Noninvasive Mechanical Ventilation in Patients with Severe Pneumonia

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9.1 Epidemiology and Etiology

Community-acquired pneumonia (CAP)—pneumonia occurring within 48 h after hospital admission or more than 2 weeks after discharge—leads to hospitalization rates of 20–35 % in Europe, with figures in Spain being even higher at 22–61 %. A substantial proportion of these cases (10 %) are defined as severe. These patients must be admitted to the intensive care unit (ICU) because of the possible need for ventilatory or hemodynamic support. Their mortality rate can be as high as 40 % [1]. In the rest of Europe the incidence of CAP is 5–11 cases per 1,000 person-years, and in Spain it drops to 1.6–1.8 cases per 1,000 person-years, with men and the elderly most often affected and mostly in winter [1].

The etiology of CAP varies according to the geographic area and the population studied. The causal microorganisms also differ depending on whether the patients are admitted to hospital and whether t they require admission to the ICU. An etiological diagnosis is made in 40–60 % of cases. For those admitted to ICU, most

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Spanish and European studies have found that the most common pathogen is *Streptococcus pneumoniae*, followed (although with variability in the percentages and depending on the series of cases) by *Legionella pneumophila*, *Staphylococcus aureus*, and Gram-negative bacilli (GNB). Prevalence is generally lower for *Haemophilus influenzae*, whereas it is the flu virus that most commonly causes CAP. A history of alcoholism or bronchoaspiration suggests an anaerobic or GNB etiology. In patients with chronic obstructive pulmonary disease (COPD), the most common culprits are *H. influenzae*, *Pseudomonas aeruginosa*, and *Moraxella catharralis*. *Aspergillu*s spp. is the least common. In people infected with the human immunodeficiency virus (HIV), *Pneumocystis jirovecii* predominates [1].

Community-acquired pneumonia is generally characterized by signs and symptoms of lower respiratory tract infection accompanied by new infiltrates on chest radiography. In the elderly the symptoms may be limited to confusional states, worsening of underlying illness, or metabolic disorders, which leads to delayed diagnosis in up to 30 % of these patients.

9.2 Pathophysiology

Pneumonia is defined as inflammation of the lung parenchyma caused by various microorganisms leading to accumulation of exudates in the adjacent bronchioles and alveoli. The result is decreased distensibility of the lungs and reduced pulmonary gas exchange.

The main aim of noninvasive ventilation (NIV) in these patients is to improve oxygenation and reduce the workload of the respiratory muscles, thereby alleviating dyspnea. In acute situations such as the pneumonic process, the most important factor determining improvement in the gasometric parameters is the mean airway pressure. Any positive change in the mean airway pressure reflects increased lung volume and consequently a better ventilation/perfusion ratio.

During acute respiratory failure (ARF), there is an extremely close relation between the patient's breathing pattern and the workload imposed on the respiratory muscles. Thus, the more the elastic and resistive loads increase, the greater is the muscle pressure necessary to maintain the same volume and flow. This is illustrated by the equation of motion for gas flow:

$$\text{Muscle pressure} = (\text{elasticity} \times \text{volume}) + (\text{resistance} \times \text{flow})$$

Respiratory failure leads to an increase in the respiratory workload, which is followed by a reduction in circulating volumes and an increase in the respiratory rate.

Positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) essentially increase functional residual capacity, decrease intrapulmonary shunt, recruit alveoli, and improve lung compliance. This chain of events leads to a reduction in the elastic retraction forces that the respiratory muscles have to overcome, thereby reducing the respiratory workload. Pressure support ventilation (PSV) reduces inspiratory effort, and therefore also dyspnea, much more

effectively. Also, because an inverse relation has been observed between the pressure applied with PSV and the respiratory rate, and another directly proportional relation between PSV and the circulating volume, it may also have a beneficial effect on oxygenation. This occurs because it decreases the respiratory workload and oxygen consumption, establishing a better ventilation/perfusion ratio as the result of producing larger tidal volumes. The combination of PSV and PEEP—because it represents an inspiratory aid and counteracts the potential intrinsic PEEP (responsible for the extra effort the inspiratory muscles have to make to overcome the pressure gradient and achieve inspiratory flow)—contributes to reducing the pressure and, consequently, the workload of the respiratory muscles. In clinical practice, it is accepted that the application of both PSV and PEEP can be the most appropriate ventilation method in this situation. So long as a balance is found between the optimal level of PEEP (to improve oxygenation) and the optimal level of PSV (to reduce the activity of the accessory muscles and respiratory rate and improve thoracoabdominal synchrony) the efficacy, at least initially, is similar to that of conventional mechanical ventilation.

