REVIEW

Hypercapnic encephalopathy syndrome: A new frontier for non-invasive ventilation?

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Non-invasive ventilation; Hypercapnic encephalopathy; Endotracheal intubation; Acute respiratory failure; Respiratory intensive care unit; Sedation

Summary
According to the classical international guidelines, non-invasive ventilation is contraindicated in hypercapnic encephalopathy syndrome (HES) due to the poor compliance to ventilatory treatment of confused/agitated patients and the risk of aspirative pneumonia related to lack of airways protection. As a matter of fact, conventional mechanical ventilation has been recommended as "golden standard" in these patients.

However, up to now there are not controlled data that have demonstrated in HES the advantage of conventional mechanical ventilation vs non-invasive ventilation. In fact, patients with altered mental status have been systematically excluded from the randomised and controlled trials performed with non-invasive ventilation in hypercapnic acute respiratory failure. Recent studies have clearly demonstrated that an initial cautious NPPV trial in selected HES patients may be attempt as long as there are no other contraindications and the technique is provided by experienced caregivers in a closely monitored setting where ETI is always readily available.

The purpose of this review is to report the physiologic rationale, the clinical feasibility and the still open questions about the careful use of non-invasive ventilation in HES as first-line ventilatory strategy in place of conventional mechanical ventilation via endotracheal intubation.

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Introduction

"Hypercapnic encephalopathy syndrome" (HES) is a heterogeneous and potentially reversible wide spectrum of neurologic alterations (from cognitive defects, psychomotor agitation and confusion with asterixis to soporosis status, delirium and coma) occurring in the presence of acute respiratory failure (ARF) with severe decompensated respiratory hypercapnic acidosis.

Patho-physiology of HES is not fully understood as its clinical manifestations are not always clearly connected with PaCO₂ levels and several pulmonary and extra-pulmonary factors are involved. The mechanism which may better explain HES is dependent on the acidosis of cerebrospinal fluid and of brain interstitial tissue (Table 1, Fig. 1). Acute respiratory acidosis has a greater impact on liquor pH than metabolic acidosis; in fact, differently from hydrophilic molecules, CO₂ passes very quickly through the haemato-encephalic barrier because of its high liposolubility. Accordingly, symptoms of HES are correlated stronger with the changes in cerebrospinal pH than with those of arterial pH and/or PaCO₂. The role played by both hypoxaemia and non-controlled oxygen-therapy (i.e. high inspiratory oxygen fractions (FiO₂)) may be not irrelevant (Fig. 1).

From the clinical point of view, none of the three most common used neurological scores have been validated to assess HES severity: Glasgow coma scale (GCS), encephalopathy score (ES), Kelly–Matthay scale (KMS) (Table 2). Although GCS is the tool which has been mostly used in the clinical practice, this 15-point scoring system was originally built to assess and monitor changes in the level of consciousness occurring after head injury. ES is a 4 level-scale which was introduced by Brochard et al. to assess neurological dysfunctions in patients with hypercapnic ARF; the main limitation of this tool is the lack of specificity and clarity (i.e. same level of scale for different consciousness disturbances). The 6-level KMS is the only tool which was specifically designed to evaluate neurological alterations in patients ventilated in Intensive Care Unit (ICU) and who has been recently shown to have a prognostic value in HES patients treated with non-invasive positive pressure ventilation (NPPV) in a Respiratory High-Dependency Unit (RHDU).

NPPV has reached the highest level of scientific evidence as first-line ventilatory technique to treat episodes of ARF occurring in COPD exacerbations, cardiogenic pulmonary oedema, immunosuppressed patients and during the transition from invasive ventilation to spontaneous breathing. Conversely, the effectiveness of NPPV in other acute diseases (e.g. pneumonia and acute lung injury) and in specific clinical conditions (e.g. patients with impairment of sensorium and/or difficulty in removing secretions) has not still been demonstrated.

This paper is an up-date of the role of non-invasive ventilation to treat HES; alterations of consciousness due to primitive neurological diseases (e.g. stroke) and to other metabolic/toxic causes are excluded.

