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#### **Review Paper**

## Noninvasive ventilation for acute exacerbations of asthma: A systematic review of the literature

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#### ARTICLE INFORMATION

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#### ABSTRACT

Background: Asthma is a chronic disease characterised by reversible airway obstruction caused by bronchospasm, mucous and oedema. People with asthma commonly experience acute exacerbations of their disease requiring hospitalisation and subsequent utilisation of economic and healthcare resources. Noninvasive ventilation has been suggested as a treatment for acute exacerbations of asthma due to its ability to provide airway stenting, optimal oxygen delivery and decreased work of breathing.

*Objectives*: This paper is a systematic review of the available published research focused on the use of noninvasive ventilation for the treatment of acute exacerbations of asthma to determine if this treatment provides better outcomes for patients compared to standard medical therapy.

Method: Database searches were conducted using EBSCOhost, MEDLINE and PubMed. Search terms used were combinations of 'noninvasive ventilation', 'BiPAP', 'CPAP', 'wheez\*' and 'asthma'. Articles were included if they were research papers focused on adult patients with asthma and a treatment of noninvasive ventilation, and were published in full text in English. Included articles were reviewed using the National Health and Medical Research Council (Australia) evidence hierarchy and quality appraisal tools. Results: There were 492 articles identified from the database searches. After application of inclusion/exclusion criteria 13 articles were included in the systematic review. Studies varied significantly in design, endpoints and outcomes. There was a trend in better outcomes for patients with acute asthma who were treated with noninvasive ventilation compared to standard medical therapy, however, the variability of the studies meant that no conclusive recommendations could be made.

Conclusion: More research is required before noninvasive ventilation can be conclusively recommended for the treatment of acute exacerbations of asthma.

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#### 1. Introduction

This paper presents findings from a systematic review of the literature on the use of noninvasive ventilation (NIV) for the treatment of acute asthma. Asthma is a significant issue in health that has a large economic, physical and psychological impact worldwide. It has been suggested that NIV is an appropriate treatment for acute exacerbations of asthma. The purpose of this systematic review is to examine the current state of the evidence for the use of NIV as a treatment for acute exacerbations of asthma in adults. Examining the literature allows identification of the basis for this

therapy and a veritable account of the current evidence so that clinicians can determine best practice. Designations will be given to the levels of evidence and the literature critically examined to provide recommendations for future research in this area.

#### 2. Background

Asthma is defined as "a chronic disease characterised by reversible airway obstruction caused by bronchial smooth muscle contraction, airway inflammation and increased secretions". Unlike many diseases, asthma is a public health problem that affects countries regardless of the level of development. It is currently estimated that more than 334 million people have asthma internationally. This review is focused on patients who present to hospital with moderate to severe asthma. Approximately 5–10% of asth-

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matic patients experience a severe asthma attack each year and, of those who are admitted to hospital, 10% require intensive care unit (ICU) admission.<sup>3</sup> It is important to note that patients with severe asthma do not commonly show signs of impaired gas exchange until the later stages of the attack when their respiratory system loses the ability to compensate.<sup>3</sup> In 10–26% of cases patients with acute asthma will present to the emergency department with hypercapnia.<sup>3</sup> These patients have a greater likelihood of airway obstruction, high respiratory rate and pulmonary paradoxus compared to their non-hypercapnic counterparts. In-hospital mortality rates for patients with severe asthma who require ICU admission have been reported to be between 3.2–9.8%, with higher mortality rates seen in those patients who require invasive ventilation.<sup>4–6</sup>

Noninvasive ventilation refers to the provision of respiratory support without an invasive airway and has been proposed to treat the pathophysiological changes associated with acute asthma.<sup>7</sup> During acute asthma, the patient's work of breathing is significantly increased to overcome high airway resistance.<sup>8</sup> Expiration becomes active (rather than passive) to overcome the resistance caused by obstructed small airways. As acute asthma progresses, the higher work of breathing is unable to overcome the increasingly small airway diameter which results in low expiratory flow rates and incomplete alveolar emptying. The consequence of this is intrinsic positive end expiratory pressure (PEEP) which places a large workload on the inspiratory muscles, reduces lung compliance and adds a threshold load.<sup>8</sup> Noninvasive ventilation can decrease work of breathing by providing inspiratory positive airway pressure which assists the patient to overcome high airway resistance. Expiratory positive airway pressure also assists with respiration due to the stenting effect of continuous positive airway pressure (CPAP) on the airways and subsequent decrease in hyperinflation of the alveoli. Another benefit of NIV is the ability to deliver optimal fraction of inspired oxygen.<sup>9,10</sup> Noninvasive ventilation also enables the patient to maintain spontaneous respiration which is important in asthma as the contraction of the diaphragm during respiration allows for ventilation in the areas of the lungs that receive the best perfusion.<sup>11</sup> Using NIV as a treatment for patients with asthma exacerbations is aimed at facilitating bronchodilation, preventing acute respiratory failure in patients who have not yet developed impaired gas exchange, preventing intubation in patients with mild/moderate asthma exacerbation and as an alternative to intubation in patients with severe respiratory failure refractory to standard medical therapy.<sup>3</sup>

