Noninvasive mechanical ventilation in acute respiratory failure

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ABSTRACT: Mechanical ventilation (MV) has been indicated in the treatment of acute respiratory failure (ARF) if conservative treatment fails. Invasive MV is associated to a variety of complications. The recent innovations of noninvasive methods of MV (NMV) avoid the complications of invasive MV, whilst ensuring a similar degree of efficacy. A review of the literature from 1989 to 1995 shows that use of NMV in ARF has been reported in several studies involving more than 400 patients most of them COPD. NMV was successful from 51 to 91%, the severity of ARF being widely different among the different studies. Most of the studies compared effectiveness of NMV with historical groups of patients treated with "conventional" medical therapy whilst controlled studies of NMV versus ET intubation are lacking. Type of mask, mode of ventilation, compliance to treatment, type of patient and severity of disease may influence the success rate.

Success with NMV was associated with less severely abnormal baseline clinical and functional parameters and to less severe levels of acidosis assessed during an initial trial of NMV. Therefore, NMV may be useful in selected patients with ARF. Patients should have clinical and physiological evidence of ARF and should be sufficiently cooperative. It is commonly said that NMV should be avoided, and endotracheal (ET) intubation performed in patients with haemodynamic instability, uncontrolled arrhythmias, gastrointestinal bleeding, high risk for aspiration. With these limitations NMV in selected patients with ARF is well tolerated and may be useful in avoiding ET intubation in most cases of COPD and with a wide range of success rates in other disease. This in turn has several advantages in terms of avoiding complications of invasive MV, reducing the length of stay in ICU and probably the number of ICU readmissions. Side effects of NMV seem less severe than those induced by invasive MV.

In conclusion in selected patients a trial of noninvasive mechanical ventilation, as an adjunct to medical therapy, should be instituted at an early stage of ARF episodes before severe acidosis ensures, to avoid ET intubation.

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For more than 30 yrs, acute respiratory failure (ARF) has been one of the most frequent causes of admission to the Intensive Care Unit (ICU) [1]. The treatment of ARF is described as conservative if the patient is managed without intubation or tracheostomy and mechanical ventilation (MV). Many cases of ARF can be treated in a conservative way. MV via endotracheal (ET) tube or tracheostomy has been indicated if conservative treatment fails. Classic indications for MV are: deterioration of consciousness; cardiac or respiratory arrest; exhaustion or extreme fatigue [2]. The aims of MV are shown in table 1. MV makes it possible: 1) to obtain time for the cause of ARF to subside; and 2) to let the respiratory muscles (RM) rest and recover [3]. However, it is still difficult to predict which patients will require MV and when it should be instituted. Furthermore, there is no general agreement about which kind of ventilatory support is preferable.

<table>
<thead>
<tr>
<th>Table 1. – Objectives of mechanical ventilation [3]</th>
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</thead>
<tbody>
<tr>
<td>Improve pulmonary gas exchange</td>
</tr>
<tr>
<td>Reverse hypoxaemia</td>
</tr>
<tr>
<td>Relieve acute respiratory acidosis</td>
</tr>
<tr>
<td>Relieve respiratory distress</td>
</tr>
<tr>
<td>Decrease oxygen cost of breathing</td>
</tr>
<tr>
<td>Reverse respiratory muscle fatigue</td>
</tr>
<tr>
<td>Alter pressure-volume relations</td>
</tr>
<tr>
<td>Prevent and reverse atelectasis</td>
</tr>
<tr>
<td>Improve compliance</td>
</tr>
<tr>
<td>Prevent further injury</td>
</tr>
<tr>
<td>Permit lung and airway healing</td>
</tr>
<tr>
<td>Avoid complications</td>
</tr>
</tbody>
</table>

Complications of invasive mechanical ventilation

For several decades, mechanically-assisted intermittent positive pressure ventilation has been performed,
initially, by installing an artificial airway, the ET tube, and, in the event of prolonged ET intubation, later performing a tracheostomy. MV exposes the patient to a variety of complications resulting from the intubation procedure, during the course of ventilation, after removing the tube or due to tracheostomy [4]. A prolonged attempt at intubation may result, infrequently but dangerously, in cardiac arrest, generalized seizures and gastric distension. Self-extubation, mechanical dysfunction of the ET tube and cuff leaks may necessitate reintubation and result in increased mortality [5]. Injury to the pharynx, larynx and trachea can occur at the points of contact between the mucosa and the tube or cuff, resulting in ulceration, oedema, and haemorrhage with potential long-term complications, i.e. stenosis; furthermore, tracheostomy may result in loss of voice [6]. In patients requiring periodic MV, a deflated, fenestrated tracheostomy may impair RM performance during spontaneous breathing [7].

In addition to local damage, the ET tube places the patient at significant risk of developing nosocomial infections, mainly sinusitis and ventilator-associated pneumonia. Sinusitis due to nasotracheal intubation occurs from occlusion of the sinus ostia and is increasingly recognized as a cause of unexplained fever and sepsis in ventilated patients [8]. ET intubation is the single most important predisposing factor for nosocomial pneumonia as it bypasses the mechanical defences of the upper airways [9, 10]. It causes local injury, which predisposes patients to colonization of the trachea by pathogenic bacteria. In addition, the portion of the upper trachea between the inflated cuff and the vocal cords behaves as a reservoir for secretions originating from the sinuses, the nasal and oral cavity, the pharynx and the stomach. Such secretions can be introduced as a bolus into the lung by even minor ET tube manipulation [11]. Decrease in cardiac output (CO), barotrauma, and increase in work of breathing (WOB) due to the added space of the ET are additional problems of MV via an ET [12]. Up to 20% of mechanically-ventilated patients are not able to tolerate discontinuation of MV due to complete dependence on the machine and on the people who control them. Need for MV may lead to RM atrophy and related weaning difficulties [13, 14].

### Noninvasive mechanical ventilation

The recent innovations of noninvasive methods of MV (NMV) in the treatment of chronic respiratory insufficiency has led to the attempt to avoid the complications of invasive MV, ensuring at the same time a similar degree of efficacy. Both intermittent negative pressure ventilation (INPV) and positive pressure ventilation by face or nasal mask have recently been used for this purpose. This review deals mainly with noninvasive positive pressure ventilation.