9.3 Prognosis

A series of severity criteria from the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) are used in clinical practice to determine the need for ICU admission. A simple points scale, SMART-COP, is now available that seems to predict the need for ventilatory or vasoconstrictor support quite accurately. Also recently published is the REA-ICU scale, which identifies patients who are likely candidates for ICU admission during their first 3 days in hospital (Table 9.1) [1]. The incorporation of inflammatory biomarkers such as C-reactive protein and procalcitonin may improve the predictive capacity of these scales and allow better categorization of patients at high risk of dying [2]. Once in the ICU, the PIRO system, published only a few years ago, correctly identifies those whose lives are seriously at risk [3].

The prognosis depends on a number of factors, such as underlying disease; high Acute Physiology, Age, and Chronic Health Evaluation II (APACHE II) or the Simplified Acute Physiology Score II (SAPS II); hemodynamic status; multiple-organ involvement; nutritional and immune system status; degree of hypoxemia; time since onset; type of germ; both early and correct administration of the antibiotic.

The objective of NIV—defined as the administration of ventilatory assistance without endotracheal intubation—is to provide and ensure adequate ventilation and oxygenation while the medical treatment takes effect. The indications for NIV have been gradually increasing, and it is now used systematically during ARF in patients with COPD, cardiogenic pulmonary edema, or immunosuppression. However, there is a lack of consensus on its use in ARF secondary to pneumonia acquired outside the hospital. In this chapter, we review the available evidence on the application of NIV in patients with CAP.

Table 9.1 Criteria for severe community-acquired pneumonia

ATS and IDSA criteria	SMART-COP scale	REA-ICU scale
Major criteria:		
ARF requiring mechanical ventilation	SBP <90 mmHg (2 points)	Male (1 point)
Septic shock	Multilobar infiltrates (1 point) RR ≥ 25 resp/min for patients ≤ 50 years and ≥30 resp/min for patients >50 years (1 point)	Co-morbidity ≥1 (1 point) RR ≥ 30 resp/min (1 point) Leukocytes < 3×10^9 or ≥ 20×10^9/L (1 point)
Minor criteria:		
Systolic blood pressure (SBP) < 90 mmHg Multilobar infiltrates $PaO_2/FiO_2 < 250$ Confusion BUN (blood urea nitrogen) >20 mg/dL RR > 30 resp/min Leukopenia < 4×10^9/L Thrombocytopenia < 100×10^9 platelets/L Hypothermia < 36 °C	HR > 125 bpm (1 point) Confusion (1 point) Hypoxemia: $PaO_2 < 70$ mmHg or oxygen saturation ≤93 % for patients ≤50 years and <60 mmHg or oxygen saturation ≤ 90 % for patients > 50 years or $PaO_2/FiO_2 < 250$ (2 points) Albumin < 3.5 g/dL (1 point) Arterial pH < 7.35 (2 points)	HR ≥ 125 bpm (1 point) Age < 80 (1 point) Multilobar infiltrates or pleural effusion (2 points) $SatO_2 < 90$ % or $PaO_2 < 60$ mmHg (2 points) Arterial pH < 7.35 (2 points) BUN ≥ 11 mmol/L (2 points) Sodium < 130 mEq/L (3 points)
		Risk of admission to ICU:
The presence of one major criterion or three minor criteria suggest admission to ICU	Three or more points predict the need for ICU	≤3 points 1.1 % 4–6 points 5.5 % 7–8 points 11 % ≥9 points 27.1 %

9.4 Patient Selection: Factors Predicting Success or Failure of Noninvasive Mechanical Ventilation

Although the success of NIV depends primarily on the type of patient selected, there are a number of factors that are predictive of success or failure. Guidelines on NIV recommend using this ventilatory system according to clinical and gasometry criteria, excluding patients for whom it might be contraindicated. Classic potential candidates for NIV are those with a $PaO_2/FiO_2 < 200$ who develop progressive respiratory acidosis with pH ≤ 7.35 and have a sustained respiratory rate (RR) of more than 24 respirations per minute accompanied by active contraction of the accessory muscles or paradoxical abdominal motion. The exclusion criteria are well known. It must be remembered that to try to guarantee success patients must meet a series of criteria before NIV is applied (Table 9.2).

