Non-invasive ventilation in acute respiratory failure: a randomised comparison of continuous positive airway pressure and bi-level positive airway pressure

A M Cross, P Cameron, M Kierce, M Ragg, A-M Kelly

Original Article

Methods:
This prospective, randomised study was conducted in the emergency departments of three Australian teaching hospitals: The Royal Melbourne Hospital, Geelong Hospital, and Western Hospital. The study was approved by the relevant clinical research and ethics committees.

Patients presenting to the ED in acute respiratory failure deemed by the treating clinician to require NIV support were randomly assigned to receive either CPAP or BiPAP in addition to standard medical treatment. For the purposes of this study acute respiratory failure was defined by any one of the following inclusion criteria: SaO2 <90% on air, SaO2 <93% on >6 litres O2/min, inability to speak in sentences or respiratory rate >25/min. These criteria were selected to reflect current practice; enabling rapid clinical assessment and initiation of treatment before arterial blood gas analysis has been performed and to include what has traditionally been defined as type 1 and 2 respiratory failure.

Exclusion criteria were: obtundation (to the point of being unable to cooperate or protect the airway), traumatic and congenital causes of respiratory failure (for example, cystic fibrosis, Duchenne’s muscular dystrophy), pneumothorax, gross radiological lobar pneumonia, endotracheal intubation, and a decision to withhold or withdraw treatment made by the clinician in consultation with the patient and/or next of kin.

Abbreviations: CPAP, continuous positive airway pressure; BiPAP, bi-level positive airway pressure; APO, acute pulmonary oedema; NIV, non-invasive ventilation; COAD, chronic obstructive airways disease; PEEP, positive end respiratory pressure.
For both groups NIV was started with a \( \text{FiO}_2 \) of 70% at the initial level of ventilation within five minutes of arrival in the ED. The level of ventilatory support was increased in a stepwise fashion (table 1) every 5–15 minutes as clinically indicated. Optimal NIV was defined as the lowest pressure level of NIV and lowest \( \text{FiO}_2 \) that maintained \( \text{SaO}_2 > 90\% \) or \( \text{PaO}_2 > 60 \text{ mm Hg} \) without further deterioration of any clinical parameters. Weaning followed the reverse sequence and started once the patient had remained stable (by clinical and biochemical parameters) for 30 to 60 minutes.

If a patient randomised to CPAP treatment was diagnosed as having an acute exacerbation of COAD and was not improving after one to two hours of treatment the study protocol allowed for crossover to BiPAP. Such a crossover was considered a failure of CPAP.

Need for endotracheal intubation, and, thus, failure of NIV, were as previously described: respiratory arrest, respiratory pauses with loss of consciousness, psychomotor agitation (making nursing care impossible and requiring sedation), HR < 50 with loss of alertness and haemodynamic instability with systolic BP < 70. Additionally, the clinician could elect to intubate the patient if it is felt their condition was not improving satisfactorily or worsening. If intubation was required within 15 minutes of the start NIV this was judged to be an inappropriate application of NIV rather than a failure of treatment and these patients were excluded from analysis.

Standard treatment was defined according to the condition being treated. For acute pulmonary oedema; intravenous frusemide and nitrates (via any route, aiming for systolic blood pressure of 120–140 mm Hg and stopped if systolic blood pressure < 100 mm Hg). For acute exacerbations of asthma or COAD; \( \beta \)-agonists (initially continuous nebulised 0.5% salbutamol then, if required, intravenous infusions of adrenaline (epinephrine) 0.25–2.0 \mu g/min or salbutamol 5–20 \mu g/min) and parenteral corticosteroids (hydrocortisone 250 mg). For pneumonia; ceftriaxone 1 g intravenously.

Data collected included age, sex, half hourly observations (HR, RR, BP, temperature, \( \text{SaO}_2 \) and Glasgow coma score), blood gas pressures (on arrival, at one hour, and at two hourly intervals thereafter), complications, outcome of NIV (improved, worsened, or admitted with NIV continuing), whether further ventilatory support (standard or NIV) was needed during the admission, disposition (standard ward compared with coronary care, high dependency, or intensive care unit), hospital length of stay, ICU length of stay, and inhospital mortality.

The primary analysis included all patients on an “intention to treat” basis. This study was powered to detect a one hour difference in the duration of NIV. This time frame was selected as being the minimal reduction in treatment duration that would make a significant difference, from a practical point of view, in a busy ED. A subgroup analysis was conducted on the group of patients with APO.

Data were analysed using the two sample Wilcoxon rank sum (Mann-Whitney) test and Fisher’s exact tests, as indicated.

RESULTS

Altogether 101 patients were enrolled in the study (CPAP 51, BiPAP 50). There were no significant differences in age, sex, vital signs, or arterial blood gas measurements on presentation between the groups (table 2).

Seventy one patients (70%) were diagnosed as having had COAD (21%), eight had pneumonia (8%), and one had asthma (1%).

The duration of NIV for the two modalities was not significantly different for either the overall group or the APO subgroup (table 3). In the overall group, the median duration of CPAP was 123 minutes (range 10–338) and, for BiPAP, 132 minutes (range 20–550) \((p = 0.206)\). For the APO subgroup the median duration of CPAP was 123 minutes (range 35–338) and 133 minutes (range 30–530) for BiPAP \((p = 0.320)\).