**Negative pressure techniques**

INPV came into use in the second half of the nineteenth century during poliomyelitis epidemics. Development of a subatmospheric pressure around the thorax and abdomen results in air being drawn into the lungs through the mouth and nose. When the pressure around the chest wall returns to that of the surrounding air, expiration occurs passively owing to the elastic recoil of the lungs and chest wall. Excellent reviews of negative pressure devices have been published [15, 16]. Several studies have pointed out the efficacy of INPV in reducing electrical and mechanical activity of the inspiratory muscles (IM), thus allowing them to rest [17]. Ventilation with an “iron lung” was found to show a linear relationship between the increase in venous pressure and the mean pressure applied to ventilate normal humans [18]. On the other hand, no significant change in CO and haemodynamics was found during INPV by cuirass ventilators in chronic obstructive pulmonary disease (COPD) patients [19]. All negative pressure ventilators restrict motion and back pain is a common problem. INPV has been associated with rib fractures, pneumothorax, obstructive sleep apnoeas and lower oesophageal sphincter dysfunction, both in normal subjects and in COPD patients [20–22].

Chronic hypercapnic respiratory insufficiency resulting from neuromuscular and skeletal disorders is the main indications for INPV [23, 24]. Studies that have been published on the effects of INPV in COPD patients during ARF episodes are presented in table 2. INPV has been used to avoid the need for ET intubation during episodes of ARF in neuromuscular and skeletal disorders [28]. On the other hand, during the poliomyelitis epidemic, mortality decreased from 87% to 40% when INPV was replaced by positive pressure ventilation [29].

The place of INPV in acute exacerbations of COPD is still discussed. Iron lung, cuirass and poncho-wrap ventilators have been successfully used in exacerbations of COPD [25–27, 30, 31]. A review of the papers listed in table 2 revealed that in no case was INPV used in place of invasive MV; the severity of ARF was defined

<table>
<thead>
<tr>
<th>First author [Ref.]</th>
<th>COPD patients</th>
<th>INPV</th>
<th>Schedule</th>
<th>Control</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>CORRADO [25]</td>
<td>9</td>
<td>7.33</td>
<td>5.7</td>
<td>9.0</td>
<td>7.37</td>
</tr>
<tr>
<td>MONTSERRAT [26]</td>
<td>20</td>
<td>7.32</td>
<td>6.4</td>
<td>7.9</td>
<td>7.38</td>
</tr>
<tr>
<td>SAUER [27]</td>
<td>17</td>
<td>7.34</td>
<td>6.2</td>
<td>9.8</td>
<td>7.39</td>
</tr>
</tbody>
</table>

INPV: intermittent negative pressure ventilation; COPD chronic obstructive pulmonary disease; $P_{aO_2}$: arterial oxygen tension; $P_{aCO_2}$: arterial carbon dioxide tension.
by a mean pH not less than 7.32, and use of control populations was variable.

In conclusion, these studies on the effects of INPV during ARF in COPD patients may be considered preliminary and "physiological" rather than clinical: as a consequence, at the moment, there is no indication for the generalized use of INPV during ARF.

**Positive pressure techniques**

Intermittent positive pressure ventilation is aimed at delivering a tidal volume ($V_T$) and then allowing passive exhalation, either to atmospheric pressure or to a set positive airway pressure. The technique can be used to control ventilation entirely or to increase spontaneous respiratory efforts. Increasing gas exchange can be achieved for conscious subjects only if the ventilator cycles into inspiration in response to the initiation of a spontaneous breath by the patient, a process described as "triggering" ("assisted ventilation"). If there is no spontaneous inspiratory effort or it is too weak to trigger the ventilator, an automatic cycle must be imposed to ensure that gas exchange continues ("controlled ventilation"). The so-called assist/control mode can be used to ensure that breaths are triggered or imposed according to the capability of triggering the ventilator. Intermittent positive pressure ventilation delivered via a nasal, face or mouth mask (NIPPV) has been used in the short- and long-term treatment of chronic hypercapnic respiratory insufficiency from neuromuscular and thoracic disorders, from COPD and cystic fibrosis, with controversial results. It is usually delivered by standard volume-cycled ventilators in assisted or controlled mode [32].

Pressure support ventilation (PSV) is an assisted mode of ventilation supplying a set level of positive airway pressure during spontaneous respiratory efforts. PSV can either totally or partially unload IM during spontaneous inspiration supplying a set level of positive airway pressure during spontaneous inspiratory efforts. PSV can be used to control ventilation supplying a set level of positive airway pressure. The technique can be used to control ventilation entirely or to increase spontaneous respiratory efforts. Increasing gas exchange can be achieved for conscious subjects only if the ventilator cycles into inspiration in response to the initiation of a spontaneous breath by the patient, a process described as "triggering" ("assisted ventilation"). If there is no spontaneous inspiratory effort or it is too weak to trigger the ventilator, an automatic cycle must be imposed to ensure that gas exchange continues ("controlled ventilation"). The so-called assist/control mode can be used to ensure that breaths are triggered or imposed according to the capability of triggering the ventilator. Intermittent positive pressure ventilation delivered via a nasal, face or mouth mask (NIPPV) has been used in the short- and long-term treatment of chronic hypercapnic respiratory insufficiency from neuromuscular and thoracic disorders, from COPD and cystic fibrosis, with controversial results. It is usually delivered by standard volume-cycled ventilators in assisted or controlled mode [32].

Pressure support ventilation (PSV) is an assisted mode of ventilation supplying a set level of positive airway pressure during spontaneous respiratory efforts. PSV can either totally or partially unload IM during spontaneous breathing. Total unloading occurs when the only effort made by the patient is to trigger the breath. PSV allows the patient to maintain control of inspiratory and expiratory time and to interact with a set pressure to determine the ultimate flow and $V_T$ [33]. PSV via nasal mask (NPSV) has also been used in chronic respiratory insufficiency, in restrictive thoracic disease and COPD [34–36].

**Physiological studies.** NIPPV delivered in control mode is able to significantly reduce electromyographic (EMG) activity of the IM both in obstructive and in restrictive patients [37], the reduction being greater than with INPV [38]. Oesophageal ($P_{oes}$) and transdiaphragmatic pressures ($P_{dia}$) are also reduced by NIPPV in control mode, confirming that NIPPV is also able to rest IM from a mechanical point of view [38].

In stable COPD patients, NPSV increases minute ventilation and $V_T$, and reduces breathing frequency ($f_R$), whilst improving gas exchange; it is able to reduce diaphragmatic EMG activity (Et), $P_{dia}$ and the IM oxygen consumption as assessed by the pressure-time product (P*$P_{dia}$) [39]. Similar results are reported during ARF episodes in COPD [40]. The addition of external positive end-expiratory pressure (PEEP) is able to further reduce diaphragmatic effort and oxygen consumption both in stable COPD and during acute exacerbations [39, 41]. NPSV with and without PEEP may also be applied by means of portable ventilators [42]. In stable COPD, a reduction in CO and oxygen delivery has been observed with NPSV with and without PEEP, which was, however, of negligible clinical relevance [43].