Apart from the variables predictive of NIV failure in patients with hypercapnic ARF, Antonelli et al. [4, 5] described a series of variables in patients with hypoxemic ARF (AHRF) and those who develop acute respiratory distress syndrome (ARDS) that identify those in whom the risk of failure is high. In AHRF patients

Table 9.2 Factors predictive of noninvasive ventilation success

Experience of the medical and nursing teams
Sufficient human resources
Early institution
Adequate instruction and positioning of the patient (sitting up)
Manual fixing of the mask, preventing leaks
Check tolerance and fit of the system (if possible, use helmet in AHRF), with strict "foot of bed" monitoring, especially during the first 6–8 h
Normal facial geometry. Intact dentition
Absence of bronchorrhea
Good neurological status
Haemodynamically stable
Adequate analgesia and/or sedation if agitated (if possible with remifentanil)
Low APACHE II and SAPS II scores
Abnormalities in acid–base balance mild
Adjust PSV and PEEP (4 cm of H_2O in single-tube systems to prevent reinhalation of CO_2) to reduce the RR to <25 resp/min and the activity of the accessory muscles and to achieve a tidal volume of 8 mL/kg
Initially adjust FiO_2 to achieve $SatO_2 \geq 90$ %
Clinical, gasometric, and acid–base balance improvement after 60–120 min of NIV
Try to maintain the NIV for at least the first 24 h without interruption

they are being >40 years of age, SAPS II ≥ 35, $PaO_2/FiO_2 \leq 146$ after 60 min of NIV, and the presence of CAP. For ARDS patients they are SAPS II > 34 and $PaO_2/FiO_2 \leq 175$ after 60 min of NIV.

Various authors have described a number of variables predictive of success or failure of NIV in groups of patients with CAP. In 2010, Carron et al. [6] reported on a small group of patients with severe CAP, regardless of high SAPS II scores, low PaO_2/FiO_2 ratio and low pH on admission, unsatisfactory gasometric response and acid–base balance, and increased respiratory rate and oxygenation index (OI) after application of NIV for 60 min. The OI (mean airway pressure × FiO_2 × 100/PaO_2) is an oxygenation parameter that serves as the most reliable independent predictor of NIV failure in the latter group of patients. In a larger group of patients with H1N1 pneumonia, Masclans et al. [7] reported that involvement of one quadrant on chest radiography, hemodynamic stability, and a Sequential Organ Failure Assessment (SOFA) score <8 are predictors of NIV success. Carrillo et al. [8] also reported that progression of the infiltrate on chest radiography within the first 24 h of NIV, a SOFA score ≥ 7 and heart rate ≥ 104 bpm, $PaO_2/FiO_2 < 144$, and bicarbonate < 23 mEq/L after 60 min of NIV are predictors of NIV failure in patients with severe CAP.

Nevertheless, questions have to be raised while clinical trials are being conducted in patients with AHRF: (1) What patients should be selected, and what criteria should be met to obtain better results? Earlier application of NIV is probably more efficient. (2) What is the role of corticosteroids during the acute phase, and what effect do they have on patients with CAP who undergo NIV [9]? (3) How long

should we wait, and when is the most appropriate time to resort to endotracheal intubation in the event of no improvement after instituting NIV? Most authors generally advise moving on to endotracheal intubation if the recognized standard criteria are met and if no clinical or gasometric improvement is observed within 60–120 min as delay can result in high morbidity/mortality rates.

9.5 Factors Determining Adequate Synchronization Between Patient and Ventilator

Noninvasive ventilation requires a respirator that applies positive pressure resulting in a transpulmonary pressure gradient, adequate tubing system and sensor systems, and above all an interface that adapts perfectly to the patient and enables adequate synchronization of the patient with the respirator. Although the main cause of mechanical failure of NIV is intolerance of the interface. Despite reports of the transparent helmet system improving comfort and reducing complications deriving from this technique, there are a number of factors inherent to the respirator that can critically affect adequate synchronisation. Among these factors are the following.