Ventilatory strategies in hypercapnic encephalopathy

Management of HES should be based on: 1) close monitoring in units with an adequate level of expertise (i.e. ICU, RHDU); 2) "etiologic treatment" towards the precipitating condition (i.e. pneumonia, COPD exacerbation, heart decompensations) plus "controlled oxygen-therapy" (e.g. to avoid PaCO₂ rebound by an injudicious use of O₂); 3) mechanical ventilation to quickly correct gas exchange and neurological status; 4) "protection of airways" in patients without efficient cough to prevent pulmonary infections (i.e. "ab ingestis" and bronchial mucous retention); 5) "control" of psychomotor agitation which may occur at

Table 1  Pathogenetic mechanisms of Hypercapnic Encephalopathy Syndrome.

| 1) Intra-cranic hypertension secondary to vasodilatation of resistance cerebral arteries |
| 2) Cerebrospinal fluid and brain tissue acidosis with: |
| - increased cerebral blood flow and oedema |
| - lower levels of cerebral phosphocreatine |
| - higher lactate/pyruvate ratio, higher cerebral levels of glucose-6-phosphate and fructose-6-phosphate with impaired Krebs cycle metabolism of carbohydrates |
| - increased aminoacids metabolism with higher cerebral levels of ammonium and glutamine |
| 3) Cerebral hypoxia due to arterial systemic hypoxemia |
| 4) Rebound effect of high FiO₂ on PaCO₂ and pH from: hypoventilation due to suppressed hypoxic stimulus drive; altered ventilation/perfusion ratio; Haldane effect |
| 5) Neurotropic drugs (i.e. benzodiazepines, opioids) |
| 6) Impaired cardiovascular and renal function |
| 7) Alterations of hydro-electrolytic balance |
| 8) Primitive coexistent cerebral diseases (i.e. chronic atherosclerotic encephalopathy) |
either the onset of HES episode or during the “awakening phase” of a comatose patient.2

According to the Consensus Conference, international reviews and states of the art, NPPV is contraindicated in HES (i.e. GCS < 10), while endotracheal intubation (ETI) is recommended and, therefore, conventional mechanical ventilation (CMV) considered the "golden standard" ventilatory strategy.15,17 These statements are based on both the poor/lack compliance to NPPV of confused/agitated HES patients and the risk of aspirative pneumonia related to NPPV-induced gastro-distension, weak cough and lack of airways protection. Moreover, some clinical studies identified neurological impairment as a negative prognostic factor for NPPV outcome.18–21

However, up to now there are not controlled data that have demonstrated the advantage of CMV vs NPPV in HES.

Table 2  Clinical tools for the assessment of neurological impairment in critically ill patients.

<table>
<thead>
<tr>
<th>Glasgow Coma Scale (GCS)</th>
<th>Verbal response (V)</th>
<th>Motor response (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes open (E)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneously (4 p.)</td>
<td>Oriented (5 p.)</td>
<td>Obey verbal command (6 p.)</td>
</tr>
<tr>
<td>To verbal stimulation (3 p.)</td>
<td>Confused (4 p.)</td>
<td>Localises pain (5 p.)</td>
</tr>
<tr>
<td>To painful stimulation (2 p.)</td>
<td>Inappropriate words (3 p.)</td>
<td>Defend from painful stimulus (4 p.)</td>
</tr>
<tr>
<td>No open (1 p.)</td>
<td>Incomprehensible sounds (2 p.)</td>
<td>Decorticate rigidity (3 p.)</td>
</tr>
<tr>
<td></td>
<td>No response (1 p.)</td>
<td>Decerebrate rigidity (2 p.)</td>
</tr>
</tbody>
</table>

GCS = E + V + M; range from 3 (worst neurological impairment) to 15 points (normal sensorium)

Encephalopathy score (ES)

| Grade 0 = normal |
| Grade 1 = hypertonia or cogwheel rigidity without an abnormality in consciousness |
| Grade 2 = tremor, asterixis, or daytime sleepiness |
| Grade 3 = confusion or agitation |
| Grade 4 = prostration or vigil coma |

