

Nitric oxide reduced the use of extracorporeal membrane oxygenation but not death in infants with hypoxic respiratory failure

The Neonatal Inhaled Nitric Oxide Study Group. **Inhaled nitric oxide in full-term and nearly full-term infants with hypoxic respiratory failure.** *N Engl J Med.* 1997 Feb 27; 336:597-604.

Objective

To determine the effectiveness of inhaled nitric oxide in reducing mortality or the need for extracorporeal membrane oxygenation (ECMO) in mature and nearly mature infants with hypoxic respiratory failure.

Design

Randomised, double-blind, controlled trial with 120-day follow-up.

Setting

Centres throughout Canada and the United States.

Patients

235 infants born at ≥ 34 weeks of gestation who were ≤ 14 days old, required assisted ventilation for hypoxic respiratory failure, and had an oxygenation index of ≥ 25 on 2 measurements made ≥ 15 minutes apart. Exclusion criteria were congenital heart disease,

congenital diaphragmatic hernia, or a decision not to provide full treatment.

Intervention

114 infants were allocated to nitric oxide (20 ppm), and 121 were allocated to control gas (100% oxygen). Infants who had partial pressures of arterial oxygen (PaO_2) increased by ≤ 20 mm Hg after 30 minutes were also studied for a response at 80 ppm or with control gas.

Main outcome measures

Mortality or need for ECMO and change in PaO_2 , oxygenation index, and alveolar-arterial oxygen gradient.

Main results

16 infants (14%) in the nitric oxide group died compared with 20 infants (17%) in the control group {95% CI for the 3% absolute difference -7%

to 12%}* ($P = 0.60$). 44 infants (39%) in the nitric oxide group received ECMO compared with 66 infants (55%) in the control group ($P = 0.014$) (Table). Infants in the nitric oxide group had a greater improvement in PaO_2 , oxygenation index, and alveolar-arterial oxygen gradient. Nitric oxide was not discontinued in any infant because of toxic effects.

Conclusion

Nitric oxide reduced the use of extracorporeal membrane oxygenation but did not reduce mortality in mature and nearly mature infants with hypoxic respiratory failure.

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*Numbers calculated from data in article.

Effect of nitric oxide vs 100% oxygen[†]

Outcome at 120 days or death	Nitric oxide EER	100% oxygen CER	RRR (95% CI)	ARR EER - CER	NNT (CI)
Need for ECMO	39%	55%	29% (7 to 47)	16%	7 (4 to 31)

[†]Abbreviations defined in Glossary; RRR, ARR, NNT, and CI calculated from data in article.

Commentary

This study is important because, in conjunction with other recent work (1), it provides clear evidence that inhaled nitric oxide can influence the outcome for mature infants with hypoxic respiratory failure. However, at present, the benefit shown relates to the short-term measure of a reduced need for ECMO. Full interpretation of these data will not be possible until information becomes available relating to neurodevelopmental outcome at 2 years of age. It will be important to confirm that the use of nitric oxide has not, for example, delayed the use of ECMO and as a result increased late morbid conditions.

The implications of this study for prac-

tice are complex. The data add support to the role for inhaled nitric oxide in mature infants with hypoxic respiratory failure, although the continuing lack of information about anything other than short-term toxicity remains a concern. Information from a few open investigations about the response of preterm infants to nitric oxide suggests that the data from this study should not be extrapolated to this group of infants.

The clinical challenge in using nitric oxide for mature infants is to introduce it into care and assess the infants' response at a stage where, if no response is seen, referral for ECMO still remains an option (2).

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References

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2. UK Collaborative ECMO Trial Group. UK Collaborative randomised trial of neonatal extracorporeal membrane oxygenation. *Lancet.* 1996;348:75-82.