**Clinical studies of NIPPV in ARF of COPD**

**Success rate.** Meduri et al. [44] were the first to publish a report dealing with noninvasive face mask ventilation in patients with ARF. They treated six patients with hypercapnia and four with ARF meeting the clinical and objective criteria for MV, which was delivered with pressure control and PSV via a tightly strapped, clear face mask. No patient dropped out of the study because of inability to deliver adequate ventilation or to improve oxygen exchange; three patients (30%) eventually required ET intubation. The mask was generally well-tolerated. All patients had a nasogastric tube placed on suction, and none vomited or aspirated. The physiological response was considered similar to that which would have been achieved with conventionally delivered ventilation.

Since that time, NMV has been widely used in ARF episodes. A review of the literature from 1989 to 1995 shows that use of NMV in ARF has been reported in several studies involving more than 400 patients, most of them with COPD. NMV was successful in 51–91% of cases, the severity of ARF as assessed by the level of respiratory acidosis being widely different among the different populations under study [44–48]. Most of the studies compared effectiveness of NMV with historical groups of patients treated with "conventional" medical therapy, whilst controlled studies of NMV versus ET intubation are lacking. In these studies, success was defined as the ability of NMV to improve gas exchange, and to avoid ET intubation and death in the ICU. Some studies published on the clinical effects and success rate of NMV in COPD patients during ARF episodes are presented in table 3.

**Modality of ventilation.** In a subsequent open study, Meduri et al. [49] treated 18 patients with hypercapnic ARF (83% from COPD or asthma) with NMV consisting of continuous positive airway pressure (CPAP) and NPSV or intermittent mandatory ventilation. NMV was successful in avoiding intubation in 13 of the 18 patients (72%). NPSV was set at 10–20 cmH$_2$O to achieve a frequency ($f_R$) <25 breaths·min$^{-1}$ and a $V_T$ >7 mL·kg$^{-1}$. The mean duration of NMV was 25 h, pH increased by 27%, arterial carbon dioxide tension ($P_aCO_2$) decreased by 24%, and $f_R$ decreased by 44%, with an ICU survival rate of 94%.

The most quoted paper dealing with NPSV during ARF is that by Brochard et al. [40], who in a study controlled with matched historical patients treated 13 COPD patients with ARF by means of NPSV 12–20 cmH$_2$O. NPSV induced an increase in pH of 38%, and a decrease in $P_aCO_2$ of 26%. Only one of their 13 patients (8%) needed ET intubation as compared with 11 of the 13 historical controls (84%) treated with conventional therapy. Two patients in each group died (15%). As compared with
the controls, patients treated with NPSV needed a shorter mean duration of ventilatory assistance (3 vs 12 days) and a briefer stay in the ICU (7 vs 19 days). No side-effects were noted during this study, and with NPSV <25 cmH2O the patients did not observe inflation of the stomach.

NIPPV by nasal mask was used by FOGGIO et al. [50] in a retrospective study on 25 COPD patients with acute exacerbations, in which patients unable to tolerate NMV were the control population treated with standard medical therapy. NIPPV was delivered by means of a "domestic" volume-cycled ventilator in controlled mode with a VT of 15 mL·kg⁻¹ and an inspiratory/expiratory (I/E) ratio of 1:3. NIPPV was applied for 1 h four times a day for 6 days a week. Improvements in blood gases, maximum inspiratory pressure (MIP) and airflow obstruction were similar to those in control patients. The relevant side-effects are listed in table 4.

NIPPV by means of a volume-cycled ventilator in controlled mode and delivered through a customized nasal mask was used by BENHAMOU et al. [51] to evaluate the possible role of NMV in ARF episodes when invasive MV was questionable. They studied 30 patients (mean age 76 yrs), in all of whom clinical or physiological parameters indicated the need for MV, but ET intubation was either not applied because of the age and the physiological condition of the patients, or was postponed. NMV was continuous during the first 12 h and the following nights, and was then intermittent during the day. Twenty one patients (70%) improved clinically within a few hours. Progressive correction of arterial blood gases (ABG) was observed. Eighteen patients (60%) were able to be successfully weaned from NMV. Clinical tolerance was said to be satisfactory in 23 (76%) patients and poor in seven patients (24%). These authors claimed a success in 60%, but two more deaths after weaning reduced the number of patients able to be discharged home to 16 (53%).

NPSV and NIPPV by face mask were compared in the treatment of ARF in 16 and 13 COPD patients, respectively, by VITACCA et al. [52]. Both NPSV and NIPPV improved ABG. Thirteen percent of patients submitted to NPSV and 22% of patients submitted to NIPPV required ET intubation. These authors retrospectively compared the need for ET intubation of these patients (as a whole 17%) with 35 COPD patients in ARF treated with medical therapy in the same institution, 16 (45%) of whom required ET intubation.

BOTT et al. [53] reported the first prospective randomized clinical trial of NIPPV compared with conventional therapy in patients with acute exacerbations of COPD. Thirty patients were randomized to receive NIPPV and 30 patients received conventional therapy. Nasal ventilation was more effective than conventional therapy in lowering (by 15%) PaCO₂ and reversing acidosis. Four

