Negative Noninvasive Mechanical Ventilation: External Negative Pressure Ventilation (ENPV)

8

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8.1 Introduction

In patients with acute respiratory failure (ARF), ventilation can be supported during the inspiratory phase either by inflating the airways (intermittent positive pressure ventilation, IPPV), or by external negative pressure ventilation (ENPV), applied around the thorax (and abdomen) by "*body ventilators*." These ventilators include

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the iron lung, portable lung (Portalung), pneumowrap, chest cuirass, pneumobelt, and rocking bed and should be reserved for patients with an intact upper airway.

In respiratory mechanics, the term "negative pressure" refers to the fact that the pressure in certain districts (pleuro-pulmonary) is slightly less positive than the atmospheric pressure although this does not imply that the pressure is always less than zero.

ENPV assists respiration by intermittently applying a sub-atmospheric pressure only around the thorax (when the cuirass is employed), or around both thorax and abdomen when it is performed by poncho or pneumowrap ventilator. It can be delivered also by a whole-body ventilator (i.e., "*iron lung*" or tank ventilator) (IL).

It should be taken into account, however, that ventilators acting externally to the chest can also act during the expiratory phase, hence the so-called biphasic ventilation.

Authoritative authors consider ENPV more physiological than IPPV because it comes closest to physical respiratory mechanics [1].

8.1.1 Operation of External Ventilators (ENPV)

The IL is an electrically powered pressure-controlled ventilator, which does not allow presetting of inspiratory flow or tidal volume, which – as mentioned above – depends on the interaction between the pressure (negative or positive) inside the ventilator and the mechanical properties of the patient's respiratory mechanics. The pressure inside the ventilator was initially provided by a mechanical system (cylinder/piston) and the frequency being regulated by a variator existing between the motor and the piston. This mechanical system was able to generate sine-like pressure waves.

The presence of two discharge valves (acting in the inspiratory and expiratory phases) of the air present inside the tank made it possible to vary said pressure waves, thus modulating the regime of sinusoidal waves both in relation to the pressure and to the time of execution of the inspiration/exhalation, and thus regulating the passage from the inspiratory phase to the expiratory phase. Therefore, this ventilation pattern could be called time-triggered and time-cycled. In more recent years, ventilators acting externally to the chest use air turbines with sufficient flow rates to create high pressures even in an entire chest, as in the so-called IL.

With the latest IL models (©C900 Iron lung. Officine Coppa Biella—Italy) (Fig. 8.1), it is possible to carry out not only controlled ventilation – by setting in-expiratory pressures and times – but also assisted ventilation, by means of two systems: either by a patient-generated negative pressure at the nares that triggers the machine or by patient activation of a thermistor trigger sensitive to T° differences at the nares between the in-expired air that triggers a breath.

This device allows patients to initiate the preset mechanical act according to their needs, considering that the response time of the device is in the order of a few milli-sec.

Fig. 8.1 Iron Lung C900 (®Officine Coppa, Biella, Italy)

The increased interaction between patient and ventilator by assisted ventilation has also facilitated "weaning" from the ventilator (at positive pressure) in the intubated patient [2]. It has been shown that a microprocessor-based iron lung capable of thermistor triggering was able to perform assisted ENPV with a marked reduction in diaphragm effort and a low rate of non-triggering inspiratory effort both in normal individuals and in patients with an acute exacerbation of COPD [3].

8.1.2 Ventilation "Mode"

As to delivered pressures, ENPV can be delivered by four modes: (1) *cyclical negative pressure ventilation*; (2) *negative/positive (or biphasic) pressure ventilation*; (3) *bilevel negative pressure ventilation (Bilevel NPV)*; and (4) *continuous negative pressure ventilation* (CNPV) (Fig. 8.2).

In *cyclical negative pressure ventilation,* negative pressure is applied *in the inspiratory phase only*, with exhalation being entrusted to the elastic return of the lungs ("*lung elastic recoil*") (i.e., *inspiratory Pressure:* iP = −30; *expiratory Pressure:* eP = 0).