- *Inspiratory sensitivity*. Flow-triggered inspiration is preferable to pressure-triggered inspiration. If the trigger is too sensitive, the machine auto-triggers (cycles triggered by the ventilator, not triggered by the effort of the patient). With NIV, the auto-trigger tends to occur because of leaks or a poorly fitting interface. The ventilator interprets the increase in flow which attempt to compensate the leak as ventilation demand from the patient, triggering unwanted assisted cycles.
- *Time between the inspiratory effort and flow administration*. The longer the interval, the greater is the respiratory workload. There have been reports of increased delay in the administration of flow in patients receiving PSV with the helmet system, causing a delay between the start of the inspiratory effort and obtaining pressure in the system. This situation has led to discomfort and poor coordination.
- *Inspiratory ramp or flow rate*. In certain situations, a steep ramp allows delivery of flow in less time, reducing the sensation of "air hunger" and onset of the auto-PEEP, thereby making it more comfortable.
- *Expiratory sensitivity*. The patient sometimes terminates the inspiration before the respirator reaches the inspiratory flow-cycle threshold (in PSV, this often happens when 25 % of the peak flow rate is reached). This synchronization fault is called long-cycle asynchrony. In this case, an increase in the expiratory threshold sensor makes it possible to optimize the synchrony between patient and ventilator. In other instances, it may be due to the tidal volume being too high, which would have to be dealt by decreasing the PSV. Short-cycle asynchrony (when the patient's inspiratory time is longer than that of the respirator) tends to occur when chest wall/lung compliance is low or the patient is being underventilated. It can be resolved by reducing the expiratory threshold sensor or increasing the PSV.

- *PEEP valves*. The most suitable PEEP valves are threshold resistors. The external PEEP level necessary to reduce ineffective efforts due to auto-PEEP should never exceed 80 % of the auto-PEEP level. To lessen the problem of auto-PEEP, the bronchodilator treatment can be increased or the PSV reduced.
- *Humidification system*. The most appropriate humidification system is perhaps the surface humidifier (active humidification with an electric guide). Heat and moisture exchangers should be ruled out as they lead to increased dead space and cause an increased respiratory workload.
- *Leak compensation system*. Leaks can cause trigger failure and lengthen the inspiratory time in the PSV mode, leading to intolerance and failure of the NIV. This problem can be resolved by producing the cycle with a secondary safety feature that is usually time-controlled or changing to a pressure-limited, time-cycled ventilator mode.

In general terms, the success of NIV depends on the patient selected and where NIV is applied (i.e., in an ICU), the experience of the team, the type of ventilator (avoiding ventilators that were not designed for NIV), the humidification system and interface used, and adjustment of the ventilator parameters. Applying NIV in patients with ARF secondary to pneumonia should be done exclusively in ICUs because the ICU nursing staff has more experience, the patient can be closely monitored, and endotracheal intubation can be performed if necessary.

9.6 Experience in Acute Hypoxemic Respiratory Failure

Acute respiratory failure secondary to CAP has traditionally been treated with oxygen therapy delivered using face masks. Because of increased respiratory workload and refractory hypoxemia in some situations, however, it has been necessary to resort to endotracheal intubation and connection to mechanical ventilation. In view of the fact that invasive mechanical ventilation is not a risk-free technique and can cause a variety of complications—ventilator-associated pneumonia, complications related to the sedation/analgesia, damage to the trachea and lungs, organ dysfunction—over the last few years the indications for NIV have been extended based on studies that have produced strong evidence for its use [10]. It is now used systematically in patients with COPD or cardiogenic pulmonary edema, those who have undergone thoracic surgery, and immunosuppressed patients.