#### 3. Importance of this topic to critical care nursing

This topic is of importance to critical care nurses broadly but is especially relevant for those working in the emergency department (ED) and ICU. An American study that examined the location of patients at time of NIV initiation found that 38% of all NIV starts occurred in the ICU and 36% of NIV starts occurred in the ED. 12 Of those patients who were started on NIV in the ED, 70% were later transferred to an ICU for continuation of their NIV treatment. 12 This was similar to Canadian studies which found that 32–62% of NIV starts occurred in the ED and 27% in the ICU. 13–15 In Australia, it has been estimated that 56% of all patients started on NIV outside of the ICU are transferred to the ICU. 16 It must also be considered that ICU and ED nurses are commonly members of the medical emergency team who can also be responsible for commencing NIV on the wards. 16,17

#### 4. Aims

The aim of this systematic review is to examine the current available evidence for the use of NIV as a treatment for acute exacer-

**Table 1**Hierarchy of evidence for interventional studies.<sup>22</sup>

| Level | Intervention   |
|-------|--|
| I     | A systematic review of level II studies                                      |
| II    | A randomised controlled trial  |
| III-1 | A pseudorandomised controlled trial  |
| III-2 | A comparative study with concurrent controls:                                |
|       | <ul> <li>Non-randomised experimental trial</li> </ul>                        |
|       | Cohort study   |
|       | <ul> <li>Case-control study</li> </ul>                                       |
|       | <ul> <li>Interrupted time series with a control group</li> </ul>             |
| III-3 | A comparative study without concurrent controls                              |
|       | Historical control study   |
|       | <ul> <li>Two or more single arm study</li> </ul>                             |
|       | <ul> <li>Interrupted time series without a parallel control group</li> </ul> |
| IV    | Case series with either post-test or pre-test/post-test outcomes             |

bations of asthma. There is currently no consensus in international guidelines for the use of NIV for asthma<sup>18–20</sup> thus it is important to review the evidence on this topic and provide clinicians with a contemporary critique of the literature. This review aims to determine if the scientific literature recommends NIV as a safe treatment for these patients and whether it provides better clinical outcomes compared to standard medical therapy alone. The clinical outcomes of interest are mortality, ICU and hospital length of stay, and dyspnoea scores.

#### 5. Method and data evaluation

Database searches were conducted using EBSCOhost, MEDLINE and PubMed. Search terms used were combinations of 'noninvasive ventilation', 'BiPAP', 'CPAP', 'wheez\*' and 'asthma'. Inclusion criteria were studies that focused on a sample group with asthma, the treatment of NIV, those that were published in English, and those with research designs. Studies were excluded if they focused on patients aged younger than 18 years. There was no limit set on date of publication. Studies were initially shortlisted for inclusion based on article title. Abstracts were then examined against the inclusion and exclusion criteria and relevant papers shortlisted again. At the time of full text evaluation, a review of the reference list was also undertaken to identify any omitted relevant research. The studies that met the inclusion criteria were individually examined and rated according to the level of the evidence (Table 1) and quality appraisal tools (Appendix A and the GRACE Checklist).<sup>21</sup>

The quality appraisal tool used to appraise the randomised controlled trials (RCTs) is recommended by the National Health and Medical Research Council<sup>23</sup> (NHMRC) and has been developed by the NHMRC from the Cochrane Handbook for Systematic Reviews of Interventions. Broadly, the evidence provided by the RCTs is rated as Level II according to the hierarchy of interventional studies. The initial intention of this review was to conduct a meta-analysis of study results; however, this was unable to be accomplished due to differing study endpoints and variable hypotheses used in the RCTs, and subsequently a systematic review was conducted.<sup>24</sup> Observational studies were therefore also included and evaluated according to the GRACE Checklist which has previously been tested for validity.<sup>21</sup>

#### 6. Results

The literature search returned a possible 490 matches which were shortlisted according to title and then again by abstract content before being reviewed in full. Fig. 1 shows the selection process that was undertaken as per the PRISMA reporting flow chart.

Thirteen articles were included in the review of which seven were RCTs, two were retrospective cohort studies, two were interrupted time series without a parallel control group, one was a

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