The clinical effectiveness and cost-effectiveness of heated humidified high-flow nasal cannula compared with usual care for preterm infants: systematic review and economic evaluation

Nigel Fleeman,[1]* James Mahon,[2] Vickie Bates,[1] Rumona Dickson,[1] Yenal Dundar,[1] Kerry Dwan,[1,3] Laura Ellis,[4] Eleanor Kotas,[1] Marty Richardson,[1] Prakesh Shah[5] and Ben NJ Shaw[6]

[1]Liverpool Reviews and Implementation Group, University of Liverpool, Liverpool, UK
[2]Coldingham Analytical Services, Berwickshire, UK
[3]Cochrane Editorial Unit, Cochrane Collaboration, London, UK
[4]Patient representative (parent of premature infants)
[5]Departments of Paediatrics and Institute of Health Policy, Management and Evaluation, University of Toronto, Mount Sinai Hospital, Toronto, ON, Canada
[6]Neonatal Unit, Liverpool Women's NHS Foundation Trust, Liverpool, UK

*Corresponding author

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Scientific summary

Effectiveness of HHHFNC compared with usual care for preterm infants

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Scientific summary

Background

Respiratory problems are one of the most common causes of morbidity in preterm infants. Clinically, respiratory distress syndrome presents with early respiratory distress and infants are treated with several modalities for respiratory support. These include mechanical endotracheal ventilation, nasal continuous positive airway pressure (NCPAP), oxygen, nasal intermittent positive-pressure ventilation (NIPPV) and the heated humidified high-flow nasal cannula (HHHFNC). HHHFNC is gaining popularity in clinical practice, but there is a lack of convincing evidence for the relative effectiveness of HHHFNC over any other modality.

Objectives

The aim of this systematic review and economic evaluation was to answer the question: what is the clinical effectiveness and cost-effectiveness of HHHFNC compared with usual care for preterm infants? We conducted a primary analysis of HHHFNC to usual care following ventilation and a secondary analysis of HHHFNC to usual care with no prior ventilation. Usual care was considered to consist of NCPAP, oxygen or NIPPV. The primary outcome measure of the review was treatment failure as defined by a need for reintubation (primary analysis) or a need for intubation (secondary analysis).

Methods

The following databases were searched for relevant published literature on 8 September 2014:

- MEDLINE and MEDLINE In-Process & Other Non-Indexed Citations (via OvidSP)
- EMBASE (via OvidSP)
- Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effectiveness, Health Technology Assessment database
- ISI Web of Science, Science – Citation Index Expanded and ISI Web of Science, Proceedings (Index to Scientific and Technical Proceedings)
- PubMed (limited to the last 6 months).

In addition, we searched seven trial and research registers and bibliographies of previous reviews and retrieved articles. All databases were searched from 2000 to 8 September 2014, apart from PubMed which was searched from 1 March to 9 September 2014. The searches were then updated on 12 January 2015.

Search terms included a combination of index terms (for the study population) and free-text words (for the technologies involved). No methodological filters or other limits were employed.

The citations identified by the search strategy were assessed for inclusion through two stages by two independent reviewers. First, all titles and abstracts were screened to identify all potentially relevant citations and, second, inclusion criteria were applied to full-text articles.

The results of the data extraction and quality assessment for each study were presented in structured tables and as a narrative summary. All summary statistics were extracted for each outcome and, when possible, data were pooled and a meta-analysis was carried out using a fixed-effects model.

Heterogeneity was explored through consideration of the study populations (e.g. differences in gestational age), interventions (e.g. starting flow rate for HHHFNC or starting pressure for NCPAP), outcome definitions (e.g. different definitions for reintubation) and, in statistical terms, by the chi-squared test for homogeneity and the I^2 statistic.

No studies were identified at the scoping stage that explored the relative cost-effectiveness of HHHFNC compared with NCPAP; therefore, a de novo economic analysis was undertaken.

Results

Nine papers reporting on seven randomised controlled trials (RCTs) were included in the review. Four RCTs (735 infants) were relevant to the primary analysis (preterm infants treated following ventilation) and three RCTs (124 infants) were relevant to the secondary analysis (infants treated who had not received prior ventilation). Overall, the RCTs included in the review were of satisfactory methodological quality, although it was not possible to blind administrators or participants in any study.

