TITLE: Heated, Humidified High-Flow Nasal Cannula for Pediatric Patients: Clinical Effectiveness, Cost-Effectiveness, and Guidelines

DATE: 17 November 2016

RESEARCH QUESTIONS

1. What is the clinical effectiveness of heated, humidified high-flow nasal cannula therapy for pediatric patients?

2. What is the cost-effectiveness of heated, humidified high-flow nasal cannula therapy for pediatric patients?

3. What are the evidence-based guidelines regarding heated, humidified high-flow nasal cannula therapy for pediatric patients?

KEY FINDINGS

One health technology assessment, two systematic reviews, eight randomized controlled trials, and one evidence-based guideline were identified regarding heated, humidified high-flow nasal cannula therapy for pediatric patients.

METHODS

A limited literature search was conducted on key resources including Medline, PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2011 and November 3, 2016. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.
SELECTION CRITERIA

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

<table>
<thead>
<tr>
<th>Table 1: Selection Criteria</th>
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<tbody>
<tr>
<td><strong>Population</strong></td>
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<tr>
<td><strong>Intervention</strong></td>
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<tr>
<td><strong>Comparator</strong></td>
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| **Outcomes** | Q1: Clinical effectiveness (e.g., benefits and harms, patient quality of life)  
Q2: Cost-effectiveness  
Q3: Guidelines and recommendations for use of these devices in the pediatric population |
| **Study Designs** | Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines |

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, economic evaluations, and evidence-based guidelines.

One health technology assessment, two systematic reviews, eight randomized controlled trials, and one evidence-based guideline were identified regarding heated humidified high-flow nasal cannula therapy for pediatric patients. Due to the volume of relevant literature identified, non-randomized studies have been included in the appendix.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

One health technology assessment\(^1\) assessed the clinical and cost-effectiveness of heated humidified high-flow nasal cannula (HHHFNC) compared with usual care for preterm infants. There was a significant difference between HHHFNC and nasal continuous positive airway pressure (NCPAP) favoring HHHFNC in regards to nasal trauma leading to a change in treatment. There were no significant differences between groups in treatment failure, death, bronchopulmonary dysplasia, pneumothorax, intraventricular hemorrhage, apnoea, and acidosis.\(^1\) Because there was no evidence of a difference in effectiveness between the two treatments, a cost-minimization analysis was undertaken and HHHFNC was found to be less costly than NCPAP but the lifespan of the equipment may impact this finding.

Two systematic reviews\(^2,3\) were identified. One review\(^2\) identified two trials that found no difference between different models of equipment that were used to deliver humidified high flow nasal cannula for preterm infants. The second review examined HHHFNC compared with conventional respiratory support for infants with bronchiolitis.\(^3\) The review included one randomized controlled trial (RCT) comparing HHFNC with oxygen delivery via a head box. Median oxygen saturation was initially higher in the HHFNC group but was similar between
groups at 24 hours. The authors determined there was not enough evidence to determine whether HHNFC was effective for the management of infants with bronchiolitis.

One guideline from the British Thoracic Society was identified regarding the respiratory management of children with neuromuscular weakness.\textsuperscript{12} The guideline recommends that humidification “be considered in children who use non-invasive ventilation (NIV) and who have tenacious airway secretions.”\textsuperscript{12}

Eight relevant RCTs were identified.\textsuperscript{4-11} The main study results and conclusions are summarized in Table 2.

