Use of Inhaled Nitric Oxide for Infants ≤ 29 Weeks Gestation in Two Tertiary Neonatal Units from the United Kingdom

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Background:

There is a lack of data to support the benefit of iNO (inhaled nitric oxide) use in premature infants with respiratory failure¹. Despite this the rate of use in this population is rising².

Aims:

1. Assess use of iNO in infants born $\leq 29/40$ with hypoxic respiratory failure
2. Compare outcomes of babies born $\leq 29/40$ who received iNO to babies $\leq 29/40$ who didn't receive iNO
3. Identify co-existing variables which may influence outcomes in infants receiving iNO

Outcomes in iNO Use

- Overall mortality of infants receiving iNO in both centres was 48%.
- Based on combined data from both centres at $\leq 29/40$ the overall odds of dying were 6.3 times greater in infants who received iNO at any time (Odds ratio 6.3221 $p < 0.0001$).
- The odds of dying were higher in St Mary's: odds ratio 9.02 ($p < 0.0001$) vs St George's: odds ratio 4.57 ($p < 0.0001$).
- No statistically significant prognostic markers influencing outcomes in infants receiving iNO were identified.

Method:

Retrospective analysis of electronic neonatal unit Badger Net database for all infants $\leq 29/40$ admitted in two tertiary neonatal units in United Kingdom; St. George's University Hospital (London) and St. Mary's Hospital (Manchester), from 2010 to 2015 (total infants 1412).

Outcomes for infants who received iNO were compared to infants who did not receive iNO. Impact of confounding variables on measured outcomes for infants receiving iNO were also analysed.

Outcomes measured:

Mortality, day of death, intraventricular haemorrhage, days ventilated, days in oxygen, chronic lung disease, pneumothorax, retinopathy, cystic PVL.

Variables analysed: Ethnicity, gender, gestational age, birth weight, presence of chorioamnionitis, steroid course, singleton or multiple birth, day iNO initiated, duration of iNO use, indication for iNO use.

iNO Use

- 108 (8%) infants received iNO over period of 6 years.
- There was no significant increase in use over the time period analysed.
- The majority of infants receiving iNO were 24 weeks gestation (26%).

Percentage of infants at St George's who died depending on day of nitric initiation

Percentage of infants at St Mary's who died depending on day of nitric initiation

St Mary's odds of dying if iNO ≤ 15 days vs ≥ 15 days: 1.47 (0.48 to 4.49, $p = 0.49$)
St George's odds of dying if iNO ≤ 15 days vs ≥ 15 days 0.53 (0.18 to 1.57 $p = 0.25$)

Survival data for infants receiving iNO vs those not receiving iNO up to 100 days of life

iNO use and survival

Conclusions

- The odds of dying are 6.3 times greater in all infants who received iNO. This suggests iNO use is an indicator of disease severity.
- Practices differ between centers in use of iNO, based on the survival outcomes. At St Mary's fewer and more sicker patients receive iNO in comparison to St George's and hence the odds of dying are greater. At St Mary's more infants died if they received iNO ≤ 15 days of life; although impact of day of initiation of iNO on survival was not statistically significant.
- Survival curve suggests that iNO delays death by approximately 10 days compared to mortality in babies born $\leq 29/40$ who did not receive iNO.
- Further studies are needed to identify whether iNO use is independently associated with death or other adverse outcomes.