducing mortality and improving the oxygenation index associated with pulmonary haemorrhage in all six of the studies identified where it was the primary treatment method. HFOV is an effective management in treating pulmonary haemorrhage and in improving OI, with a significant decrease in oxygenation index seen 1 h post-HFOV in one study and decreased alveolar-arterial gradient in two studies. These effects may be attributed to an increase in mean arterial pressure, but more evidence is required to identify the exact aetiology of these improvements.

Barnes ME, Feeney E, Duncan A et al. Pulmonary haemorrhage in neonates: Systematic review of management. Acta Paediatr. 2021: Epub ahead of print

<https://onlinelibrary.wiley.com/doi/10.1111/apa.16127>

Evidence Level: I

Can surfactant treatment be beneficial in pulmonary haemorrhage?

A small RCT in which VLBW infants in the neonatal intensive care unit were randomised to either receive one of two natural surfactants (poractant alfa and beractant; n = 21 each group) found both were equally effective in improving oxygenation and ventilatory indexes following pulmonary haemorrhage (Bozdağ, 2015). There was a mortality rate of 23 neonates within 72 h of the occurrence of pulmonary haemorrhage and 5 of the 13 surviving infants developed chronic lung

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disease. However, due to the size of the study groups, no statistically significant conclusions were drawn regarding the mortality or long-term morbidity rate.

A retrospective case series from Amizuka et al. found that 21 of 26 neonates treated with single-dose surfactant 3.0 ± 1.3 h after the onset of haemorrhagic pulmonary oedema showed a good response at 1 h following administration. There were no reported deaths or instances of long-term disability in neonates treated with surfactant therapy

A retrospective cohort study by Yen et al. suggested that surfactant was beneficial in treatment of severe pulmonary haemorrhage. A statistically significant improvement in alveolar-arterial oxygen difference and oxygenation index in the 2- to 4-h period post-administration was observed, compared with the group who did not receive surfactant.

Amizuka T, Shimizu H, Niida Y et al. Surfactant therapy in neonates with respiratory failure due to haemorrhagic pulmonary oedema. *Eur J Pediatr.* 2003; 162: 697-702

Bozdağ Ş, Dilli D, Gökmen T et al. Comparison of two natural surfactants for pulmonary hemorrhage in very low-birth-weight infants: a randomized controlled trial. *Am J Perinatol.* 2015; 32: 211-8

Yen TA, Wang CC, Hsieh WS et al. Short-term outcome of pulmonary hemorrhage in very-low-birth-weight preterm infants. *Pediatr Neonatol.* 2013; 54: 330-4
<https://www.sciencedirect.com/science/article/pii/S1875957213000752?via%3Dihub>

Evidence Level: III

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