Review
Clinical review: Long-term noninvasive ventilation

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Abstract

Noninvasive positive ventilation has undergone a remarkable evolution over the past decades and is assuming an important role in the management of both acute and chronic respiratory failure. Long-term ventilatory support should be considered a standard of care to treat selected patients following an intensive care unit (ICU) stay. In this setting, appropriate use of noninvasive ventilation can be expected to improve patient outcomes, reduce ICU admission, enhance patient comfort, and increase the efficiency of health care resource utilization. Current literature indicates that noninvasive ventilation improves and stabilizes the clinical course of many patients with chronic ventilatory failure. Noninvasive ventilation also permits long-term mechanical ventilation to be an acceptable option for patients who otherwise would not have been treated if tracheostomy were the only alternative. Nevertheless, these results appear to be better in patients with neuromuscular/-parietal disorders than in chronic obstructive pulmonary disease. This clinical review will address the use of noninvasive ventilation (not including continuous positive airway pressure) mainly in diseases responsible for chronic hypoventilation (that is, restrictive disorders, including neuromuscular disease and lung disease) and incidentally in others such as obstructive sleep apnea or problems of central drive.

Introduction

After the successful use of tracheostomy and intermittent positive pressure ventilation (IPPV) in the 1950s to treat acute bulbar poliomyelitis [1], some patients were discharged at home with long-term mechanical ventilation via tracheostomy (invasive) or mouth piece (noninvasive) [2,3]. However, it was only in the 1980s after the introduction of noninvasive positive pressure ventilation (NIPPV) through facial interfaces in the intensive care unit (ICU) that long-term NIPPV was considered as a standard of care to treat selected patients following an ICU stay. NIPPV is now a predominant technique for long-term home ventilation [4]. It is also well recognized that NIPPV allows patients treated for acute failure from chronic respiratory insufficiency to be discharged from hospital and also prevents readmissions [5,6]. These beneficial effects have been reported for both chronic obstructive pulmonary disease (COPD) and neuromuscular/parietal disorders [6]. Depending on the underlying diseases and the severity, IPPV is either continuously mandatory to avoid death in cases of complete or quasi-complete paralysis or is used nightly, producing enough improvement to allow free time during the daytime for spontaneous breathing. This clinical review will address the use of NIPPV (not including continuous positive airway pressure (CPAP)) in the different diseases for which it is currently proposed.

Methods of NIPPV and their uses
Interfaces

The need to select an appropriate and properly fitted interface cannot be overemphasized due to its impact on the quality of ventilation [7]. The aim is to reach a compromise between different objectives: to minimize leaks, improve comfort and implement the mask easily. A wide variety of different factory-made masks of different designs, shapes, sizes and materials is now available. It is usually possible to find a mask that suits most individuals. Because of this, the initial practice of custom made interfaces for different individuals is now seldom needed, even if it remains probably the best interface [7,8]. There are currently four different types of interfaces: nasal masks, which are used predominantly [8,9]; facial masks covering the nose and the mouth; nasal pillows; and mouthpieces [9], which are now essentially indicated in the case of daytime ventilation [10]. Mouthpieces may afford an excellent interface to provide adjunct daytime ventilation in neuromuscular patients who are unable to maintain acceptable diurnal arterial blood gases without frequent intermittent periods of assistance. The mouthpiece is positioned close to the patient's mouth where it is intermittently captured to take a few assisted breaths from the ventilator and subsequently released. An advantage

ABG = arterial blood gas; ALS = amyotrophic lateral sclerosis; BPAP = bilevel positive airway pressure; COPD = chronic obstructive pulmonary disease; CPAP = continuous positive airway pressure; $EtCO_2$ = end-tidal CO_2; ICU = intensive care unit; IPPV = intermittent positive pressure ventilation; NIPPV = noninvasive positive pressure ventilation; $PaCO_2$ = partial pressure of arterial carbon dioxide; PaO_2 = partial pressure of arterial oxygen; PEEP = positive end-expiratory pressure; SpO_2 = pulse oximetry; $TcCO_2$ = transcutaneous CO_2.

of this is that the face is free from face-attached interfaces. Patients needing assistance night and day may use a combination of interfaces.