Kelly–Matthay score (KMS)

| Grade 1 = alert, follows complex 3-step command |
| Grade 2 = alert, follows simple commands |
| Grade 3 = lethargic, but arousable and follows simple commands |
| Grade 4 = stuporous (only intermittently follows simple commands even with vigorous attempts to arouse the patient) |
| Grade 5 = comatose, brain stem intact |
| Grade 6 = comatose with brain stem dysfunction |

Figure 1  Pathogenesis of Hypercapnic Encephalopathy Syndrome. CBF: cerebral blood flow; CSF: cerebrospinal fluid; ICP: intracranic pressure; V/Q: ventilation/perfusion ratio.
fact, patients with altered mental status have been systematically excluded from the randomised controlled trials (RCTs) performed with NPPV in hypercapnic ARF. Furthermore, some observational studies have not confirmed that HES is a negative predictor for NPPV success. Conversely, some points are in favour of the rationale employ of NPPV in HES:

1) the similar efficacy of NPPV vs CMV in terms of unloading respiratory muscles, gas exchanges improvement and in-hospital mortality in severely acidotic COPD patients in whom mechanical ventilation is mandatory; furthermore, the application of non-invasive negative pressure ventilation via iron lung (ILV) has turn out to be as effective as CMV in severe hypercapnic ARF.

2) the reduced risk of ventilator associated pneumonia (VAP) with NPPV in place of CMV to treat ARF due to the avoidance of endotracheal tube and the less number of invasive devices; moreover, an RCT demonstrated the usefulness of NPPV in severe community-acquired pneumonia (CAP) occurring in COPD patients.

3) the physiologic barrier of the upper and lower oesophageal sphincters (respectively tone of 40 and 32 cm H2O) against the risk of gastro-distension during NPPV.

4) the role of NPPV as “ceiling therapy” or as “tool to buy time in the end-of-life decisions” in HES patients with “end-of-stage” chronic respiratory disorders.

5) the reduced costs of treating COPD patients without multi-organ failure (MOF) in RHDU vs ICU.

Non-invasive ventilation in hypercapnic encephalopathy: where we are?

The first and larger trial on the use of non-invasive ventilation in HES is the retrospective study of Corrado et al. conducted in an RHDU with iron lung applied to 150 cases of hypoxaemic–hypercapnic coma with severe acidosis. The authors reported ILV success in avoiding ETI of 70% and an hospital mortality of 24% with a quick sensorium recover (median time = 4 h). The outcome resulted stratified depending on HES severity, being worst for GCS ≤ 5. Only 5 patients developed pulmonary aspiration, but all of them survived. Unfortunately, ILV is available in few centres which have acquired a great experience with this ventilatory technique.

The majority of data are about non-invasive ventilation in HES patients reported the use of NPPV delivered via nasal and full-face mask.

The first attempt of using NPPV in HES is found in Benhamou et al. study, where nasal NPPV succeeded in 60% of ARF patients, most of them showing an altered level of consciousness; specifically, two out of 3 cases with a GCS = 3 were responsive to NPPV. Then, only few case reports and clinical series including a limited number of HES patients treated with NPPV were published. More recently, some non-RCT studies have demonstrated the feasibility of NPPV to successfully treat HES patients.

A prospective uncontrolled ICU Spanish study, Diaz et al compared the efficacy of NPPV applied via facial mask to 95 patients with GCS ≤ 8 vs that achieved in 863 patients with GCS > 8. Surprisingly, the rate of NPPV success was slightly but significantly greater in comatose than non-comatose patients (80% vs 70.1%; p = 0.0434) without significant difference in-hospital mortality (26.3% vs 33.2%; p > 0.05). Moreover, 1 h of NPPV quickly and significantly improved blood gases, diastolic pressure and sensorium in comat group, with quick normalisation of mental status (mean time = 4.1 h) in 85.3% of cases. By applying the multivariate analysis, GCS after 1 h of NPPV and the degree of MOF at ICU admission were the only parameters which independently predicted NPPV failure. The main limitation of the study is the heterogeneous distribution of the diseases between the two groups: compared to GCS ≥ 8 group, GCS ≤ 8 group showed a greater prevalence of more NPPV-responsive diseases, like COPD (69.5% vs 25.5%), respect to that of disorders in whom the likelihood of NPPV success is lower, as CAP or ARDS (8.4% vs 22.5%).

