Inhaled nitric oxide reduces the utilization of extracorporeal membrane oxygenation in persistent pulmonary hypertension of the newborn

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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 in persistent pulmonary hypertension of the newborn.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with a gestational age of more than 35 weeks, absence of lethal chromosomal abnormality or intracranial haemorrhage with severity above grade I, and severe gas exchange abnormality (as defined by an alveolar-arterial oxygen tension difference of above 600 torr or an oxygenation index of above 40).

Setting
Tertiary care, children's hospital. The study was carried out in Wisconsin, USA.

Dates to which data relate
The effectiveness and resource use data were collected between January 1993 and December 1995. The price year was not reported.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
Although no details were reported, the costing was presumably undertaken on the same patient sample as that used in the effectiveness study.

Study sample
No power calculations were reported. A total of 50 patients out of 103 neonates referred for rescue therapy during the study period were included in the study. Of these, 29 were admitted when inhaled nitric oxide was unavailable (due either to its permanent unavailability or to the concurrent use by other patients of the single delivery system at the institution), while the remainder (21 patients), were admitted when this delivery system was available. The final number of patients who met ECMO criteria was 21 and 16 for the control and intervention groups, respectively.
Study design
A retrospective cohort study performed in a single centre. The outcomes were assessed at 28 days of age.

Analysis of effectiveness
The analysis was based on the intention to treat principle. The primary health outcome measures were complication-free survival and functional outcome, which was assessed by means of a ranked functional outcome index ranging from 4 (alive without apparent organ damage) to 0 (dead). Physiologic responses and safety data were also compared for the treatment group relative to their own baseline values. A logistic regression analysis was used in order to adjust for differences in patient characteristics between groups. Nevertheless, the groups were found to be comparable in terms of age, weight, gender, underlying diagnoses, oxygenation index, alveolar-arterial oxygen tension gradient, surfactant and high-frequency oscillatory ventilation administration before ECMO or nitric oxide, and evidence of persistence pulmonary hypertension of the newborn with extra pulmonary right to left shunt.

Effectiveness results
The survival rate without chronic lung disease (oxygen therapy at 28 days) and intracranial haemorrhage of any type was 10% and 69% (p=0.001) for the control and intervention groups, respectively. The relative risk ratio was 7.22 (95% CI: 1.85 - 28.1). The ranked functional outcome index was 2.19 (+/- 12.5) and 3.36 (+/- 0.96) in the control and intervention groups, respectively (p=0.003). The logistic regression analysis showed that the only characteristic significantly associated with each health outcome measure in terms of complication-free survival and functional outcome was the availability of inhaled nitric oxide therapy.

Measure of benefits used in the economic analysis
The authors did not derive a summary measure of effectiveness for the economic analysis, but reported various outcome measures. The main health outcomes were complication-free survival and the ranked functional outcome index.

Direct costs
No details about the methodology employed in the cost analysis, data sources or the items included were provided. The authors referred to the total cost estimates as 'hospital costs'. The price year was not reported.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
All outcome measures used were more favourable in the intervention group.

Cost results
The 'hospital costs' per patient (standard error) in the intervention and control groups were $116,000 (+/- 70,000) and $159,000 (+/- 93,000), respectively. The difference in the costs per patient was not statistically significant.

Synthesis of costs and benefits
Costs and benefits were not combined since the intervention turned out to be the dominant strategy.
Authors' conclusions
The administration of inhaled nitric oxide to neonates with persistent pulmonary hypertension at time of initial qualification for ECMO reduced the need for ECMO compared with institutionally derived prior probability. This treatment strategy increased the number of patients surviving without chronic lung disease, intracranial haemorrhage, and tube feedings, with lower resource use. There were no adverse effects seen with the intervention in any patients. Therefore, administration of inhaled nitric oxide to patients with severe persistent pulmonary hypertension appears to safely improve gas exchange, reducing the need for ECMO while improving clinical outcome.

CRD COMMENTARY - Selection of comparators
A justification was give to comparator used which was a choice of standard therapy options (including ECMO) in the situation where inhaled nitric oxide was not available. You, as a user of this database, should consider whether this is a relevant comparator in your own setting.

Validity of estimate of measure of benefit
The internal validity of the study results may be questionable due to biases likely to arise from the retrospective nonrandomised study design used. Nevertheless, the authors analysed the known confounders thoroughly. The sample size was rather small, which may increase the role of chance in the statistical analysis.

Validity of estimate of costs
The authors did not discuss any aspects of costing estimations or even the cost results in the paper. Since no details about the methodology and constituent elements of the estimates of 'hospital costs' were given, the quality of the results presented for this analysis cannot be assessed.

Other issues
The authors' conclusions about the health benefits seem to be justified. However, the reservations about the quality of the cost analysis must lead the reader to consider with care any conclusions concerning the cost-effectiveness or potential savings due to the study therapy. The issue of generalisability was not addressed, although evidence showing the same qualitative results found in previously published uncontrolled studies gives some idea of the potential for external validity. Due to lack of detail in the reporting of cost estimation, the generalisability of the economic analysis to other settings cannot be assessed.

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