Ventilators and modes for NIPPV

Ventilators use one of two basic methods: volume-preset and pressure-preset [9]. With volume-preset, the ventilator always delivers the tidal volume that is set by the clinician, regardless of the patient's pulmonary system mechanics (compliance, resistance and active inspiration). However, leaks at the skin-mask interface, or through the mouth when using a nasal mask, reduce the volume received by the patient. Conversely, with pressure-preset, changes in pulmonary mechanics directly influence the flow and the delivered tidal volume (lower or higher) since the ventilator delivers the set pressure throughout inspiration. In this case, leaks augment the flow and tend to maintain the tidal volume [11]. More recently, a third method has been proposed for both ICU and home ventilation. This is called pressure-preset/volume-targeted and aims to guarantee delivery of a tidal volume with the comfort of the pressure-preset method. At the present time, clinical evaluation of this third method remains poorly documented [12]. It is important to understand that NIPPV is dominated by both rapidly varying non-intentional leaks and the geometry and the resistance of the upper airway [13]. Obviously, leaks and airway resistance partly interact. In the face of these continuous changes the respective advantages and drawbacks of volume- and pressure-preset methods, which are opposite, make it difficult to predict their effects. The way inspiration begins and ends is initiated either by the ventilator or in response to a patient effort to do so, allowing one to define the main modes of ventilation: control, assist-control, and assist or spontaneous (assist or spontaneous possible only with pressure-preset).

Most home ventilators function according to only one of the methods, volume-preset or pressure-preset, but modern ones may deliver inspiration by both methods. Besides the classic circuitry, including two valves (on the inspiratory and expiratory limbs) alternately closing and opening, bilevel positive airway pressure (BPAP) ventilators are simpler and, therefore, lend themselves to home mechanical ventilation [14]. Inspiratory and expiratory pressures are alternatively established in a single circuit incorporating an intentional, calibrated leak located close to the patient or even on the mask. The theoretical disadvantage with such a circuit is the risk of variable CO_2 rebreathing. However, concern about the risk of CO_2 rebreathing has not been definitively documented [15], although the trend is to consider it as negligible provided positive expiratory pressure is applied in order to eliminate CO_2 through the intentional leak (at least 2 to 4 cmH_2O) [16]. Depending on the ventilator, all the different modes and refined settings, and even closed-loop modes usually applied in the ICU, are more or less available. Some ventilators may analyze ventilation in an on-going manner and keep the data in internal memory for further assessment. The general objective is to provide many possible capabilities in order to have enough tools to adapt and optimize patient-machine synchronization. While conceptually attractive, sufficient studies have not been performed to document or refute the advantages of such complexity in the context of noninvasive home ventilation.

Choice of the ventilator and mode

Many clinicians currently prefer a pressure-preset ventilator in assist mode as the first choice with a view to offering the best synchronization [4]. In fact, in the studies comparing volume and pressure-preset ventilators, no clear differences in the correction of hypoventilation in short-term studies [17,18] and long-term outcomes [19,20] have been shown. This is understandable since leaks and resistance changes during NIPPV alternate very quickly and when the pressure target is well achieved, the volume target is not, and *vice versa*. However, it is important to remain flexible by trying alternative approaches if problems occur with one or the other type of ventilator.

Additionally, even if new generations of BPAP ventilators tend to contain batteries, it should be noted that these batteries most often provide autonomy of only short duration. This would limit security and mobility of neuromuscular patients with hypoventilation and then shift the preference to the volume ventilator.