In the second case-control prospective Italian study performed in an RHDU, Scala et al. analysed the outcome of NPPV in three groups of COPD patients in ARF with different degrees of HES (mild, KMS = 2; moderate, KMS = 3; severe, KMS > 3) compared to that of a control group with a normal sensorium (KMS = 1), strictly matched in terms of several clinical—physiological parameters. After 1–2 h of NPPV the authors reported a significant improvement of blood gases and KMs in all groups. Rates of NPPV failure, in-hospital and 90-days post-discharge mortality were progressively worst as much severe was the degree of HES reaching the significance only between the KMS > 3 and the control group. Among the causes leading to NPPV failure, only cardiovascular complications were significantly greater in the KMS > 3 vs the control group, in accordance with the negative effects of acidosis upon myocardial inotropism and excitability and with the prognostic impact of cardiovascular comorbidities in COPD exacerbations needing NPPV. Conversely, the number of treatment failures due to an inefficient removal of secretions was similar among all groups without cases of aspirative pneumonia. The authors hypothesised that the risk of aspiration might have been minimised by the quick improvement of neurological status under NPPV.

In the third case-control study performed in a Chinese RHDU, Zhu et al. did not report a worst outcome of NPPV via face mask (ETI and hospital mortality) in a group of 22 COPD patients with GCS < 10 vs a control group of 21 subjects with GCS ≥ 10, even though pressure support, NPPV time and RHDU length of stay were significantly higher in the former group.