### Table 2: Summary of Included Randomized Controlled Trials

<table>
<thead>
<tr>
<th>First Author, Year</th>
<th>Patient Population</th>
<th>Intervention and Comparator</th>
<th>Results and Authors’ Conclusions</th>
</tr>
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</table>
| Lavizzari, 2016\textsuperscript{4} | Infants older than 28 weeks’ GA and less than 37 weeks GA with respiratory distress syndrome of prematurity N = 316 | HHHFNC versus nCPAP or BiPAP | Need for mechanical ventilation 72 hours from beginning of respiratory support  
• HHHFNC was non-inferior to nCPAP/BiPAP  
No significant difference was identified between groups in secondary outcomes:  
• need for surfactant  
• air leaks  
• bronchopulmonary dysplasia |
| Shetty, 2016\textsuperscript{5} | Infants with evolving or established bronchopulmonary dysplasia  
Median postnatal age of 30.9 weeks  
N = 20 | HHHFNC versus CPAP  
Randomized to one treatment on the first day and switched to the other treatment the second day | No significant difference was measured between groups in work of breathing, thoracoabdominal asynchrony, or mean oxygen saturation. |
| Kugelman, 2015\textsuperscript{6} | Preterm infants with RDS  
Gestational age less than 35 weeks  
N = 76 | HHHFNC (Precision Flow) versus NIPPV (SLE 2000 or 5000) | There was no significant difference in the need for endotracheal ventilation between groups.  
The rate of neonatal morbidities was similar between groups. |
| Collins, 2014\textsuperscript{7} | Preterm infants requiring non-invasive respiratory support following intubation  
Gestational age less than 32 weeks | HHHFNC (Vapotherm) and Sticky Whiskers versus nCPAP and Sticky Whiskers or Cannulaide nasal dressings | Mean nasal trauma score was significantly lower in the HHHFNC group. |
## Table 2: Summary of Included Randomized Controlled Trials

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| Klingenberg, 2014<sup>4</sup> | Infants less than 34 weeks postmenstrual age  
N = 20 | HHHFNC versus nCPAP  
Randomized to one treatment on the first day and switched to the other treatment the second day | There was no significant difference between groups in regards to mean cumulative pain scale score.  
HHHFNC was significantly better than nCPAP in the domains of child satisfaction, parental contact and interaction, and possibility to take part in care.  
Mean respiratory rate was lower with HHHFNC than CPAP. |
| Lavizzari, 2014<sup>9</sup> | Preterm infants with RDS  
Mean gestational age 31 weeks  
N = 20 | HHHFNC versus nCPAP | No significant differences were observed between groups in breathing pattern, gas exchange, lung mechanics, or total work of breathing at Prp of 2 and 4 cmH<sub>2</sub>O. |
| Collins, 2013<sup>10</sup> | Preterm infants requiring non-invasive respiratory support following intubation  
Gestational age less than 32 weeks  
N = 132 | HHHFNC (Vapotherm) versus nCPAP | There was no difference in reintubation between groups.  
Nasal trauma score was significantly lower in the HHHFNC group. |
| Yoder, 2013<sup>11</sup> | Infants in the NICU requiring non-invasive respiratory support  
Gestational age 28 to 42 weeks  
N = 432 | HHHFNC versus nCPAP | There was no significant difference in early failure, subsequent need for intubation, or adverse events between groups. |

bPAP = bilevel continuous positive airway pressure; cmH<sub>2</sub>O = centimeter of water; CPAP = continuous positive airway pressure; GA = gestational age; HHHFNC = heated, humidified high-flow nasal cannula; nCPAP = nasal continuous positive airway pressure; NICU = neonatal intensive care unit; NIPPV = nasal intermittent positive pressure ventilation; NR = not reported; Prp = retropharyngeal pressure; RDS = respiratory distress syndrome
REFERENCES SUMMARIZED

Health Technology Assessments


Systematic Reviews and Meta-analyses


Randomized Controlled Trials


Economic Evaluations
No literature identified.

Guidelines and Recommendations


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APPENDIX – FURTHER INFORMATION:

Randomized Controlled Trials

Alternate Comparator


Alternate Outcome


Non-Randomized Studies


Evidence-Based Guidelines – Possible Alternate Intervention


Clinical Practice Guidelines – Methodology Not Specified

AIRVO 2

See: AIRVO 2

Device Not Specified


PubMed: PM25414585


See: 3.5 Other therapies, page 13