Criteria to consider when deciding on the implementation of NIPPV
Signs and symptoms of hypoventilation

The presence of clinical symptoms and/or physiological markers of hypoventilation are useful in identifying clinical severity as it relates to therapeutic decision-making with regard to initiation of nocturnal NIPPV. In the course of a typically progressing disease, two successive steps occur more or less rapidly: nocturnal hypoventilation that is reversible during waking hours associated with none or a few clinical symptoms; and nocturnal and daytime hypoventilation associated with clinical symptoms that show a low respiratory reserve and should be considered an unstable state with increased susceptibility to life-threatening acute ventilatory failure that may be triggered by what may otherwise be trivial additional factors [21,22]. A sleep study continuously recording CO_2 (end-tidal ($EtCO_2$) or transcutaneous ($TcCO_2$)) and/or pulse oximetry (SpO_2) is required to document nocturnal hypoventilation, which may occur throughout all sleep stages but in some cases exclusively during rapid eye movement sleep. Daytime hypoventilation is defined by abnormally elevated partial pressure of arterial carbon dioxide ($PaCO_2$), a high serum bicarbonate level and a relatively normal pH with associated reduction of the partial pressure of arterial oxygen (PaO_2). Chronic daytime hypoventilation is an important indicator invariably associated with sleep-related hypoventilation. Thus, in the presence of diurnal hypoventilation, the reason for overnight recording is only to

Table 1

Clinical features frequently associated with alveolar hypoventilation

Shortness of breath during activities of daily living in the absence of paralysis

Orthopnea in patients with disordered diaphragmatic dysfunction

Poor sleep quality: insomnia, nightmares and frequent arousals

Nocturnal or early morning headaches

Daytime fatigue, drowsiness and sleepiness, loss of energy

Decrease in intellectual performance

Loss of appetite and weight loss

Appearance of recurrent complications: respiratory infections

Clinical signs of *cor pulmonale*

rule out obstructive or central apnea. Clinical symptoms indicating consequences of hypoventilation (Table 1) must be carefully evaluated since, even when modest, they are important for the appreciation of disease severity and prognosis and in the indication of NIPPV. Pulmonary function tests help define and quantify the ventilatory-respiratory disease but have low predictive values for chronic sleep-related hypoventilation in individual patients except in those with neuromuscular disease. Indeed, in Duchenne muscular dystrophy, hypoventilation appears only during rapid eye movement sleep, all night, or during the daytime when supine inspiratory vital capacity is <40%, <25% and <12%, respectively [21]. Similarly, a peak cough flow <160 l/min, related to expiratory muscle deficit, means an increased risk of accumulation of secretions that may worsen hypoventilation and trigger acute failure [23]. It is crucial to note that isolated reduced PaO_2 does not require mechanical ventilation but only supplemental oxygen because it does not indicate hypoventilation but only a mismatching of ventilation and perfusion.

Diseases that may potentially be treated with NIPPV
The principal diseases that may be addressed using NIPPV therapy are shown in Table 2. Except for those due to respiratory control or upper airway abnormalities, all may become severe enough to cause alveolar hypoventilation during sleep and daytime and eventually may impair the quality of life and threaten life. In neuromuscular disorders, it is important to consider the progressiveness according to each type of disease and the individual concerned.

Survival with NIPPV in different diseases
NIPPV efficacy in terms of survival compared to control treatment is important information required in order to adequately discuss NIPPV. Besides a few randomized control trials [24-27], this information comes from retrospective series compared to the usual prognosis [20,28-31]. In order