Very recently, a case-control study Scala et al. compared the hospital outcomes of 20 patients with COPD exacerbations and moderate-severe HES (i.e. KMS ≥ 3) managed by NPPV in an RHDU vs that of 20 COPD subjects (strictly matched for age, SAPS II, arterial blood gases) managed by CMV in an ICU. Gas exchange significantly improved after 2 h in both groups. In-hospital mortality, one-year mortality and tracheostomy rate were similar in the two groups, while complication rate (p = 0.027) was lower in NPPV-group due to fewer cases of nosocomial pneumonia and sepsis. NPPV-group showed also a shorter duration of ventilation (p = 0.009) than CMV-group. The authors suggested that, despite some limitations of their study (no-RCT design; different settings of care), an initial cautious NPPV trial in patients with COPD exacerbations and HES may be attempt as long as there are no other contraindications and the
<table>
<thead>
<tr>
<th>Author, year</th>
<th>Type of study</th>
<th>Setting</th>
<th>Patients/COPD</th>
<th>pH</th>
<th>PaCO₂ (mmHg)</th>
<th>PaO₂/FiO₂</th>
<th>Sensorium level</th>
<th>Need of ETI (%)</th>
<th>Hospital mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corrado, 1996</td>
<td>Retrospective (ILV)</td>
<td>RHDU</td>
<td>150/118</td>
<td>7.13</td>
<td>112</td>
<td>43.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>GCS ≤ 8</td>
<td>30</td>
<td>24</td>
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<td>Corrado, 2004</td>
<td>RCT (ILV vs CMV)</td>
<td>RHDU</td>
<td>22/22</td>
<td>7.20</td>
<td>96</td>
<td>192</td>
<td>GCS = 14 (3–15)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>18.2</td>
<td>18.2</td>
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<td>Benhamou, 1992</td>
<td>Open, prospective</td>
<td>ICU</td>
<td>30/20</td>
<td>7.29</td>
<td>65</td>
<td>44&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Altered in 60%</td>
<td>40</td>
<td>47</td>
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<td>Fernandez, 1993</td>
<td>Open, prospective</td>
<td>ICU</td>
<td>14/14</td>
<td>7.19</td>
<td>92</td>
<td>98&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Altered</td>
<td>21</td>
<td>7</td>
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<tr>
<td>Carlucci, 2001</td>
<td>Multicenter Prospective</td>
<td>ICU</td>
<td>36/NA</td>
<td>7.35&lt;sup&gt;b&lt;/sup&gt;</td>
<td>56&lt;sup&gt;b&lt;/sup&gt;</td>
<td>214&lt;sup&gt;b&lt;/sup&gt;</td>
<td>ES ≥ 1</td>
<td>53</td>
<td>NA</td>
</tr>
<tr>
<td>Conti, 2002</td>
<td>RCT (NPPV vs CMV)</td>
<td>ICU</td>
<td>23/23</td>
<td>7.20</td>
<td>85</td>
<td>168</td>
<td>KMS = 3 (5)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>52</td>
<td>26</td>
</tr>
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<td>Dueñas-Pareja, 2002</td>
<td>Open, prospective</td>
<td>RW</td>
<td>13/10</td>
<td>7.18</td>
<td>92</td>
<td>203</td>
<td>GCS ≤ 7</td>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>Confalonieri, 2005</td>
<td>Multicenter Prospective</td>
<td>ICU, RHDU, RW</td>
<td>1033/1033</td>
<td>7.28</td>
<td>80.4</td>
<td>180</td>
<td>GCS = 13.2 (2.3)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>22.8</td>
<td>13.7</td>
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<tr>
<td>Diaz, 2005</td>
<td>Open, prospective</td>
<td>ICU</td>
<td>95/66</td>
<td>7.13</td>
<td>99</td>
<td>139</td>
<td>GCS = 6.5 (1.7)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>24</td>
<td>25</td>
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<td>Scala, 2005</td>
<td>Case-control</td>
<td>RHDU</td>
<td>20/20</td>
<td>7.28</td>
<td>79.3</td>
<td>164</td>
<td>KMS = 2</td>
<td>25</td>
<td>25</td>
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<td>Scala, 2005</td>
<td>Case-control</td>
<td>RHDU</td>
<td>20/20</td>
<td>7.26</td>
<td>81.9</td>
<td>170</td>
<td>KMS = 3</td>
<td>30</td>
<td>20</td>
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<tr>
<td>Scala, 2005</td>
<td>Case-control</td>
<td>RHDU</td>
<td>20/20</td>
<td>7.22</td>
<td>91.1</td>
<td>154</td>
<td>KMS &gt; 3</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>Honrubia, 2005</td>
<td>RCT (NPPV vs CMV)</td>
<td>ICU</td>
<td>31/20</td>
<td>7.27</td>
<td>72.0</td>
<td>119</td>
<td>KMS = 3–5&lt;sup&gt;e&lt;/sup&gt; in 58%</td>
<td>58</td>
<td>32</td>
</tr>
<tr>
<td>Zhu, 2007</td>
<td>Case-control</td>
<td>RHDU</td>
<td>43/43</td>
<td>7.18</td>
<td>102</td>
<td>168</td>
<td>GCS = 7.5 (1.9)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>27.3</td>
<td>13.6</td>
</tr>
<tr>
<td>Scala, 2007</td>
<td>Case-control (NPPV vs CMV)</td>
<td>RHDU</td>
<td>20/20</td>
<td>7.22</td>
<td>88.2</td>
<td>162</td>
<td>KMS = 3–5&lt;sup&gt;e&lt;/sup&gt;</td>
<td>35</td>
<td>25</td>
</tr>
<tr>
<td>Claudett, 2008</td>
<td>Case-control (NPPV vs CMV)</td>
<td>ED</td>
<td>12/12</td>
<td>7.18</td>
<td>75.3</td>
<td>103&lt;sup&gt;a&lt;/sup&gt;</td>
<td>GCS = 5.6 (1.3)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>16.7</td>
<td>16.7</td>
</tr>
<tr>
<td>Scala, 2011</td>
<td>Case-control (NPPV vs CMV)</td>
<td>RHDU</td>
<td>15/15</td>
<td>7.27</td>
<td>76.0</td>
<td>163</td>
<td>KMS = 3.4</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