### Table 3. – Published studies on the effect of NMV during ARF in COPD patients

<table>
<thead>
<tr>
<th>First author</th>
<th>Patients</th>
<th>NMV</th>
<th>Schedule</th>
<th>Control</th>
<th>Results</th>
<th>Type of mask employed</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEDURI</td>
<td>18</td>
<td>CPAP+ NPSV</td>
<td>25 h</td>
<td>Open</td>
<td>7.37</td>
<td>9.5 kPa</td>
</tr>
<tr>
<td>BROCHARD</td>
<td>13</td>
<td>NPSV</td>
<td>7.6 h for 2–8 days</td>
<td>13 Historical</td>
<td>7.40</td>
<td>6.3 kPa</td>
</tr>
<tr>
<td>FOGGIO</td>
<td>25</td>
<td>NIPPV</td>
<td>4×1 h for 6 days-week⁻¹ (3 weeks)</td>
<td>24 ST Retrospective</td>
<td>7.36</td>
<td>7.6 kPa</td>
</tr>
<tr>
<td>BENHAMOU</td>
<td>20</td>
<td>NIPPV</td>
<td>At first 12 h + night, then individually</td>
<td>Open</td>
<td>7.34</td>
<td>8.4 kPa</td>
</tr>
<tr>
<td>VITACCA</td>
<td>13</td>
<td>NIPPV</td>
<td>69 h</td>
<td>35 ST</td>
<td>7.40</td>
<td>7.5 kPa</td>
</tr>
<tr>
<td>Bott</td>
<td>30</td>
<td>NIPPV</td>
<td>7.6 h for 5–9 days</td>
<td>30 ST Prospective randomized</td>
<td>7.38</td>
<td>7.6 kPa</td>
</tr>
<tr>
<td>FERNANDEZ</td>
<td>14</td>
<td>NPSV</td>
<td>8±4 h</td>
<td>Open</td>
<td>7.31</td>
<td>8.8 kPa</td>
</tr>
<tr>
<td>KRAMER</td>
<td>11</td>
<td>NPSV</td>
<td>3.8±1.4° days</td>
<td>12 ST Prospective randomized</td>
<td>NR 7.9**</td>
<td>91 Nasal</td>
</tr>
<tr>
<td>BROCHARD</td>
<td>43</td>
<td>NPSV</td>
<td>6 h</td>
<td>42 ST Prospective randomized</td>
<td>7.31</td>
<td>8.9** kPa</td>
</tr>
</tbody>
</table>

NR: nonreported; **: from the figure. NMV: noninvasive mechanical ventilation; ARF: acute respiratory failure; CPAP continuous positive airway pressure; NPSV: pressure support ventilation via nasal mask; NIPPV: noninvasive intermittent positive pressure ventilation; ST: standard therapy; PS: pressure setting; VT: tidal volume; I:E: inspiratory/expiratory ratio. For further abbreviations see legend to table 2. °: mean±SD.
patients allocated to receive NIPPV did not receive this therapy because they were unable to tolerate it or due to lack of co-operation (due to neurological status). A comparison of the 26 patients who were treated with NIPPV compared with the 30 patients who received conventional therapy demonstrated a significant reduction in mortality (1 of the 26 (3.8%) versus 9 of the 30 (30%)). However, when the four patients who did not tolerate NIV were included, the mortality with NIV increased to 3 out of 30 (10%), being not significantly modified on an intention-to-treat basis. Breathlessness was significantly improved in the treated group. The difference in survival for the two groups led the authors to recommend NIPPV in all patients admitted with an acute exacerbation of COPD and ventilatory failure who do not respond promptly to conventional therapy. It is worthwhile mentioning that many control group patients in the study by BOTT et al. [53] died without being endotracheally intubated, which may have influenced mortality.

FERNANDEZ et al. [54] studied 12 COPD patients during 14 episodes of acute exacerbation of chronic respiratory failure, who failed to improve with intensive medical therapy and showed impairments in severe respiratory acidosis and/or hypercapnic encephalopathy leading their attending physicians to recommend MV. In these circumstances, a trial of NPSV with a level of pressure support adjusted to obtain a VT >400 mL was attempted. If the patient deteriorated, ET intubation and standard MV were performed. Mean $P_{a,CO_2}$ decreased by 27%, and arterial pH increased. Three episodes were unsuccessful (21%) and one of the patients (8%) died in the intensive care unit (ICU).

In a recent randomized, prospective trial of NIV versus standard therapy, KRAMER et al. [55] used a simple portable ventilator to deliver NPSV in the patient flow-triggered/time triggered (S/T) mode through a nasal mask to COPD and non-COPD patients with ARF. Ventilation was initiated using a backup rate of 12 breaths-min$^{-1}$. The inspiratory positive airway pressure was set at 8 cmH$_2$O and the expiratory positive airway pressure at 2 cmH$_2$O. The need for intubation was reduced from 73% in the standard therapy group to 31% in the NPSV group. Among COPD patients, the reduction was even more relevant with 67% of control patients requiring intubation compared with 9% of NPSV patients.

In the largest multicentric, randomized, prospective study of NIV versus standard medical therapy in 85 COPD patients, BROCHARD et al. [56] showed that the use of 20 cmH$_2$O of NPSV significantly reduced the need for ET (11 out of 43 (26%) vs 31 out of 42 (74%) for NPSV and standard therapy, respectively). In the subgroup successfully treated with NPSV, a significant improvement was noted in the respiratory rate as well as in arterial oxygen tension ($P_{a,O_2}$) at 1 h (by 61%) and $P_{a,CO_2}$ at 12 h (by 14%). In addition, the frequency of complications was significantly lower in the NPSV group (16 vs 48%). The in-hospital mortality rate was also significantly reduced with NPSV (4 out of 43 vs 12 out of 42). Ten of the 12 deaths in the standard-treatment group and 3 of the 4 in the NPSV group occurred during mechanical ventilation. These authors concluded that in selected patients with acute exacerbations of COPD, NIV may reduce the need for ET, the length of the hospital stay and the in-hospital mortality rate.

Other uncontrolled studies of noninvasive positive pressure ventilation during ARF in COPD patients have recently been reported [57–59].

### Table 4. – Side-effects during noninvasive positive pressure ventilation assessed in published studies

<table>
<thead>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of mask</td>
<td>Face</td>
<td>Nasal</td>
<td>Nasal tailored</td>
<td>Face</td>
<td>Nasal</td>
</tr>
<tr>
<td>Aspiration</td>
<td>5.6</td>
<td>3.4</td>
<td>7</td>
<td>18</td>
<td>3.4</td>
</tr>
<tr>
<td>Gastric distension</td>
<td>8</td>
<td>7</td>
<td>21</td>
<td>18</td>
<td>3.4</td>
</tr>
<tr>
<td>Mask discomfort</td>
<td>32</td>
<td>7</td>
<td>21</td>
<td>18</td>
<td>3.4</td>
</tr>
<tr>
<td>Nose lesion</td>
<td>5.6</td>
<td>20</td>
<td>7</td>
<td>21</td>
<td>3.4</td>
</tr>
<tr>
<td>Dry nose</td>
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<td>7</td>
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<tr>
<td>Eye irritation</td>
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<td>17</td>
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<td>17</td>
<td>17</td>
<td>18</td>
<td>3.4</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>10</td>
<td>3.4</td>
<td>17</td>
<td>18</td>
<td>3.4</td>
</tr>
<tr>
<td>Claustrophobia</td>
<td>3.4</td>
<td>3.4</td>
<td>17</td>
<td>18</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Percentage values are presented. First authors only are named.
of about 7.3%. More interestingly, NPSV decreased diaphragmatic effort as assessed by PTP à. NPSV combined with CPAP induced a further reduction in PTP à by counterbalancing PEEPi, dyn, which was reduced. On the basis of these results, the authors suggested the use of low levels of PEEP (80–90% of PEEPi,dyn) to treat acute exacerbation of COPD by means of mask PSV.