to extend the analysis, it is also possible to take into account results obtained with either negative pressure ventilation [32] or tracheostomy [2]. These are informative enough and generally accepted by the medical community even if conclusions derived from them are refutable in terms of evidence-based medicine. In neuromuscular disease, NIPPV always increases survival. Approximate median increased survival times depend on the age of the patient when starting NIPPV and the comorbidities present (including extended paralysis): very long (>20 years) in the sequelae of poliomyelitis; long (10 years) in spinal muscular atrophy type 2 and 3, Duchenne muscular dystrophy, and acid maltase deficiency; short (4 years) in myotonic dystrophy; and very short (1 year) in amyotrophic lateral sclerosis (ALS). In cases of chest-wall abnormalities, NIPPV also prolongs life: 15 years in kyphosis and 7 years in the sequelae of tuberculosis. No data support a positive effect on survival in lung diseases: in COPD patients randomized trials are negative [25,26,32], and data are too scarce in cystic fibrosis or for bronchiectasis patients. However, we must note that the negative results in the trials in COPD may be related to insufficient ventilation due to a too low driving pressure.

Circumstances and indications for NIPPV
In clinical practice, NIPPV is initiated either electively or in the context of acute ventilatory failure initially treated invasively with translaryngeal intubation or noninvasively with facial interfaces [33]. In the latter circumstances, the long-term necessity for NIPPV should be reevaluated after weeks or months during follow-up since the indications for NIPPV may change as the clinical conditions improve or not. In cases of chronic and stable awake hypoventilation, the main criteria for predicting the need for NIPPV are advanced severity with clinical symptoms of hypoventilation plus a balance of several other issues, including: the main primary process explaining the hypoventilation - mechanical or lung deficit; whether the natural rate of progression has been a few years or dozens of years; the clinical severity at the time of decision making; actual symptoms and history of acute-subacute failure in the previous months; and the patient's willingness, including the family and social environment, to undertake this therapy.

Indications for NIPPV are outlined in Table 3. NIPPV is strongly indicated in patients with chest wall and neuromuscular disorders in the presence of clinical symptoms attributable to diurnal hypoventilation [34-37]. There are no validated values above which NIPPV is definitely indicated; however, many clinicians consider treatment in scoliosis and sequelae of tuberculosis with awake $PaCO_2$ >50 to 55 mmHg and a PaO_2 <60 mmHg, and in neuromuscular disease with a $PaCO_2$ around 45 to 50 mmHg and a PaO_2 <70 mmHg. In cases with clear clinical symptoms, less severe values may be considered as an indication to start NIPPV [35]. Conversely, in COPD and probably in other lung diseases, diurnal hypoventilation does not support the unequivocal utility of NIPPV [38,39]. Nevertheless, this question remains open since the

Table 2

Main diseases that can benefit from NIPPV classified according to the cause and progressiveness of the respiratory impairment

Parietal disorders (PFT abnormal; $\downarrow$ VC, $\downarrow$ FEV1, $\rightarrow$ FEV1/VC, $\downarrow$ RV, $\downarrow$ TLC)

Chest wall	
Kyphoscoliosis	No worsening
Sequelae of tuberculosis	Slow worsening
Obesity hypoventilation syndrome	Depends on obesity
Neuromuscular disorders	
Spinal muscular atrophy	No worsening
Acid maltase deficit	Slow worsening (>15 years)
Duchenne muscular dystrophy	Intermediate worsening (5 to 15 years)
Myotonic myopathy	Intermediate worsening (5 to 15 years)
Amyotrophic lateral sclerosis	Rapid worsening (0 to 3 years)

Lung diseases (PFT abnormal; $\rightarrow$ or $\downarrow$ VC, $\downarrow$ FEV1, $\downarrow$ FEV1/VC, $\uparrow$ RV, $\uparrow$ TLC)

COPD	Continuous worsening
Bronchiectasis, cystic fibrosis	Continuous worsening

Predominant ventilatory control abnormalities (PFT normal)

Ondine's curse	Improvement?
Cheyne-Stokes breathing	Depends on heart failure

Upper airway abnormalities (PFT normal)

Obstructive sleep apnea	No worsening

Symbols indicate actual compared to theoretical values: $\downarrow$, decrease; $\uparrow$, increase; $\rightarrow$, normal. COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 second; NIPPV, noninvasive positive pressure ventilation; PFT, pulmonary function test; RV, residual volume; TLC, total lung capacity; VC, vital capacity.