ILV = Iron lung ventilation; NPPV = non-invasive positive pressure ventilation; COPD = chronic obstructive pulmonary disease; CMV = conventional mechanical ventilation; RCT = randomized controlled trial; NA = not available; GCS = Glasgow Coma Scale; KMS = Kelly–Matthay Scale; ES = Encephalopathy Score; ICU = Intensive Care Unit; RHDU = Respiratory High-Dependency Unit; ED = Emergency Department; RW = Respiratory Ward; ETI = endotracheal intubation.

<sup>a</sup> PaO₂ (mmHg).
<sup>b</sup> Arterial blood gases in all 108 patients submitted to NPPV, with and without hypercapnic encephalopathy.
<sup>c</sup> Mean (range).
<sup>d</sup> Mean (standard deviation).
<sup>e</sup> Range.
technique is provided by experienced caregivers in a closely monitored setting where ETI is always readily available.

Similarly, in the second case-control study performed in a South-American Emergency Department (ED) comparing NPPV vs CMV in treating HES patients, Claudett et al.49 did not report any differences in the clinical outcomes of the studied 24 patients. It has to be remarked the high mean values of PaO2 (about 100 mmHg) in the population which suggested that an inadequate O2-therapy may have contribute to HES development; thus may have overestimated the NPPV success.

The comparability of the findings of the different studies about the application of NPPV in HES is difficult to be performed, due to the heterogeneity in the severity of altered level of consciousness, in the typology of the population recruited (underlying diseases, comorbidities, arterial blood gases), in the setting and in the modality of treatment. Concerning the type of the treated respiratory disorders, the majority of the available data in favour of the successful use of NPPV in HES are referred to COPD exacerbations. This is in accordance with the experience of Phua et al.52 who clearly showed that in a multivariate analysis the likelihood of NPPV failure is significantly greater in non-COPD compared to COPD patients.

Another confounding factor is the different clinical tool chosen in the published studies to assess the level of neurological dysfunction. The degree of HES as measured by the three available systems (GCS, ES, KMS)10–12 cannot be compared due to the different way to assess mental impairment that was used by each one. It may be believed that for highest levels of dysfunction which identify the condition of “hypercapnic coma” (i.e. GCS < 8, ES > 3, KMS > 4) the chance of NPPV success is substantially reduced.

It should be underlined that in these studies NPPV was applied almost continuously in the first 24–48 h till the recovery of alertness and the improvement in blood gases.

The "integrated use" of ILV and NPPV is likely to expand the success in HES patients, as suggested by the "real world" study in whom the need of ETI was strongly reduced in a large series of patients with exacerbations of chronic respiratory disorders.53

It’s important to highlight that a great deal of these data on the success of non-invasive ventilation in patients with altered mental status were achieved in centres (ICU and RHDU) with a good experience in NPPV and/or ILV,54 a strong motivation for non-invasive techniques of monitoring and of ventilatory support, an immediate access to CMV and a quick management of complications occurring in critical patients.

**Drawbacks for non-invasive ventilation in hypercapnic encephalopathy**

The first limitation for the feasibility and the success of NPPV in HES is the lack of co-operation in agitated patients who could not cope with the mask and the pressurised air pushed by the ventilator.14 Despite the assistance provided by an experienced nurse team, severe patient-ventilator asynchrony, major air leaks and patient’s attempts in removing the interface may make impossible for the physician to provide an adequate NPPV therapy leaving as the only option the assistance with CMV under heavy pharmacological sedation.

