Cost-effectiveness of inhaled nitric oxide in near-term and term infants with respiratory failure: eighteen- to 24-month follow-up for Canadian patients

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Inhaled nitric oxide (INO) was compared with oxygen administration in near-term and term infants with severe respiratory failure.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised newborns of at least 34 weeks' gestation with severe respiratory failure. Severe respiratory failure was determined by at least two oxygenation indices reading greater than or equal to 25, at least 15 minutes apart. The oxygenation index was defined as the mean arterial pressure multiplied by the ratio of FiO2 to PaO2. Infants older than 14 days or with congenital heart disease and congenital diaphragmatic hernia were excluded.

Setting
The setting was tertiary care (regional neonatal intensive care units). The economic analysis was conducted in Canada.

Dates to which data relate
The dates to which the data related were not reported. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single prospective study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients (except patients who were lost to follow-up) as that used in the effectiveness study.

Study sample
No power calculations to determine the sample size were reported. Initially, 96 infants were included in the trial and were randomised to the INO (n=49) or oxygen (n=47) intervention.

Study design
The study was a randomised controlled trial, which was conducted in 9 Canadian neonatal units. The authors stated that the study was double-blinded, but they did not provide any details of the blinding. In addition, the method of randomisation was not specified. The duration of follow-up was between 18 and 24 months. Of the original 96 enrollees, 20 died (7 in the INO group and 13 in the oxygen group). Of those who survived, 8 were lost to follow-up (5 in the INO group and 3 in the oxygen group). The remaining sample for analysis contained 88 patients (including the 20 patients who died), 44 infants in each group.

Analysis of effectiveness
The analysis of the clinical study was based on the treatment allocations, except that patients lost to follow-up were excluded. The authors stated that the patients lost to follow-up were comparable between the groups in terms of important characteristics.

The primary health outcomes used in the analysis were mortality rates, clinical outcomes and a variety of developmental indicators. These indicators included cerebral palsy, seizure disorder, vision or hearing loss, and mental or performance delay as measured by scores of less than 70 on the Bayley Scales of Infant Development (see Other Publications of Related Interest). Several aggregate measures of outcome were developed. These were counts of deaths, counts of children with poor health, counts of children with disabilities, and counts with any of the three adverse outcomes. Health service utilisation measures were used as indicators of general health problems following discharge of the infant. The two groups appear to have been comparable at randomisation for several characteristics.

Effectiveness results
The difference in mortality rate was not statistically significant between the INO and oxygen groups (7 versus 13; p=0.224).

There was no significant difference in the composite measure of outcome (death or at least one health problem or disability) between the two groups.

Other aggregate outcome measures were also no different between the interventions.

In the survivors who did not drop out, 2.7% of the infants under INO had seizure disorders after hospital discharge, compared with 22.6% of the infants under oxygen, (p=0.019).

Clinical conclusions
Infants who received INO generally did better than those who received oxygen, and experienced significantly lower seizure disorders.

Measure of benefits used in the economic analysis
The authors did not develop a summary benefit measure. A cost-consequences analysis was therefore performed.

Direct costs
A modified societal perspective was adopted. The resources included all government costs and family private costs beyond normal care that were related to the infant's development in the first 18 to 24 months of life. The private costs to the family were not specifically identified, but may have included the drug prescriptions. Lost parental income was excluded from the analysis. The costs were for the initial hospitalisation, and standard medical services above routine care and developmental services received until follow-up. The hospitalisation costs included the neonatal intensive care, ECMO, physician services, surfactant, and air transport from the neonatal intensive care unit and from the ECMO referral centre. Resource use was estimated from case report forms. The unit costs were estimated from provincial data for Alberta or financial data from the Capital Health Authority of Edmonton, Alberta. The costs and the quantities were reported separately. The dates to which the data related were not reported. The price year was not reported. A discount rate of 5%, as recommended by the Canadian Coordinating Office for Health Technology Assessment, was used.
Statistical analysis of costs
A statistical analysis of the costs was performed using Student's t-test.

Indirect Costs
No indirect costs were included in the analysis.

Currency
Canadian dollars (Can$). The exchange rate was Can$1 = US$0.67.

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The costs per infant in the INO group were $4,800 greater than the costs per infant in the oxygen group ($23,907 versus $19,195). The difference was not statistically significant, (p=0.148).

There were no statistically significant differences in the costs when considering the breakdown of post follow-up costs for survivors who were not lost to follow-up.

Synthesis of costs and benefits
Not applicable.

Authors’ conclusions
Inhaled nitrogen oxide (INO) would be preferable to oxygen since it was more effective, with no difference in the costs.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator, oxygen, was clear. The comparator was chosen because it represented the standard care for newborns with severe respiratory distress in the authors' setting. You should consider whether this is a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The estimate of effectiveness was based on a double-blind, randomised controlled trial. However, the methods of randomisation and blinding were not described. The study sample may have been representative of the study population. The patient groups were shown to have been comparable at analysis. However, the sample size was very small, suggesting a lack of power calculations. Appropriate statistical analyses were undertaken to take potential biases and confounding factors, particularly between survivors who were not lost to follow-up and patients who were lost, into consideration.

Validity of estimate of measure of benefit
The authors did not develop a summary benefit measure. A cost-consequences analysis was performed.
Validity of estimate of costs
Although the authors reported that the costs were estimated from a societal perspective, the indirect costs were not included. The exclusion of these costs (social and financial consequences of care arrangements for the mothers) might have biased the results of the cost analysis. The costs incurred by the family were unclear. The costs and the quantities were reported separately. A statistical analysis of the costs was performed. The authors performed appropriate currency conversions. Discounting was unnecessary since all costs were incurred in one year. The price year was not stated.

Other issues
The limitation of the generalisability of the results to other settings or countries was addressed. Adequate comparisons were made with studies dealing with the same topic. The authors enrolled near-term and term infants with respiratory failure, and this was reflected in the authors' conclusions. The authors highlighted the limitations of their study. They do not appear to have reported their results selectively.

Implications of the study
The authors commented that their findings suggested the use of INO was favourable.

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Other publications of related interest

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