A prospective controlled trial of albuterol aerosol delivered via metered dose inhaler-spacer device (MDI) versus jet nebulizer in ventilated preterm neonates

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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
The health interventions examined in the study were two techniques for the delivery of bronchodilators (albuterol aerosol) in premature infants: metered dose inhaler-spacer device (MDI) and Jet nebulisers.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised premature infants (24 to 34 weeks of gestation), ventilated for respiratory distress syndrome in the neonatal intensive care unit (NICU).

Setting
The setting was hospital. The study was carried out at the Departments of Pediatrics and Respiratory Care, Albert Einstein Medical Center, Philadelphia, Pennsylvania, USA.

Dates to which data relate
The dates during which data on both effectiveness and resource use were gathered were not reported. The price year was not indicated.

Source of effectiveness data
A single study was used as the source for the effectiveness evidence.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
No power calculations were performed. The method of sample selection was not reported. A total of 53 preterm ventilated infants were identified: 29 patients (gestational age: 26.8 +/- 0.5 weeks; birth weight: 929 +/- 66 g; age at study: 13 +/- 4 days) were included in the MDI group and 24 patients (gestational age: 27.8 +/- 0.5 weeks; birth weight: 1,129 +/- 79 g; age at study: 11 +/- 4 days) were included in the Jet nebuliser group. No patient was excluded from the initial sample.
Study design
This was a prospective case-control study. The length of follow-up was not reported. Assessment of the outcomes was conducted 15 minutes before and after bronchodilator delivery.

Analysis of effectiveness
All patients included in the sample were accounted for in the analysis, thus producing, in effect, an intention to treat analysis. The primary health outcomes were heart rates, respiratory rates, oxygen saturation, dynamic lung compliance (CDYN), and expiratory airway resistance (RAWE). Groups were shown to be comparable in terms of gestational age, birth weight, age and weight at study, and pre-extubation ventilator settings.

Effectiveness results
The effectiveness results were as follows:

Heart rates increased significantly in both groups after bronchodilator delivery: from 152 +/- 3 to 157 +/- 3 per minute in the MDI group and from 137 +/- 3 to 142 +/- 3 per minute in the Jet group, (p<0.001). These differences were significantly different over time, (p=0.001), but not in terms of interaction of treatment and time, (p=0.08).

Respiratory rates also increased in both groups: from 42 +/- 3 to 45 +/- 3 per minute in the MDI group and from 43 +/- 3 to 47 +/- 3 per minute in the Jet group, (p<0.05). These were not significant over time and interaction of treatment.

The oxygen saturation was also beneficial in both groups, but the percentage increase in the Jet group was statistically greater: from 96.3% +/- 0.4% to 97.2% +/- 0.4% in the MDI group and from 96.1% +/- 0.3% to 97.8% +/- 0.3% in the Jet group, (p<0.01). These differences were not significant over time, but were significant when interaction of treatment and time was considered.

CDYN increased in both groups: from 0.83 +/- 0.10 mL/cm H2O to 0.95 +/- 0.12 mL/cm H2O in the MDI group and from 0.90 +/- 0.12 mL/cm H2O to 0.93 +/- 0.13 mL/cm H2O in the Jet group, (p<0.05). These differences were not significant over time and interaction of time and treatment.

RAWE decreased statistically significantly in both groups: from 188 +/- 19 cm H2O/L/s to 142 +/- 12 cm H2O/L/s in the MDI group and from 161 +/- 21 cm H2O/L/s to 138 +/- 14 cm H2O/L/s in the Jet group, (p<0.001). Not significant over time, and treatment and time interaction.

Clinical conclusions
The analysis of the effectiveness showed that both methods of delivery were equally effective in improving patients’ conditions. The Jet nebuliser showed a slightly, but significantly, greater beneficial effect in terms of oxygen saturation in comparison with the MDI device.

Measure of benefits used in the economic analysis
Health outcomes were left disaggregated and no summary benefit measure was used, therefore a cost-consequences analysis was conducted.

Direct costs
Discounting was not relevant given the short time horizon of the study. Unit costs and quantities of resources were reported. The cost/resource boundary adopted appears to have been that of the hospital. The cost items included were the device (Jet nebuliser and MDI-spacer), the albuterol bottle (for 200 doses), and the saline solution. The estimation of costs and quantities was based on actual data, but the source of costs was not reported. The period of collection of quantities of resources consumed during the study was not reported. The price year was not indicated.
Statistical analysis of costs
Statistical analyses of costs were not carried out.

Indirect Costs
Indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analyses were conducted.

Estimated benefits used in the economic analysis
See effectiveness results above.

Cost results
The cost of one MDI treatment was 2 cents and 10 cents for the Jet nebuliser.

Synthesis of costs and benefits
Not relevant.

Authors’ conclusions
The authors concluded that both albuterol delivery devices were, in general, equally effective in improving short-term infants’ conditions, and costs of a single dose were not high for either. However, the authors suggested the adoption of MDI-spacer because delivery times were shorter compared to Jet nebulisers.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The interventions were chosen because they represented widely used delivery devices for ventilated preterm infants. You, as a user of this database, should assess whether they represent routine health interventions in your own setting.

Validity of estimate of measure of effectiveness
The analysis of the effectiveness was based on a prospective case-control study, which appeared appropriate to the study question. However, although study groups were generally comparable at baseline, the lack of randomisation could have limited the internal validity of the analysis. In addition, the sample size was not large and power calculations were not conducted. The time horizon of the study analysed only short-term effects of the interventions and the period of collection of effectiveness data was not reported.

Validity of estimate of measure of benefit
Health outcomes were left disaggregated and a cost-consequences analysis was conducted. It would have been interesting to have had a summary benefit measure to assess the impact of the interventions on patients’ health and include patient’s or caregivers’ preferences.

Validity of estimate of costs
The analysis of costs included limited information and the perspective of the analysis was not clearly stated. Statistical analyses of costs were not conducted. The price year and the period of collection of quantities of resources were not reported. No cost comparison between the study groups was actually conducted. These features limit the external validity of the results.

**Other issues**

The issue of the generalisability of the study to other settings was not addressed and the lack of sensitivity analyses reduced the external validity of the analysis. The authors made some interesting comparisons of their findings with those from other studies.

**Implications of the study**

The authors pointed out that the study results should be applicable only to infants who are recovering from lung disease. Moreover, MDI should be used because, in addition to the shorter delivery times and lower cost, it does not require adjustment of ventilator flow and does not cause cooling of the ventilatory gas.

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