MIRO et al. [64] used mask CPAP in seven patients with hypercapnic ARF, in an attempt to avoid ET intubation. Mask CPAP was started at 5 cmH2O and then increased to a maximum of 10 cmH2O depending on the clinical response. In five patients (71%), CPAP significantly improved ABG but one of them was withdrawn from mask ventilation due to necrosis from the face mask and was, therefore, intubated. In two out of the seven patients, ABG deteriorated even with CPAP of 10 cmH2O and one of these (14%) was intubated. No barotrauma or adverse haemodynamic effects were associated with CPAP.

FERNANDEZ et al. [54] were able to add PEEP (5.7±0.8 cmH2O) to counterbalance “suspected” but not assessed PEEPi in four out of their 14 cases of ARF treated by NPSV. No increase in the leakage around the mask occurred. In these patients, the use of external PEEP only diminished the apparent inspiratory effort. In some cases, patients spontaneously referred to an alleviation of dyspnoea when PEEP was added. Unfortunately, no objective measurement is reported.

Duration of NMV and length of stay in the ICU. A review of the literature shows NMV was used 4–20 h·day–1 for 1–9 days. In the controlled study by BOTT et al. [53], both patients undergoing NMV and the control group remained in hospital for 9 days. In the study by BROCHARD et al. [40], the need for ventilatory assistance was ≥1 and 12±11 days for the group treated by a noninvasive and invasive approach, respectively. Patients in their study remained in ICU 7±3 versus 19±12 days for NMV and ET intubation, respectively. FERNANDEZ et al. [54] reported an ICU stay of 5±2 versus 17±8 days for NPSV and ET intubation, respectively. In a recent retrospective study by VITACCA et al. [66], duration of NMV ranged 4 h to 11 days (mean 2.6±2.0 days) in comparison to invasive MV which lasted 19±10 days (range 2–84 days). Patients submitted to NMV remained in the ICU for 10±8 days, whilst patients undergoing ET intubation remained in the ICU for 24±12 days. Patients in the study by KRAMER et al. [55] used the ventilator for an average of 3.8±1.4 days, and among patients who used NPSV successfully the average duration of use during the first 24 h was 20.1±0.4 h. In that study, NPSV did not significantly reduce duration of ventilator use, hospital length of stay, mortality or charges in comparison to standard therapy. In the recent multicentric prospective, randomized study by BROCHARD et al. [56], the mean hospital stay was significantly shorter for patients receiving NPSV (23±17 vs 35±33 days).

Mortality. Conventional medical treatment of COPD patients with ARF was associated with an overall mortality ranging 12–29% [67, 68]. Table 5 shows the immediate mortality in the ICU of COPD patients with ARF treated with either invasive or noninvasive MV. Comparison of rates between studies is difficult as the criteria for inclusion of patients, settings of MV, medical treatment and medical practices (e.g. less or more frequent use of mechanical ventilation in different countries) are different. As a whole, the survival rate of NMV seemed better, although it is conceivable that patients submitted to invasive MV would have been more severe [25, 40, 49, 51–54, 56, 69–76].

Determinants of success. Since promising results have been observed with NIPPV and NPSV, NMV is increasingly being used in the treatment of ARF in COPD patients. The success rate of these techniques is different according to different authors, even in the same department [50, 52]. The type of mask employed, mode of ventilation, compliance to treatment, patient characteristics and severity of disease treated may influence the success rate [77]. Up to the present time, controlled studies of NMV versus ET intubation are lacking, so that the use of NMV as an alternative to ET intubation, might, in case of failure, be considered as unduly delayed ET intubation. It is, therefore, important to identify parameters able to predict the outcome of NMV.

In the study by MEDURI et al. [49], a significant initial (after 1 h of treatment) improvement in PAo2 (16% decrease) and in pH (pH>7.30) but not pulmonary function in a stable state predicted success. BENAHMOU et al. [51] studied the initial characteristics in a group of patients successfully weaned from NMV and in a group of patients who died or who were secondarily intubated. These two groups did not differ in terms of age, previous respiratory tract disease, cause for the acute decompensation, ARF, or noninvasive MV. For further abbreviations see legend to Table 1.

### Table 5. – Mortality rate of COPD patients in ICU

<table>
<thead>
<tr>
<th>First author</th>
<th>[Ref.]</th>
<th>Pts</th>
<th>n</th>
<th>Mortality</th>
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<tr>
<td>NUNN</td>
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<td>GRACEY</td>
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<td>42</td>
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</tr>
<tr>
<td>STAVFUR</td>
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</tr>
<tr>
<td>BROCHARD</td>
<td>[56]</td>
<td>31</td>
<td>32</td>
<td></td>
</tr>
</tbody>
</table>

**Invasive MV**

<table>
<thead>
<tr>
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<th>[Ref.]</th>
<th>Pts</th>
<th>n</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
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<td>MEDURI</td>
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<td>18</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>BROCHARD</td>
<td>[40]</td>
<td>13</td>
<td>15</td>
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<tr>
<td>BENHAMOU</td>
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<td>13</td>
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</tr>
<tr>
<td>BOTT</td>
<td>[53]</td>
<td>30</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>FERNANDEZ</td>
<td>[54]</td>
<td>12</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>AMBROSINO</td>
<td>[76]</td>
<td>47</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>BROCHARD</td>
<td>[56]</td>
<td>43</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>CORRADO</td>
<td>[25]</td>
<td>105</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>(INPV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Noninvasive MV**

ICU: Intensive Care Unit; MV: mechanical ventilation. For further abbreviations see legend to table 1.
initial ABG, Simplified Acute Physiological Score (SAPS) [78], and level of consciousness on inclusion in the study. However, initial agitation appeared to be a poor prognostic factor. In the study by Bott et al. [53], patients who died were more acidic on admission than patients who survived (pH 7.31 versus 7.35) and more hypercapnic (P$a\text{CO}_2$ 9.4 vs 8.4 kPa), although both groups were equally hypoxic ($P$O$_2$ 5.1 vs 5.3 kPa). Fernández et al. [54] failed to demonstrate significant differences between patients not needing and those needing ET in terms of diagnosis, age, clinical status as assessed by Acute Physiology and Chronic Health Evaluation (APACHE) II score [79], ABG and haemodynamics, either on admission or before and after NMV.

