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Non-invasive ventilation in children and adults in low- and low-middle income countries: A systematic review and meta-analysis

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ABSTRACT

Purpose: We systematically reviewed the effects of NIV for acute respiratory failure (ARF) in low- and low-middle income countries.
Materials and methods: We searched MEDLINE, CENTRAL, and EMBASE (to January 2016) for observational studies and trials of NIV for ARF or in the peri-extubation period in adults and post-neonatal children. We abstracted outcomes data and assessed quality. Meta-analyses used random-effect models.
Results: Fifty-four studies (ten pediatric/$n = 1099$; 44 adult/$n = 2904$), mostly South Asian, were included. Common diagnoses were pneumonia and chronic obstructive pulmonary disease (COPD). Considering observational studies and the NIV arm of trials, NIV was associated with moderate risks of mortality (pooled risk 9.5%, 95% confidence interval (CI) 4.6–14.5% in children; 16.2% [11.2–21.2%] in adults); NIV failure (10.5% [4.6–16.5%] in children; 28.5% [22.4–34.6%] in adults); and intubation (5.3% [0.8–9.7%] in children; 28.8% [21.9–35.8%] in adults). The risk of mortality was greater ($p = 0.035$) in adults with hypoxemic (25.7% [15.2–36.1%]) vs. hypercapneic (12.8% [7.0–18.6%]) ARF. NIV reduced mortality in COPD (relative risk [RR] 0.47 [0.27–0.79]) and in patients weaning from ventilation (RR 0.48 [0.28–0.80]). The pooled pneumothorax risk was 2.4% (0.8–3.9%) in children and 5.2% (1.0–9.4%) in adults. Meta-analyses had high heterogeneity.
Conclusions: NIV for ARF in these settings appears to be effective.

1. Introduction

Acute respiratory failure (ARF) is a common indication for intensive care unit (ICU) admission in children [1] and adults [2,3] in low- and middle-income countries. Infection-related ARF is among the leading causes of death in adults and children in these countries [4-6], and non-communicable causes of ARF, such as chronic obstructive pulmonary disease (COPD) [7] and congestive heart failure (CHF) [8], are becoming increasingly common. Despite a high burden of critical illness, ICUs are sparse [9,10] and resources are constrained in many low- and middle-income countries [11]. The availability of invasive mechanical ventilation (MV) in low-income countries is limited [12], and its use in the sickest of patients is associated with a high risk of mortality [9].

Non-invasive ventilation (NIV) for ARF, compared to MV, reduces mortality and need for endotracheal intubation (ETI) in selected pediatric [13,14] and adult [15] populations in high-resource settings. Although NIV benefits patients with acute hypercapneic respiratory failure (arterial carbon dioxide tension [$PaCO_2$] >50 mmHg and pH <7.35), its effect is less certain in hypoxemic respiratory failure, defined as arterial oxygen tension (PaO_2) <60 mmHg with a normal or low $PaCO_2$ [15]. NIV also benefits selected patients who are weaning from MV [16]. Furthermore, NIV has been shown to be cost-effective in ICU [17] and ward [18] settings, and thus represents an attractive option in low- and low-middle income countries [19,20]. Therefore, we conducted a systematic review of the literature on NIV for ARF and the peri-extubation period in low- and low-middle income countries. Our

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main objective was to describe the patient populations and outcomes of NIV in this setting; our secondary objective was to summarize trials of NIV versus standard management (including MV) for COPD that enrolled patients from these countries.

2. Materials and Methods

2.1. Search Strategy

We searched MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), and EMBASE from inception until 1 January 2016 without age or language restrictions. We used a highly sensitive search strategy with keywords and MeSH terms for NIV, low- and low-middle income countries, country names, and ARF (Supplementary file, item 1). We included countries categorized as 'low income' or 'low-middle income' in the World Bank [21] list of economies in 2012. Two reviewers (KM, AL) independently reviewed all citations and retrieved the full text of any citation considered potentially relevant by either reviewer. References of included articles were also reviewed for relevant studies.

2.2. Study Selection

We included observational studies and randomized controlled trials (RCTs) of children (age > 28 days) and adults that investigated NIV for treatment of ARF or in the peri-extubation period. We considered the latter situation because faster liberation from MV in resource-constrained areas would allow more patients not eligible for NIV or who failed NIV to be treated with MV. We divided studies in the peri-extubation period into those examining NIV for patients after a failed spontaneous breathing trial (SBT) on MV and those examining NIV use post-extubation (including after surgery). Studies that described both NIV and MV were included if outcomes of patients treated non-invasively were reported separately. We excluded studies of NIV for chronic respiratory failure, as defined by the author or if NIV was used in the out-patient setting. Two reviewers (KM, AL) independently screened citation titles and abstracts. Disagreements were settled by consensus.