In the primary analysis, three studies compared HHHFNC with NCPAP. It was possible to pool data for at least two trials comparing HHHFNC with NCPAP in a meta-analysis for three efficacy outcomes: need for reintubation < 7 days, bronchopulmonary dysplasia and death. No statistically significant differences were reported between arms [reintubation: risk ratio (RR) 0.76, 95% confidence interval (CI) 0.54 to 1.09; bronchopulmonary dysplasia: RR 0.92, 95% CI 0.72 to 1.17; death: RR 0.56, 95% CI 0.22 to 1.44]. No statistically significant differences were reported in individual trials between arms for any other efficacy outcomes. Regarding adverse events, the only statistically significant difference between arms (favouring HHHFNC over NCPAP) was for nasal trauma leading to a change of treatment (RR 0.21, 95% CI 0.10 to 0.42). No statistically significant differences were reported between arms for pneumothorax, intraventricular haemorrhage, necrotising enterocolitis, apnoea or acidosis. Generally, individual trials reported numerically fewer of these adverse events (and also nosocomial sepsis and gastrointestinal perforation, reported in only one study) with HHHFNC than with NCPAP. With the exception of nasal trauma rates and nasal trauma score (which favoured HHHFNC over NCPAP), differences between arms in individual studies were not, however, statistically significant.

In the secondary analysis, one study compared HHHFNC with NIPPV and two studies compared HHHFNC with NCPAP; one RCT was a crossover trial (2 × 24 hours). Two studies reported on treatment failure but a statistically significant difference between arms was not found in either study [reintubation rates of HHHFNC (28.9%) compared with NIPPV (34.2%) and respiratory failure with HHHFNC (15.3%) compared with NCPAP (13.3%)]. Neither of these studies reported a statistically significant difference for any of the secondary outcomes of interest to our review. The third study was the only study to report on quality of care, in which parents were more likely to favour HHHFNC over NCPAP for the following reasons: (1) child satisfaction, (2) contact and interaction, and (3) opportunities to take part in care. Only the study comparing HHHFNC with NIPPV reported on adverse events. These appeared to be numerically higher in the HHHFNC arm than in the NIPPV arm, but no statistically significant differences between arms were reported.

For the primary analysis, with no difference in primary outcome being reported and the only difference in secondary outcomes being in rates of minor nasal trauma, a cost-minimisation analysis was undertaken. For the secondary analysis there is no evidence on the primary outcome and, as such, no economic analysis was undertaken.

Costs for equipment were taken from the NHS Supply Chain (www.supplychain.nhs.uk). Assumptions were made about the lifespan of equipment and its rate of utilisation to estimate the costs of equipment per preterm infant. Weekly consumable costs were provided by a clinician working in a NHS neonatal unit.

Our analysis suggests that HHHFNC would cost less than NCPAP if:

- the capital equipment (flow generator or humidifier machines) for HHHFNC and NCPAP lasts 5 years
- the capital equipment is in use for 80% of the time
- preterm babies require HHHFNC or NCPAP for an average of 43.5 days before discharge.

This finding of HHHFNC being cost saving compared with NCPAP is sensitive to the assumed lifespan of the equipment and the cost differential of consumables. If the equipment lasts, on average, more than 6.8 years or the cost of consumable equipment is approximately £16 per week per preterm infant higher with HHHFNC than NCPAP, then NCPAP will cost less than HHHFNC.

Conclusions

There is a lack of convincing evidence to suggest that HHHFNC is superior or inferior to usual care, in particular compared with NCPAP. This is true for preterm infants who have been treated following ventilation and for those who have received no prior ventilation. The results of one small trial suggest that parents do, however, prefer HHHFNC to NCPAP.

There is also uncertainty regarding whether or not HHHFNC can be considered cost-effective because the lack of clinical evidence precluded us from conducting an analysis of cost–utility or cost-effectiveness. The results of our cost-minimisation analysis suggest that HHHFNC may cost less than NCPAP, but there is much uncertainty around the assumptions employed and it is quite possible that HHHFNC could cost more than NCPAP. As the overall cost of either HHHFNC or NCPAP is small compared with the cost of preterm neonatal care as a whole, and the potential cost differences between the systems are even smaller, the financial case for HHHFNC over NCPAP, or vice versa, is not compelling.

More RCT evidence comparing HHHFNC with usual care (in particular NCPAP) is required to inform the evidence base for both the clinical effectiveness and the cost-effectiveness of HHHFNC. Ideally, a large and adequately powered trial is required to compare HHHFNC with NCPAP for preterm infants who were previously ventilated and for preterm infants who have not received prior ventilation. Based on available evidence, it is possible that further research could include evidence derived from a non-inferiority trial.

Study registration

The study is registered as PROSPERO CRD42015015978.

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