Soo Hoo et al. [80] evaluated the efficacy of nasal mechanical ventilation in COPD patients and hypercapnic respiratory failure and tried to identify predictors of its success or failure in a prospective study of 12 patients treated during 14 episodes of ARF (mean pH 7.25 ± 0.09; mean P$a\text{CO}_2$ 9.7±2.1 kPa). NMV was performed with a volume ventilator and was successful in 50% of cases. There was no differences in age, prior pulmonary function and ABG, admission ABG, or respiratory rate between those patients successfully treated and those patients who failed NIPPV. unsuccessfully treated patients appeared to have a greater severity of illness, as indicated by a higher APACHE II score (mean 21 ± 4 vs 15 ± 4). Unsuccessfully treated patients were edentulous, had pneumonia or excess secretions, and had pursed-lip breathing, factors that prevented adequate mouth seal and contributed to greater mouth leakage than in successfully treated patients. Successfully treated patients were able to adapt more rapidly to the nasal mask and ventilator with greater and more rapid reduction in P$a\text{CO}_2$, correction of pH, and reduction in respiratory rate. Brochard et al. [56] found that NPSV was less effective in the patients with more severe clinical disturbances as assessed by SAPS, and encephalopathy score. In that study, gas exchange was not different between patients treated successfully and unsuccessfully with NPSV.

With the aim of identifying simple parameters recorded in a hospital setting useful for the early prediction of whether or not COPD patients may be successfully treated with NMV, we have recently retrospectively analysed 59 episodes of ARF in 47 COPD patients treated with NMV by means of either NPSV (25 cases) or NIPPV (34 cases) delivered through either a nasal (31 cases) or a facial (28 cases) mask. According to survival and to the need for ET intubation, each episode was considered as successful (46 episodes; 78%) or unsuccessful (13 episodes; 22%). NMV was able to significantly reduce P$a\text{CO}_2$ in both groups. NPSV was successful in 84% and NIPPV in 73%. Clinical and radiological evidence of pneumonia was the cause of ARF in 39% of unsuccessful episodes but only in 9% of successful ones. Success with NMV was associated with less severely abnormal baseline clinical and functional parameters, and to less severe levels of acidosis assessed during an initial trial of NMV. The logistic regression analysis demonstrated that baseline pH maintained a significant predictive effect, indicating that all other variables were in some way dependent on it. By this analysis, baseline pH showed a sensitivity of 97% and a specificity of 71%. The severity of the episode of ARF as assessed by clinical and functional compromise and the level of acidosis and hypercapnia during an initial trial of NMV, therefore, have an influence on the likelihood of success with NMV and may prove useful in deciding whether to continue with this treatment [76]. Facial masks were successful in 78% and nasal masks in 77% (unpublished data); therefore, the mode of ventilation and type of mask used do not seem to influence the outcome of NMV in acute exacerbations of COPD. Both Ambrosino et al. [76] and Brochard et al. [56] found that NMV was less likely to be effective in patients with more severe physiological disturbances at the outset, suggesting that once decomposition has been well-established the cycle of deterioration may not be broken with the use of NMV [81].

On the other hand, in patients with ARF from causes other than COPD, Wysoki et al. [82, 83] proposed NPSV by face mask as an alternative to ET intubation. Only in hypercapnic but not in normocapnic patients was NPSV associated with a reduction in the rate of ET intubation, in the length of ICU stay and in the mortality rate. In both groups of patients, gas exchange improved after 1 h on NPSV. Pennock et al. [84] in similar patients could not find any pretreatment parameters that favoured successful outcome.

**Long term survival.** Survival at 1 yr in COPD patients undergoing ET intubation and MV is variable but nevertheless quite low [70–75, 85–94]. Survival rates at one year obtained in different studies of COPD patients who underwent MV are shown in table 6. Recently, Vitacca et al. [66] have retrospectively evaluated the short- and long-term prognosis in COPD patients submitted to NMV for ARF. Thirty nine patients submitted to NMV through face masks (mean pH 7.28; P$a\text{CO}_2$ 10.9 kPa) were compared to 27 historical control patients (mean pH 7.26; P$a\text{CO}_2$ 9.9 kPa) submitted to MV through ET intubation when clinical and functional conditions had further deteriorated because the medical therapy failed and NMV was not available at the time. The mortality rate was 20 and 26% in ICU, 18 and 48% at 3 months, and 30 and 63% at 1 yr, in NMV patients and in controls, respectively. The number of new ICU admissions during the follow-up was 0.12 versus 0.30 per patient annually in NMV and patients undergoing ET intubation, respectively.

Corrado et al. [25] showed that the overall survival rate during the first year of their patients treated by Table 6. — One year mortality rate in patients undergoing invasive and noninvasive mechanical ventilation

<table>
<thead>
<tr>
<th>First author</th>
<th>Ref.</th>
<th>Pts</th>
<th>MV modality</th>
<th>Mortality %</th>
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</thead>
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<td>Corrado</td>
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<td>NIPPV</td>
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</tr>
<tr>
<td>Gillespie</td>
<td>[70]</td>
<td>54</td>
<td>ET</td>
<td>44</td>
</tr>
<tr>
<td>Kaelin</td>
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<td>ET</td>
<td>59</td>
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<td>Gracey</td>
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<td>ET</td>
<td>61</td>
</tr>
<tr>
<td>Stauffer</td>
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<td>ET</td>
<td>44</td>
</tr>
<tr>
<td>Nava</td>
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<td>42</td>
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<td>Vitacca</td>
<td>[66]</td>
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<td>Vitacca</td>
<td>[66]</td>
<td>30</td>
<td>NIPPV/NPSV</td>
<td>30</td>
</tr>
</tbody>
</table>

ET: endotracheal (intubation). For further abbreviations see legends to tables 2 and 3.
means of iron lung was 82%. These patients made monthly visits to the hospital. This fact, rather than the difference in modality of ventilation (mask ventilation versus iron lung) might explain the better 1 yr survival of patients in the study by Corrado et al. [29], underlining the usefulness of a regular programme of outpatient control.

Diseases other than COPD

Martin et al. [95] showed that in induced asthma CPAP reduced the load on the IM, improving their efficiency and decreasing the energy cost of their action. In patients with severe acute asthma, Shivaram et al. [96] reported that low levels of CPAP (5 and 7.5 cmH2O) by nasal mask produced a significant decrease in breathing frequency and dyspnoea compared with a control group. Neither group of patients showed significant changes in spirometry or blood gases. That different modalities of NMV may have a role in the management of patients with severe acute asthma is still to be confirmed by clinical controlled studies [97].