clinical trials are underpowered and secondary parameters, such as some components of the quality of life or hospitalization days, may have improved. Some observational series suggest better results [40,41]. Presently, we may admit NIPPV as an option in COPD patients with symptoms of hypoventilation contributing to recurrence of acute-subacute failure, provided that long-term oxygen and drug therapy have already been optimally adjusted. During early stages with only isolated nocturnal hypoventilation, NIPPV is not mandatory but could be optional in kyphoscoliosis and neuromuscular diseases [42]. In the latter, when worsening is both inevitable and rapid (for example, ALS), NIPPV is valuable at an early stage provided that this is an acceptable therapeutic option for the patient.

NIPPV use in some other diseases may also deserve consideration even if clinical experience remains inconclusive. Obesity hypoventilation syndrome is dominated by morbid obesity impeding ventilation, frequent obstructive apnea and

more or less reversible decreased reactivity of the respiratory centers [43]. In acute-subacute as in chronic situations, NIPPV has been shown to reverse hypoventilation [44,45]. However, considering the high prevalence of obstructive apnea, CPAP is a simpler and efficient treatment. In addition, CPAP reduces the resistance of the pharynx, which leads to a light reduction of the work of breathing. This may be another reason for the reversal of the hypoventilation. Cheyne-Stokes breathing with central and obstructive apnea in the context of severe cardiac insufficiency has been shown to negatively influence the clinical situation and survival [46]. Conventional NIPPV or a new modality, such as adaptive servo-ventilation, has been shown to alleviate apnea and improve cardiac function [47,48]. Nevertheless, no conclusion about the utility of nocturnal NIPPV in terms of survival and main outcomes is available. In addition, a recent large study comparing oxygen and CPAP, which also alleviates apnea and improves cardiac function, does not prove the clinical superiority of CPAP in terms of survival [49]. Pure obstructive sleep apneas in the context of obstructive sleep apnea could be suppressed with NIPPV. Some authors have proposed NIPPV as a second-line treatment in the case of CPAP failure. However, this is not supported with enough conclusive study to be recommended [50]. Ondine's curse, in children, is characterized by the lack of metabolic response of the respiratory centers during sleep and is responsible for severe nocturnal hypoventilation. The usual treatment is tracheostomy and nocturnal ventilation. Some clinical experience suggests that, after years, tracheostomy might be converted in some cases to nocturnal NIPPV. Obviously, such options must remain in the hands of specialized teams [51].

Management of NIPPV
Initiation and settings for nocturnal ventilation
The main goal of NIPPV, which in the best circumstances is used solely during the night, is to improve arterial blood gases up to nearly normal values without discomfort and sleep disruption. However, day time mechanical ventilation in chronic respiratory insufficiency is as good as night time ventilation. The reduction of hypercapnia depends more on the duration of the ventilation than on whether the patient is asleep or awake [52]. The objective when there is residual muscle ability to breathe is to provide enough improvement to allow comfortable time off the ventilator. Even if there is no absolute recommendation, it is good general practice to proceed in three steps. The first step consists of selecting and adjusting the ventilator settings while the patient is awake, insuring physiological adequacy and patient comfort for at least one or two hours. One study, done on awake cystic fibrosis patients, found that clinical observation is as efficient as the use of physiological measurements, including esophageal pressure, in setting the ventilator parameters [53]. Another in patients with COPD and neuromuscular disease has shown that using physiological measurements does not improve ventilation during the day but improves ventilation and sleep quality during the night [54,55].