Although only a small number of patients (13–30 %) with AHRF (defined as ARF caused by a series of processes other than COPD with $PaO_2/FiO_2 < 200$) are potential candidates for NIV. For years now, nonrandomized studies have shown favorable results. Early, however, with the exception of patients with cardiogenic pulmonary edema, improvements were demonstrated only in oxigenation and not in the need for intubation. Wysocki et al. [11] were the first to conduct a randomized trial in patients with AHRF due to various causes, discounting patients with COPD. They compared PSV and PEEP with oxygen therapy and found that NIV did not significantly reduce the endotracheal intubation or mortality rates in the ICU. Upon analyzing the subgroups with $PaCO_2$ below or above 45 mmHg, they found that

these rates were significantly reduced only in those with $PaCO_2$>45 mmHg. Later, among other studies conducted, the multicenter, randomized, prospective study by Delclaux et al. [12] compared CPAP by mask versus oxygen therapy in patients with ARF and bilateral lung infiltrates (due to various causes). Altogether, 54 and 55 % of the patients in the two groups, respectively, had pneumonia. Patients with COPD or respiratory acidosis were excluded. The authors found that although NIV improved oxygenation it did not reduce the need for endotracheal intubation or the mortality rates. Antonelli et al. [13] conducted a randomized, controlled study comparing NIV (PSV and PEEP) with invasive ventilation in immunocompetent patients with ARF (including a small proportion with pneumonia and excluding patients with COPD). They found that NIV improved oxygenation to the same extent as conventional invasive ventilation and significantly reduced both the need for endotracheal intubation (although this was not the primary endpoint) and the number of cases of pneumonia and sinusitis inherent to this invasive technique. Although they found no significant differences between groups regarding the mortality rate (only a trend toward increased survival in the NIV group), it is worth noting that the overall mortality rate was 28.1 % in the group assigned to NIV and 46.8 % in the invasively ventilated group. The Antonelli et al. study stimulated and gave new impetus to the interest in NIV. Since then, a number of randomized, controlled clinical trials have been conducted in both immunocompetent and immunosuppressed patients with AHRF.

Noninvasive ventilation has been shown to have clear clinical benefits in immunosuppressed patients, reducing the need for endotracheal intubation and its inherent complications. However, because of the heterogeneity of the population studied, results in immunocompetent patients have been conflicting owing to the cover-up effect that some AHRF subgroups have over others with a different etiology. Also, no clear improvement was demonstrated in the parameters studied.

We next describe the principal randomized studies conducted on patients with ARF of different etiologies, including pneumonia, in most of which NIV is compared with standard medical treatment. There are also a few studies that compared NIV with endotracheal intubation. We conclude the chapter by discussing studies, both randomized and observational, that focused almost exclusively on patients with pneumonia.

In 2000, Martin et al. [14] published a randomized clinical trial in which they compared PSV and PEEP with standard medical treatment in heterogeneous groups of ARF patients, with and without COPD. They found that NIV significantly reduced endotracheal intubation rates both overall and in the non-COPD subgroup, although it did not decrease the number of days in the ICU or the mortality rate. The results for the COPD group were not statistically significant. These results are in contrast with those of the Wysocki et al. study [11], although it is true that the intubation rate was three times higher in the standard treatment group. This study was pioneering in that it demonstrated that NIV reduces the need for endotracheal intubation in patients with AHRF, suggesting that the benefits of this NIV method are not limited to patients with hypercapnic ARF. These results were subsequently corroborated by a systematic review carried out in 2004 by Keenan et al. [15], who also

stated that it produced a clear improvement, although their study had limitations due to population difference among the patients included. After observing discrepancies, however, they suggested that certain types of ARF should be carefully selected and controlled in the ICU.

Multicenter, randomized clinical trials were published by Ferrer et al. [16] and Honrubia et al. [17]. Ferrer et al. [16] studied patients with AHRF due to various causes (mainly pneumonia, acute pulmonary edema, chest trauma, and ARDS). They included 19 immunosuppressed patients and rejected those with hypercapnia. They compared NIV with high-concentration oxygen therapy, with a primary endpoint of the need for endotracheal intubation. They found that NIV improved oxygenation. Also, it significantly reduced the respiratory rate, the number of intubations, and the mortality rate compared to the control group. It was particularly effective in the subgroup of patients with pneumonia. This contrasted with a previous prospective, cohort study run by Antonelli et al. in 2001 in which pneumonia was identified as one of the predictive factors for NIV failure. This trial was the first to show that NIV reduced the risk of endotracheal intubation in patients with AHRF without chronic respiratory disease.