2.3. Data Abstraction

Two authors (KM, AL) independently abstracted data from included studies. Data elements included study demographics (country of origin, hospital type, hospital setting); patient demographics (age, gender, Acute Physiology and Chronic Health Evaluation [APACHE] II [22] score); NIV type (bilevel positive airway pressure [BPAP, with inspiratory support above expiratory pressure] or continuous positive airway pressure [CPAP] machine, delivered by mechanical ventilator, or bubble CPAP or ventilator CPAP in children); NIV interface (face mask, full face mask, or nasal prongs); etiology of ARF; risk factors for NIV failure or mortality; and outcomes. For RCTs, we abstracted data from the NIV group. For RCTs in patients with COPD or in the peri-extubation period,

Table 1
Randomized controlled trials and observational studies of non-invasive ventilation in children with acute respiratory failure.

Study, country, setting	Study design[a]	Hospital type, setting	Study arms		Study population (%)[b]	Patient characteristics	
			NIV type, NIV interface, n total (NIV)	Control, n		Female, %	Age, mean months
Cam et al. [32] Vietnam[c], Urban	Retrospective observational	Not reported	Ventilator CPAP Nasal prongs, 25	n/a	Severe pneumonia	Not reported	4·8
Cam et al. [28] Vietnam[c], Urban	RCT	Not reported ICU	Ventilator CPAP Nasal prongs, 18	Oxygen, 19	Dengue shock syndrome	50·0%	79·2
Kinikar et al. [34][f] India[c], Urban	Prospective observational	Public Pediatric ICU	Bubble CPAP Nasal prongs, 36	n/a	H1N1 influenza (50%)	42·0%	150·0
Kinikar et al. [35][g] India[c], Urban	Retrospective observational	Public Pediatric ICU	Bubble CPAP Not reported, 92 (16)	n/a	H1N1 influenza	53·0%	30·0
Wilson et al. [30] Ghana[c], Rural	RCT	Public ED	Bubble CPAP (immediate) Face mask, 31	Bubble CPAP (delayed), 38	Malaria (49%); other diagnoses not given	36·2%	14·4
Balfour-Lynn et al. [31] Ghana[c], Rural	Pre/Post observational	Public Pediatric ward	Ventilator CPAP Face mask, 129	n/a	Malaria (31%); septicemia (24%); pneumonia/bronchiolitis (16%)	55·7%	Not reported
Walk et al. [37] Malawi[d,e,] Urban	Prospective observational	Public Step-down unit/ED	Bubble CPAP Nasal prongs, 77	n/a	Pneumonia (86%); HIV co-infection (22%)	49·0%	4·8
Chisti et al. [29] Bangladesh[d,e], Urban	RCT	NGO Pediatric ICU	Bubble CPAP Nasal prongs, 79	(1) Low flow oxygen, 67 (2) High flow oxygen, 79	Severe pneumonia	Not reported	9·0
Jayashree et al. [33] India[c], Urban	Prospective observational	Public ED	Bubble CPAP Nasal prongs, 330 (163)	n/a	Pneumonia (73%); bronchiolitis (27%)	Not reported	8·4
Machen et al. [36] Malawi[d,e,] Urban	Prospective observational	Public Acute Care Unit	Ventilator CPAP Nasal prongs, 79	n/a	Severe pneumonia	53·2%	3·7

NIV, non-invasive ventilation; RCT, randomized controlled study; ICU, intensive care unit; CPAP, continuous positive airway pressure; ED, emergency department; NGO, non-governmental organization; HIV, human immunodeficiency virus.

[a] "Prospective" refers to studies where patients were accrued after study initiation.
[b] The percentage of patients with a primary diagnosis is given if <100%.
[c] Low-middle income country as categorized by World Bank in 2012.
[d] Low income country as categorized by World Bank in 2012.
[e] Least developed country as defined by United Nations in 2013.
[f] Labeled as Kinikar (1) 2011 in Fig. 1, Panel 1.
[g] Labeled as Kinikar (2) 2012 in Fig. 1, Panel 1.

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