NMV has been used as an effective and "dignified" method of supporting patients with end-stage disease and ARF [98, 99]. Other studies dealing with medical or surgical patients with different aetiologies (from hypothyroidism to cardiogenic pulmonary oedema) and ages have also been published. Generally, improvement in ABG is reported both with NIPPV and NPSV [100–105]. CPAP delivered by face mask in patients with severe cardiogenic pulmonary oedema resulted in earlier physiological improvement and in reduction of the need for ET intubation and MV, in comparison to standard medical therapy. However, no significant difference was found in in-hospital mortality or the length of the hospital stay [103]. More recently, Lin et al. [106] confirmed that serial incremental CPAP therapy improves oxygenation and gas exchange, decreases intrapulmonary shunt and relieves the need for ET intubation in patients with acute cardiogenic pulmonary oedema. These authors failed to show any significant beneficial changes in mortality rate and hospital stay. A recent prospective randomized study by Wysocki et al. [82] suggested a lack of efficacy of NMV in non-COPD patients. Pennock et al. [84] were able to transfer the use of NPSV delivered by simple portable ventilators from an experimental setting [98] to the normal care providers of patients with ARF of different causes (80% of them surgical) with a success rate of 80%. NPSV, CPAP and continuous negative external pressure have been used in the treatment of ARF in infectious complications of acquired immune deficiency syndrome (AIDS) and lung transplantation [107, 108]. Some uncontrolled studies of ARF have also included patients with chest wall disease [49, 51, 57, 102].

Weaning from invasive mechanical ventilation

Weaning from invasive MV may be difficult in patients with increased WOB or impaired ventilatory drive. Various techniques have been used to aid weaning, including PSV. Most methods require maintenance of ET intubation and supervision in an ICU, thus causing the cost of care to increase [109, 110]. NMV was used in patients with weaning difficulties from invasive MV by means of NIPPV and NPSV after a median of 31 days of invasive MV [111]. Eighteen out of 22 patients were successfully transferred to NMV and discharged home a median of 11 days after starting this type of ventilation. Other cases of successful substitution of NIPPV for ET ventilation have been reported [112, 113].

Advantages and limitations of NIPPV

The main advantages of mask ventilation are shown in table 7. The theoretical advantages of mask ventilation include: improvement in patient comfort, reduction in the need for sedation; avoidance of the complications of ET intubation; possibility of delivering ventilation intermittently; capacity for normal swallowing, feeding and speech; physiological air warming and humidification; a physiological cough; easier weaning; meanwhile maintaining the option of ET intubation unchanged [47, 48].

Side effects. Most studies report the prevalence of side-effects only anecdotally. Studies with an assessment of side-effects are shown in table 4. Care is needed to ensure that the mask fits and is comfortable. Tolerance to the ventilator is important. Benhamou et al. [51] reported "bad tolerance" to the respirator in 17% of their cases. Vitacca et al. [52] found that compliance to NMV was better with NPSV and fewer side-effects were observed with this modality in comparison to NIPPV. In the study by Kramer et al. [55], 2 out of 11 patients (18%) failed NPSV because of nasal mask intolerance. Several commercial models are available in multiple sizes or can be constructed to conform to facial contours. A poorly fitting mask is bound to leak. Commercial masks have been associated with air leaks in 16 and 18% of patients, respectively [50, 55]. Furthermore, the amount of leakage can change and the nasal mask is easily removable. The positive pressures delivering air to the patient are felt on the face with the nasal mask, a sensation that can be uncomfortable and eye irritation and/or conjunctivitis have been reported in 16 and 17% of patients, respectively [50, 55].

All these differences can contribute to an inspiratory volume that may be changing and that is not necessarily directly proportional to the ventilator pressure as it would be with an intubated patient. To avoid air leaks, some masks incorporate a large high-compliance, low-pressure inflatable cuff for facial sealing. Some masks are filled with silicone to minimize dead space and to avoid air

Table 7. – Advantages of mask ventilation

<table>
<thead>
<tr>
<th>Intermittent delivery of ventilation</th>
<th>No need for ET intubation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of different modalities of ventilation</td>
<td>Normal swallowing, feeding and speech</td>
</tr>
<tr>
<td>Physiological air-warming and humidification</td>
<td>Physiological cough</td>
</tr>
<tr>
<td>Easier weaning</td>
<td>Unchanged possibilities of ET intubation</td>
</tr>
</tbody>
</table>

ET: endotracheal
leaks, and thin pieces of foam rubber are used to adjust the face mask for a tighter fit. Customized masks are individually moulded to the patient’s nose in silicone paste mixed in a slow catalyst. The mask is usually prepared rapidly (about 15–30 min) [51, 100].

Commercial and customized masks are secured to the head with Velcro or elastic straps. Keeping the mouth closed has been shown to be necessary to rest IM effectively [37], and the usual source of inadvertent volume loss is through the mouth in patients who sleep with their mouth open. An elasticated chin strap secured to the bands holding the mask to the head is often sufficient to control the leaks but it is rarely successful in edentulous patients. Efforts to secure the mask more firmly put pressure on the bridge of the nose, where the skin ulcerates very easily and necrosis may result. Mild skin lesions were reported in 5.6% of patients by MEDURI et al. [49], and in other studies skin reddening and/or abrasion was reported in 20% of patients [52], and nasal bridge ulcerations in 18% of patients [55]. However, in the largest series by BROCHARD et al. [56] facial skin necrosis was reported in only 1 out of 43 (2.3%) patients. The use of wound care dressing on the bridge of the nose under the mask may avoid the skin abrasions [84]. Different types of commercial nasal masks are available, some of them involving only nostrils and avoiding contact with nose skin.

Gastric distension is almost unavoidable with facial masks, and a nasogastric tube is usually inserted before initiating face mask ventilation and placed on suction. Even so, MEDURI et al. [49] reported one case (5.6%) of aspiration [49]. However, BROCHARD et al. [40] reported that when using a level of pressure support lower than 25 cmH₂O no gastric inflation was observed. Nasal masks may be related to gastric distension [50].