Honrubia et al. [17] included patients with ARF of various etiologies (pneumonia, cardiogenic pulmonary edema, patients with and without COPD), comparing NIV (PSV and PEEP) with endotracheal intubation. This and the Antonelli et al. study published in 1998 are two of the few randomized trials conducted in heterogeneous groups of patients with ARF in which NIV was compared with endotracheal intubation. The patients in the Honrubia et al. study were older, more seriously ill, and had a lower PaO_2/FiO_2 on admission. The results show a significant (58 %) decrease in the primary endpoint (endotracheal intubation) for those assigned to NIV compared to the control group (100 % of patients intubated). There was also a nonsignificant trend toward lower mortality rates when comparing the two groups and when comparing the group in which NIV failed with those assigned from the start to conventional ventilation. However, subgroup analysis showed that NIV significantly reduced the need for endotracheal intubation in patients with COPD. There was a nonsignificant trend in those who did not have COPD. At the same time, the mortality rates for patients without COPD (57 %) and for those with pneumonia in the NIV group who had to be intubated (50 %)—100 % of those with pneumonia had to be intubated—in relation to those patients assigned to intubation from the time of admission (40 and 80 %, respectively) are all lower than the 90 % rate in those assigned to NIV who required intubation in the Antonelli et al. trial.

Finally, we address the few randomized, observational studies conducted almost exclusively on patients with pneumonia. In 1999, Confalonieri et al. [18] carried out a multicenter, randomized, controlled study with conventional oxygen therapy in patients with ARF secondary to CAP. They found that NIV with PSV and PEEP significantly reduced both the primary endpoint (the number of endotracheal intubations) and the number of days in the ICU. A later analysis revealed that the only ones who benefited were the patients with COPD. These results concur with those of Wysocki et al. [11], who subsequently found, a posteriori, that the greater benefit was in the patients with hypercapnia. Moreover, the intubation rate of 37.5 % in

those without COPD who underwent NIV was slightly lower and nonsignificant in relation to the standard treatment group. This is similar to the findings published by Antonelli et al. in 1998 but with the peculiarity that in the Confalonieri et al. study the APACHE II scale was higher in the NIV group than in the standard treatment group and tended toward statistical significance.

In 2010, Cosentini et al. [19] published a randomized trial conducted in the emergency department in which they compared CPAP using the helmet system with conventional oxygen therapy in immunocompetent patients with CAP. They included patients with $PaO_2/FiO_2 > 210$ but < 285 after wearing a mask with oxygen at 50 % for at least 15 min and excluded those with respiratory acidosis, acute ischemic heart disease, and pulmonary edema. The study had to be terminated prematurely when it was found that the primary endpoint ($PaO_2/FiO_2 > 315$) was achieved in 95 % of patients assigned to CPAP at an average time of 1.5 h whereas in those assigned to conventional treatment only 30 % had reached these levels at 48 h. An important point is that only a few patients managed to sustain the primary endpoint at 60 min and 24 h after CPAP it was discontinued. These results are consistent with those reported by Jolliet et al. [20] and suggest that more sustained application of NIV in accordance with the NIV guidelines, using more comfortable systems such as a helmet, would probably avoid the mechanism of opening and closing of the alveoli and could provide greater benefits.

Among the prospective, observational studies performed, those carried out by Jolliet et al. [20] and Domeniggetti et al. [21] are important. They applied NIV (PSV and PEEP) in patients with ARF. Jolliet et al. [20] included consecutive patients with severe CAP only, excluding those with COPD and cardiogenic pulmonary edema. Domeniggetti et al. [21] included patients with severe CAP and cardiogenic pulmonary edema and excluded those with respiratory acidosis and COPD. Jolliet et al. showed that despite the initial improvement in gasometric parameters, a high percentage (66 %) of patients had to be intubated, with the mortality rate in this group reaching 50 % (none of the nonintubated group died). This was probably due to lower PaO_2 values, the large number of lung lobes affected, and inclusion of older patients compared to other series.

Domeniggetti et al. found that the NIV improved oxygenation and significantly reduced the number of intubations in patients with pulmonary edema (probably because there was more hypercapnia and lower SAPS II scores in that group). The intubation rate (38.8 %) in patients with CAP, although high, was considerably lower than that in the Jolliet group but similar to that found by Confalonieri et al. in the group assigned to NIV without COPD. The more unfavorable data in the CAP group may be the result of both the slow establishment of the initial phase and the lengthy recovery, which is typical of such inflammatory processes in the lungs.