Table 3

Typical indications for nocturnal NIPPV according to disease process and severity

Disease	Symptoms and night/day CO_2 ↑	Symptoms and only night CO_2 ↑	No/limited symptoms but night/day CO_2 ↑	Usual daily duration of NIPPV
Scoliosis	Yes	Yes	Perhaps	<12 hours
Tuberculosis	Yes	Yes	Perhaps	<12 hours
Neuromuscular stable or slow	Yes	Perhaps	Perhaps	18-24 hours
Neuromuscular intermediate	Yes	Perhaps	Perhaps	18-24 hours
Neuromuscular rapid	Yes	Yes	Yes	24 hours
COPD	Perhaps	No	No	12 hours
Bronchiectasis/cystic fibrosis	Perhaps	No	No	18-24 hours
Obesity hypoventilation	Perhaps	Perhaps	No	<12 hours

↑, Increase; COPD, chronic obstructive pulmonary disease ; NIPPV, noninvasive positive pressure ventilation.

In the second step, the clinician should judge adequacy when the patient is napping and/or during nocturnal use. To complete this step, different options according to the resources available in each center could be used. Arterial blood gas (ABG) measurements would seem ideal; however, one or a few samples during the night do not represent the rapid changes observed during several continuous hours of sleep, and the invasiveness of sampling has led most clinicians to noninvasively monitor different parameters. Ideally, a complete polysomnogram recording SpO_2 and $TcCO_2$ or $EtCO_2$, airflow, tidal volume, airway pressure, rib cage and abdomen excursion, and sleep staging permits a complete assessment [56]. When resources are not available to perform these detailed recordings, fewer measurements during overnight recordings remain informative. However, the minimal requirement is to record SpO_2 overnight in room air, assessing whether the normalization of SpO_2 accompanies a normalization, or at least an improvement, of $PaCO_2$. In addition, data related to patient tolerance, comfort, sleep quality and well-being should be obtained.

The third step is carried out after several nights of NIPPV and consists of looking for a reduction in $PaCO_2$ and augmentation of PaO_2, without dyspnea, during the day when free from ventilation to confirm that the settings are adequate. This also gives information about the necessity or not to add daylight hours of NIPPV (at first during napping and more when necessary). If the results are not satisfactory, alterations must be made to the settings and possibly the mask and the ventilator, and the effects of these checked again. In most cases, a few days are necessary to achieve success.

If one uses assist pressure-preset ventilation, 10 cmH_2O of inspiratory pressure support is a suggested starting point. If necessary, the pressure level is progressively increased to achieve evidence of improvement. Pressure support higher than 20 cmH_2O is rarely necessary. Nevertheless, one

observational series reports good results in COPD patients ventilated with higher (28 cmH_2O) pressure [41]. In COPD, the addition of an expiratory positive pressure (positive end-expiratory pressure (PEEP) or expiratory positive airway pressure (EPAP)), also necessary to decrease the rebreathing with BPAP ventilators, should conceptually improve patient triggering when intrinsic PEEP exists [57]; however, there is no long-term study proving its clinical usefulness. Depending on the ventilator capabilities and observations made of how the patient and ventilator do together, more subtle settings concerning triggers, initial flow, and inspiratory time limit could be tried. A backup frequency set close to the spontaneous frequency of the patient during sleep is a reasonable substitute to avoid central apnea induced by transitory but repeated hyperventilation exceeding the apnea threshold [58].

When employing a volume-preset ventilator, the initial suggested settings may be established by adjusting the frequency of ventilator-delivered breaths so that it approximates the patient's spontaneous breathing frequency during sleep, an inspiratory time/total breathing cycle time between 0.33 and 0.50 and a relatively high tidal volume of around 10 to 15 ml/kg to insure sufficient tidal volume in case of leaks [59].

Supplemental oxygen should be added into the ventilator circuit in those patients requiring oxygen while awake due to lung parenchyma diseases (for example, COPD, cystic fibrosis, bronchiectasis). In the absence of parenchymal disease it is only after trying to optimize all technical parameters that residual desaturation may justify additional oxygen bled into the ventilator circuit during sleep [60].