There was also no significant difference between the treatment modalities for the secondary end points in either the overall or APO groups (tables 3 and 4). None of the patients diagnosed with COAD and randomised to CPAP were crossed over to BiPAP.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Levels of non-invasive ventilatory support</th>
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<tr>
<td><strong>CPAP (cm H2O)</strong></td>
<td><strong>BiPAP—increasing PSV</strong></td>
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<tr>
<td>Initial level</td>
<td>5</td>
</tr>
<tr>
<td>Second level</td>
<td>10</td>
</tr>
<tr>
<td>Third level</td>
<td>15</td>
</tr>
<tr>
<td>Fourth level</td>
<td>20</td>
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<th>Table 2</th>
<th>Presentation characteristics</th>
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<td><strong>Group overall (n = 101)</strong></td>
<td><strong>APO subgroup (n = 71)</strong></td>
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<tr>
<td><strong>A: CPAP</strong></td>
<td><strong>B: BiPAP</strong></td>
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<tr>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td><strong>Age (y)</strong></td>
<td>74</td>
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<tr>
<td><strong>Temperature (°C)</strong></td>
<td>35.7</td>
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<tr>
<td><strong>Heart rate (beat/min)</strong></td>
<td>114</td>
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<tr>
<td><strong>Systolic BP (mm Hg)</strong></td>
<td>162</td>
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<tr>
<td><strong>Diastolic BP (mm Hg)</strong></td>
<td>87</td>
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<tr>
<td><strong>Respiratory rate (min)</strong></td>
<td>35</td>
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<tr>
<td><strong>\text{SaO}_2 (%)</strong></td>
<td>92</td>
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<tr>
<td><strong>GCS</strong></td>
<td>14</td>
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<tr>
<td><strong>pH</strong></td>
<td>7.22</td>
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</table>
The overall complication rate in this study was 8%. The complication rate was not significantly different for CPAP compared with BiPAP in either the heterogenous or the APO group (p = 1.00 for both). Of the eight patients with complications two had vomiting, three had respiratory deterioration, one cardiogenic shock, one hypotension, and one evolution of ST segment elevation on the ECG.

DISCUSSION

Emergency physicians are often confronted with patients with acute respiratory failure. On occasion it is necessary to select therapeutic interventions, including a method of NIV, before a firm diagnosis is made.

This study shows that CPAP and BiPAP are not significantly different with respect to duration of NIV, rates of complications, in-hospital mortality, disposition from the ED, hospital and ICU length of stay, or need for further ventilation in either the overall, heterogenous group, or the APO subgroup. These findings suggest that it is not important whether CPAP or BiPAP is given to patients with undifferentiated respiratory failure or those known to have APO.

An implication of this finding is that EDs considering acquisition of NIV equipment could potentially justify the purchase of a simpler, cheaper, CPAP only device with a low likelihood of compromising patient care.

The mean durations of NIV treatment compare very favourably with published experience. Mehta et al in a randomised trial in an ED setting comparing CPAP with BiPAP in acute pulmonary oedema reported mean durations of treatment of 6.4 hours (SD 5.8 hours) and 7.1 hours (SD 4.7 hours) respectively.7 Although many of the presentation characteristics of the patients and the ventilation levels in this study were similar there were two important differences: the use of nasal masks (the inability of distressed patients, unfamiliar with the device to maintain positive pressure in the airway is likely to have significantly reduced effectiveness) and the use of respiratory technicians to assess and adjust treatment would have been slower and less responsive than the bedside nurses who controlled treatment in this study. Kelly et al, in a retrospective study of CPAP for APO in an Australian ED, reported an average duration of treatment of 1.9 hours,11 very similar to this study. Most studies have been carried out in intensive care units with intermittent NIV over days to weeks.3–5,8–10,12,13

The rate of failure of NIV and need for endotracheal intubation was not significantly different between treatments for either the heterogenous or the APO group. The overall intubation rate of 9% compares favourably with the rates of 9%–24% quoted in the trials referred to above. It has been suggested there may be no means of predicting successful NIV (that is, avoidance of endotracheal intubation) on the basis of initial data.14

The obvious limitation to this study is the lack of an objective indicator as to when NIV should cease. Common practice relies on an ill defined mixture of the physician’s clinical assessment of the patient, observations, blood gas analysis, and the timing of when the physician is able to review the patient. Although these factors apply equally to patients receiving CPAP and BiPAP the duration of treatment any individual patient actually needs may be shorter than has been found in this study. Another specific limitation was the inability to blind the treating staff to the mode of treatment because the ventilator’s display indicates the modality. Other
limitations relate to the generalisability of results to other hospitals. No firm conclusions can be drawn from this study of the relative merits of CPAP and BiPAP in the emergency treatment of acute exacerbations of COAD, asthma, pneumonia, and a range of other specific causes of acute respiratory failure because low numbers in these subgroups precluded subgroup analysis.

In summary, this pilot study found there was little or no difference in duration of treatment or outcomes for ED patients with acute respiratory failure of a heterogeneous nature or for those with APO when CPAP was compared with BiPAP. No conclusions could be made when CPAP was compared with BiPAP in the setting of COAD.

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REFERENCES