**Type of mask.** It is not clear whether face masks are more effective. Theoretically, face masks allow less air leakage through the mouth, while nasal masks preserve speech and swallowing, but no prospective study has directly compared their efficacy. Although previous reports suggest that facial masks could be more efficient in ARF [40, 47, 49, 52], PENNOCK and co-workers [84, 101] successfully used a nasal mask for NMV in ARF from various causes. The number of failures due to lack of accommodation to the mask in several reports [40, 47, 49, 101] support the need for a well-tolerated and a tighter fitted mask specifically designed for this non-invasive technique. The type of the mask (nasal or facial) does not seem to play a role in the outcome of NMV. Recently, a mask that covers the whole anterior surface of the face and delivers effective ventilation via the nasal and oral routes, having a more extensive patient-mask interface and not obstructing the patient’s field of vision, has been introduced and evaluated but needs further clinical studies [114].

**Nursing.** Clearing the airways should precede mask ventilation in patients with a great amount of secretions. The effectiveness of NIPPV with all modalities depends on strict staff supervision for nurses and physiotherapists. CHEVROLET et al. [115] treated six patients with NIPPV during an episode of ARF due to restrictive and obstructive pulmonary disorders. They used a volume-cycled ventilator in assist/control mode and found that NIPPV was successful in avoiding ET intubation in only three patients suffering from a restrictive pulmonary disorder, whereas the procedure was unsuccessful in patients with obstructive disorders. Moreover, in all patients, acute NIPPV was very time-consuming for the nursing staff. In patients with restrictive disorders, a nurse needed to monitor a patient submitted to NIPPV for 41% of the duration of ventilation. In patients with obstructive disorders, a nurse needed to monitor for 91% of the NIPPV time! However, no comparison with the time consumed to deliver standard therapy is reported, and BOTTE et al. [53] found that the amount for nursing care required to treat ARF with NIPPV was not different in comparison to patients undergoing standard therapy.

In a study by KRAMER et al. [55], respiratory therapists tended to spend more time at the bedside of patients receiving NPSV than that of control patients (108±27 versus 44±15 min over an 8 h period) but the difference was not statistically significant. Furthermore, there was a significant drop in the amount of time therapists spent at the bedside of NPSV patients during the second 8 h period. In addition, therapists and nurses rated the difficulty of caring for patients receiving NPSV as no greater than for control patients. PENNOCK et al. [84] suggested that a 15–30 min period of patient-caregiver interaction when initiating ventilator support can substantially improve patient comfort and acceptance, and reduce the need for nursing care.

**General considerations**

**Selection criteria.** As a whole, these studies show that NMV may be useful in selected patients with ARF. Based on criteria used in the studies evaluated, patients should have clinical and physiological evidence of ARF, including acute respiratory acidosis, tachypnoea, use of accessory muscles of inspiration and/or abdominal paradox. Patients should be sufficiently co-operative to follow instructions related to use of the mask. It is commonly said that NMV should be avoided and ET intubation performed in patients with haemodynamic instability, uncontrolled arrhythmias, gastrointestinal bleeding, high risk for aspiration, but no specific study is available to support this (table 8) [47]. It is worth noting that in the study by BROCHARD et al. [56] only 31% of all the patients with COPD admitted during the study period met the criteria for enrollment.

**Pros and cons.** With these limitations, NMV in selected patients with ARF is well-tolerated and may be useful in avoiding ET intubation in most cases of COPD and with a wide range of success rates in other diseases.

**Table 8. – Contraindications to mask ventilation**

| Coma |
| Unco-operative patient |
| Haemodynamic instability |
| Gastrointestinal bleeding |
| Recent upper abdominal surgery |
| Need for frequent aspiration |
| Excessive airway secretions |
Several pros and cons must be noted.
1. Most of the studies on NMV have historical control populations and only three adequately controlled published trials have shown an advantage of NMV compared with conventional medical therapy [53, 55, 56]. Historical comparison of two different patient populations must be interpreted with caution because treatment strategies may change with time and such studies are considered to favour the treatment group [116]. On the other hand, a retrospective study gives information about a ‘real’ setting of operations in an ICU.
2. With the above limitations, NMV seems to be able to reduce the need for ET intubation in ARF. This, in turn, has several advantages in terms of avoiding complications of invasive MV, reducing the length of stay in an ICU and, probably, the number of ICU readmissions. On the other hand, prospective, randomized, controlled studies of noninvasive versus ET intubation are lacking.
3. Side effects of NMV seem less severe than those induced by ET MV. On the other hand, NMV may be impeded by these complications. Prevalence of some of these complications, in particular aspiration, are still to be completely assessed and their consequences evaluated.
4. The findings relating to time consumption by nursing staff [115] may be of great concern, as the use of NMV could pose a greater strain on resources than would standard practice alone. This finding was not confirmed by BOTT et al. [53], or by KRAMER et al. [55]. Other studies have suggested a reduced length of stay in the ICU of patients treated with NMV in comparison to ET intubated patients [40, 54, 56, 66]. Furthermore, one report suggested a reduction in ICU readmission when patients avoided invasive MV [66]. This observation might support a reduction in the cost of treatment of these patients, but again studies of economics are lacking. In one study reporting costs [55], no significant difference between NPSV and control patients was found in hospital charges (3.7±1.1 and 4.0±1.5 thousand dollars for NPSV and control, respectively), or in total expenses (37.6±7.9 and 33.9±6.9 thousand dollars, respectively).
5. Noninvasive ventilatory support as a substitute for intubation and mechanical ventilation has several limitations. When a patient is intubated, the caregiver can set the ventilator parameters as prescribed and assume that the ventilator will perform appropriately. NMV affords less control. Mask ventilation with "domestic" ventilators sacrifices control of the airway, choice of pressure or volume delivery waveform, sometimes control of the level of inspiratory trigger, most alarms, etc. If the delivery of ventilator support in a specific patient requires any of these features, the choice of noninvasive ventilation with a simplified ventilatory support system is not appropriate. On the other hand, the many features of modern positive pressure ventilators are not necessary in all patients requiring MV [84].

**Future studies**

Further studies are needed: 1) to evaluate the ability of NMV (if any) to be used as an alternative to ET intubation; 2) to evaluate the most appropriate selection of patients and time of intervention; 3) to find the best level of NPSV and PEEP in different kinds of patients; 4) to define the best type of mask and most appropriate ventilator in different situations (ICU, Intermediate Intensive Care Unit, pulmonary ward, etc.); and 5) to evaluate the costs of NMV in comparison to conventional therapy and to invasive MV.

In conclusion, some authors claim that noninvasive mechanical ventilation to treat acute respiratory failure should be considered investigational and reserved for carefully selected patients [47]. Our opinion is rather that, in selected patients, a trial of noninvasive mechanical ventilation should be instituted at an early stage in episodes of acute respiratory failure as an adjunct to medical therapy, before severe acidosis ensues, in order to avoid endotracheal intubation.

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