Carron et al. [6] published a prospective, observational study on patients with severe CAP who did not have COPD or cardiogenic pulmonary edema and who received PSV and PEEP with a helmet system. The NIV failed in 56 %, and the mortality rate among those who required intubation was 22 %. This rate is significantly higher than that among patients in whom the NIV was successful but still

lower than the mortality rates in patients from other studies who had to be intubated when the NIV failed. Important points are that patients in whom the NIV failed had a higher SAPS II score, a worse gasometric response, and a significantly shorter NIV application time.

Carrillo et al. [8] studied 184 consecutive patients with severe CAP (82 of whom had a history of heart disease or COPD) who underwent NIV with PSV and PEEP. The NIV was successful overall in 63 % of cases. The mortality rate was 40 % among those with AHRF (who did not have COPD or heart disease) who were intubated after NIV failure. These authors found progressive infiltration on chest radiography during the first 24 h after application of NIV, SOFA score ≥ 7, heart rate ≥ 104 bpm, $PaO_2/FiO_2 < 144$ and bicarbonate < 23 mEq/L 60 min after the application of NIV to be predictors of NIV failure. NIV failure led to an increase in the mortality rate, with an NIV duration ≥ 53 h before intubation being the variable significantly associated with a decrease in hospital survival.

Finally, although NIV has been reported to be effective in isolated cases of pneumonia caused by *Legionella* and in pregnant women with pneumonia and ARF, the results obtained in those with H1N1 virus infection have not been as good as expected. As a result, the European Society of Intensive Care Medicine and a number of studies in Spain [22] have advised against its use. However, Liu et al. [23] and Belenguer-Muncharaz et al. [24], among others, published observational studies with satisfactory, promising results in patients with H1N1 infection, albeit only in a few cases. Moreover, Masclans et al. [7] published the first large-scale, multicenter, observational cohort study of patients with H1N1 viral pneumonia, having excluded patients with COPD or acute pulmonary edema. NIV was applied in 25.8 % of all patients ($n = 685$) and in 36 % of those ventilated. The NIV was successful in 40.6 % of patients. The variables predicting success were involvement of only one quadrant, on the chest radiography, hemodynamic stability, and SOFA score <8. Unlike in other studies, the mortality rate was the same for those in whom NIV failed and those who had been intubated from the start. Nonetheless, a number of important limitations in that study must be pointed out, such as the fact that data were not obtained regarding the severity of the ARF, the lack of standardized criteria for admission to the ICU and intubation, and failure to record the NIV technique and the time elapsed from NIV failure to intubation.

The initial concerns about virus propagation and disease transmission—stemming from the facts that, depending on the type of mask, the amount of leakage, and the inspiratory pressure applied, NIV creates droplets >10 μm within a radius of 1 m—have been gradually diminishing. As a result, the World Health Organization now considers it a reasonable option so long as strict measures are put in place for respiratory protection. In contrast, it is known that the risk of contagion is high when endotracheal intubation must be used [25].

The lack of accord among the studies described can be explained by a number of factors. One such factor is the differences in the populations studied. Others are that some of studies were observational, and some included low numbers of patients. There were also limitations in the interpretation of some of the studies, and in certain cases the subgroup analyses were carried out a posteriori.

Key Major Recommendations

- At present, as stated by Ambrosino and Vagheggini [10], there is firm evidence to support the application of NIV in patients with COPD, cardiogenic pulmonary edema, or immunosuppression. The evidence is weak regarding its use in patients with ARF secondary to asthma, ARDS, or pneumonia.
- Despite the fact that there is less evidence to support the application of NIV in patients with CAP, it can be considered in carefully selected patients but always under close monitoring in the ICU.
- The greatest benefits are perhaps obtained when applied early in patients with early-stage infection by well-trained, experienced teams, when the appropiate modes and interfaces are used, the correct empirical antibiotics are prescribed and, probably, when intravenous corticosteroids are administered.
- Adequately designed studies are required that do not include heterogeneous groups of patients with hypoxemic ARF. The patients should be exclusively those with pneumonia to determine the specific situations in which this ventilation method may be effective.

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