Continuous NIPPV

In neuromuscular diseases (and to a lesser degree in end-stage lung diseases), ventilator dependency may be total when starting NIPPV or may progressively increase following the gradual worsening of the disease. In cases of continuous

need for ventilation, NIPPV could be used provided that interfaces are alternated night and day and assisted coughing is made available [37,61]. Only a very well trained team that is completely informed and conscious of the constraints and dangers involved may take such an approach in patients. Such application has been reported by different teams in stable neuromuscular patients, such as those with a sequelae of poliomyelitis, high-level spinal cord injury or Duchenne muscular dystrophy [10,62]. Alternatively, a tracheostomy may be performed to facilitate ventilatory assistance and secretion removal.

There is no clear answer as to whether, and beyond what duration, a totally ventilator-dependent patient is better or more safely ventilated by tracheostomy or NIPPV [35,63,64]. This debate will probably continue and, in the end, the decision to indicate NIPPV or to convert to tracheostomy is highly dependent on the philosophy and capabilities of the clinical team as well as that of the patient and their family environmental preferences. It is essential that discussion of such issues be started as early as possible in the patient's course, well before the imperative arises.

Swallowing dysfunction, which is responsible for frequent and massive aspirations and pneumonia and is observed during the course of ALS (frequent occurrence and is due to bulbar origin) or Duchenne muscular dystrophy (occurs seldomly and is due to muscle weakness), is an imperative indication for tracheostomy to prolong survival, although tracheostomy causes major difficulties for communication and reduces opportunities for personal interactions, leading to a locked-in state [64]. In this context, NIPPV, which may be easily stopped, could be the most reasonable option in cases of rapidly devastating diseases like ALS, and can be considered by both the patient and medical team as a limitation of care or a palliative approach [65]. This was confirmed in a study in which NIPPV in ALS patients with bulbar symptoms do not increase survival longer than controls [27].

Follow-up
Clinical follow-up and daytime ABG measurements (or their surrogates) should be conducted regularly (twice per year, for example). When possible, recordings during sleep when on NIPPV, identical to those taken when initiating NIPPV, are useful. At any time when there are unsatisfactory results, such as recurrence of clinical symptoms or hypoventilation on ABG, inadequate NIPPV must be suspected and objective evaluation during sleep must be undertaken. At the very least, overnight oximetry must be done. When NIPPV is determined to be suboptimal, a change in ventilator modality or setting and a review of the mask fitting may be indicated. Increasing the total duration of NIPPV use per day should also be considered, particularly when the underlying disease has progressed. Masks have to be regularly checked and changed or adapted as needed.

Management of complications
Air leaks during NIPPV
To some degree, leaks are present when using nasal NIPPV during sleep in all patients. The major potential adverse effects of such leaks are reduced efficiency of ventilation and sleep fragmentation [66,67]. A variety of measures, more or less efficacious, have been suggested to address problematic leaks. These include preventing neck flexion, reclining in a semi-recumbent position, discouraging the mouth from opening by use of a chin strap [67] or a cervical collar, switching to pressure-preset mode [59], decreasing the peak inspiratory pressure, increasing the delivered volume [11], optimizing the interface [7,8], and possibly switching to nasal pillows or a full face mask [68]. The effectiveness of these measures must be confirmed during sleep recordings.

Nasal dryness, congestion, and rhinitis
With reference to the CPAP literature, the side effects of nasal dryness, congestion, and rhinitis are related to a defect of humidification promoted by air leaks [69]. For patients with nasal and mouth dryness, a cold passover or a heated humidifier (the latter is more effective) can be used [70]. Heat/moisture exchangers are not well adapted in cases of leaks since the 'dry' flow from the ventilator is higher than the 'dampened' flow returning from the patient. In a large series, a minority of patients needed humidifiers [9].