Concerning the problem of psychomotor agitation and the possibility of using pharmacologic sedation to increase the compliance to NPPV in HES, a recent multi-centre survey55 demonstrated that a large majority of the physicians infrequently used sedation and analgesic therapy (<25% of cases), even though practices varies depending on geographic regions (North America higher vs Europe) and speciality (critical care specialists higher vs pulmonologists). The most common used drugs were lorazepam (North America) and morphine (Europe). The setting and the nurse-patient ratio influenced the choice of using sedation during NPPV in this survey, suggesting that only a close monitoring may allow this practice “safely” preventing the risk of a respiratory depression. So far some pilot studies56–59 reported the feasibility of different sedations during NPPV in poor/lack cooperative patients to increase the success of the ventilatory technique. However, before its routine implementation in the clinical ground, this topic need to be further investigated due to the fact that the risk-benefit balance of this practice depends on the environment, the experience of the team, the type of drug and the patient’s status.

Another important drawback for the successful use of NPPV in HES patients with a depress cough reflex is the inefficacy to spontaneously clear airways from an excessive burden of respiratory secretions1–14; this is essentially due to the kinds of interfaces used to deliver NPPV, which do not allow direct access into the Airways. Consequently, the inability to spontaneously remove respiratory secretions has been considered a contraindication to start NPPV in ARF, especially in patients with impaired consciousness and depressed cough.14–17

Few published data suggested that some non-invasive physiotherapeutic techniques may improve mucous clearance in COPD exacerbations managed with NPPV.60–62 Unfortunately, no data are available with these techniques in patients with HES and abundant restagnant secretions.

Recently, in the clinical scenario of patients with COPD decompensations who require ETI and CMV because of impaired mucous clearance and HES, Scala et al.63 postulated that the early suction of secretions with fiberoptic bronchoscopy (FBO) performed during NPPV is feasible and may also allow for the successful expanded application of NPPV. This thesis was supported by the feasibility and safety of performing a diagnostic FBO with broncho-alveolar lavage (BAL) for a suspected pneumonia under NPPV in patients with either hypoxaemic or hypercapnic ARF.64–69

In a matched case-control study Scala et al.63 compared 15 acutely decompensated COPD patients with copious secretion retention and HES due to CAP undergoing early FBO plus BAL during NPPV in an expert RHDU with 15 controls (matched for blood gases, APACHE III score, KMS, pneumonia extension and severity) receiving CMV in the ICU. Two hours of NPPV plus FBO significantly improved ABGs, sensorium and cough efficiency without major complications (cardiovascular events, emergent ETI, pneumothorax). Improvement in PaCO2 and pH, as well as hospital mortality, and durations of hospitalisation and ventilation were similar in NPPV vs CMV-groups. NPPV significantly reduced serious infectious complications compared with CMV, as well as the need for tracheostomy
Even if this NPPV strategy may be a successful alternative to CMV to manage selected COPD patients within expert units, the authors acknowledged for some potential limitations of their study (case-control design without randomisation, different settings of treatment of the two groups, applicability of the data only to units with a large expertise on NPPV and FBO). Larger RCTs are necessary to confirm this preliminary result and, therefore, to test the efficacy of the FBO—NPPV protocol applied to an earlier time-course of COPD decompensations when ETI is not mandatory by comparing NPPV alone vs NPPV with early FBO.

Conclusions

Due to the lack of protection of airways, non-invasive ventilation is traditionally not recommended in HES while CMV is considered the "gold-standard". However, recent literature data have demonstrated that the risk of pulmonary aspiration and the likelihood of NPPV ineffectiveness are surely overestimated in HES. According to these preliminary results obtained in few motivated centres, a cautious attempt of NPPV/ILV seems to be justified in selected COPD patients with HES provided that it’s performed by an high experienced team with a close monitoring and prompt availability of CMV (Fig. 2). Given the fact that these published data may be not replicated in units with lower degree of expertise and lower intensity of care, so far a large-scale application of NPPV to treat HES is not routinely recommended. Furthermore, an unduly delay in prompt intubating patients with severe ARF-related altered consciousness, may increase the risk of serious systemic complications and, eventually, of death. As a matter of a fat, further large-scale controlled studies are needed to confirm these data about the feasibility and success of NPPV/ILV in HES and, therefore, to clarify the role of sedation and FBO-based strategy to overcome the drawbacks occurring during NPPV in this series of patients.

Conflict of interest statement

The author has no conflict of interest.

References

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