Aerophagia
Aerophagia, or swallowing air, is frequently reported by patients but is rarely intolerable [71]. Minor clinical signs are eructation, flatulence and abdominal discomfort. Aerophagia is usually dependent on the level of inspiratory pressure and is more commonly seen when using volume and/or mouth-piece ventilation and in the care of patients with neuromuscular disease. The incidence decreases if the peak inspiratory pressure is kept below 25 cmH_2O pressure.

NIPPV effects (other than survival) and related mechanisms
During ventilatory assistance
As expected, when under NIPPV, ventilation and gas exchange are improved in all types of disease [19,72,73], even if significant episodes of transient hypoventilation related to mouth leaks may appear [66,67]. Duration of sleep is augmented without clear changes in its quality [65,74]. Respiratory muscles are normally put at rest but there are many exceptions due to air leaks and patient-ventilator asynchrony [75].

After ventilation
When spontaneous ventilation exists, and in the absence of major lung disease, gas exchange remains improved after NIPPV is stopped. This may persist for hours and even days before reappearance of hypoventilation [76]. The improvement reported in many studies is important in chest-wall and neuromuscular diseases but inconsistent in COPD

[72,77]. Certainly, NIPPV can account for improvements in clinical symptoms such as general well-being, appetite, exercise capability, headaches, ankle edema, and resurgence of acute failure, as well as decreasing hospitalization, increasing quality of life [78] and improving survival.

Three main explanations for these improvements after NIPPV have been proposed: improved respiratory muscle strength, resetting of the chemoreceptors, and decrease of the ventilatory load. The first hypothesis suggests that ventilatory assistance rests the respiratory muscles, thereby reversing fatigue. Indeed, inspiratory force has been found to be significantly augmented in a few studies [30,79]. The second hypothesis suggests that, in response to chronic hypercapnia and hypoxia, the chemoreceptors commanding the respiratory centers change their set point, which perpetuates hypoventilation rather than attempting to generate non-sustainable ventilatory muscle efforts [80]. The resumption of better ventilation during NIPPV would reset the centers to more normal values. The third hypothesis suggests that an improvement in respiratory chest-wall and/or lung compliance, under the effects of positive pressure ventilation, would reduce the ventilatory load and increase the efficiency of the muscles. In the studies done on scoliosis, vital capacity significantly increased [30,79]; however, in other diseases, including neuromuscular patients, the vital capacity remained unchanged. In one study, chest-wall and lung compliance did not change even though there was a nonsignificant trend towards an increase [81]. Furthermore, periodic hyperinsufflation using higher inspiratory pressures for a few minutes in scoliosis [82] and ALS [83] patients revealed an increase in compliance. It seems probable that, even if the mechanisms that explain the efficacy of NIPPV are imperfectly understood, several factors, even if not individually significant, change and interact together to improve alveolar ventilation. The minimum mandatory duration of assistance is not clearly known. However, a relationship between a decrease in $PaCO_2$ and the pressure to ventilate has been found [79]. Finally, one study reports a significant decrease in pulmonary arterial hypertension, which obviously favors clinical improvement [84].

In COPD patients, the absence of clinical results compared to those obtained for scoliosis and neuromuscular disease, even if resetting of the respiratory centers has been shown [85], could be explained by the relatively low impairment of respiratory muscles and the importance of the lesions of the lung itself and its progressiveness.

Conclusions

Chronic ventilatory support using NIPPV improves and stabilizes the clinical course of many patients with chronic ventilatory failure. The results appear to be good in patients with restrictive disorders and poor in COPD. Among the neuromuscular disorders results are better in the slowly progressing ones. The benefit of NIPPV is reflected by improvements in survival, blood gas composition and clinical stability, which help avoid the risk of acute failure and/or ICU admissions. Due to its relative simplicity and its non-invasive nature, NIPPV permits long-term mechanical ventilation to be an acceptable option for patients who otherwise would not have been treated if tracheostomy were the only alternative. In this way, nocturnal NIPPV represents a huge advance.

Competing interests

The authors declare that they have no competing interests.

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