With negative/positive pressure ventilation, the ventilator provides negative pressure ventilation in inspiration (i.e., iP = −30) and positive pressure ventilation in expiration (i.e., eP = + 30); the latter increases the lung elastic recoil in the expiratory phase.

With the Bilevel NPV, the ventilator can perform ventilation at two negative pressure levels, one higher in inspiration and one lower in expiration (i.e., iP = −35; eP = −10). In this ventilatory model, exhalation is entrusted to the pulmonary spring-back force.

During CNPV, the negative pressure delivered is of equal value in both inspiratory and expiratory phases (i.e., iP = −10; eP = −10). In this *ventilatory mode*, Insp/Exp acts are entrusted to the activation of the muscular forces (during inspiration

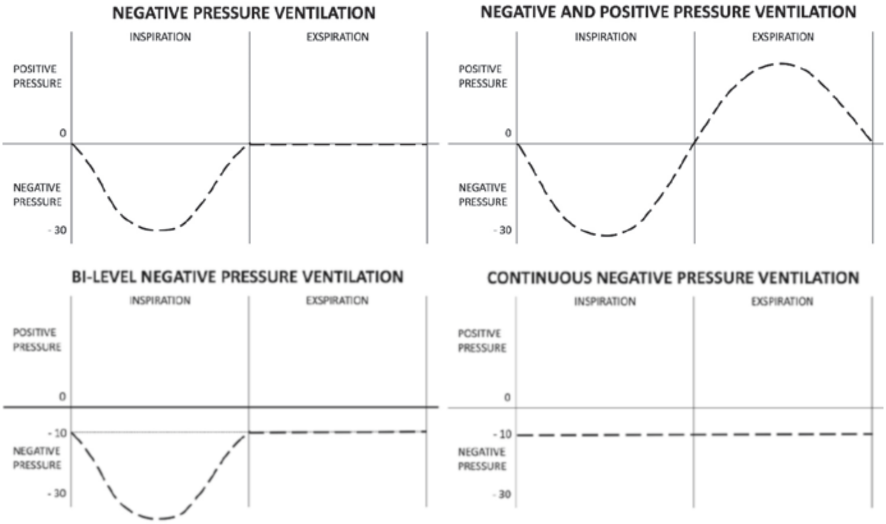

Fig. 8.2 External negative pressure ventilation: ventilation mode *(see text)*

phase) and elastic forces (in expiration phase) of the patient, which can be responsible for minimal oscillations of the pressure wave resulting from the afore-mentioned respiratory movements; in CNPV the continuous negative pressure facilitates inspiration.

As far as the flow is concerned, with ENPV it is ensured by the difference in pressure that is created between the mouth (outside the ventilator) and the alveoli, inside it. This difference in bucco-alveolar pressure is obtained by creating an area of negative peri-thoracic pressure inside the ventilator during the inspiratory phase that generates an increase in trans-pulmonary pressure (TPP) with a consequent entry of ambient air into the patient's airways, thus inflating the lungs, and increases lung volume[1].

Therefore, *in all external ventilators*, a flow of air from the mouth to the alveoli is created during inspiration due to the increase in intrapleural negativity that occurs with each inspiratory act. It follows that any event (foreign body or simple muscle spasm) acting along the mouth/airway pathway will impede flow.

Conversely, *the expiration phase* varies according to the type of ventilator used: with poncho (or pneumowrap) differently than with iron lung (IL) or cuirass.

Indeed, when using poncho or "pneumowrap," the *expiration occurs only passively (or mechanically non-assisted)* because of the elastic recoil of the lungs and

[1] The mechanism rests on Boyle's law, which establishes the relationship between pressure and volume: at a constant temperature, the volume of a given mass of gas is inversely proportional to the pressure. [P x V = constant, i.e., $P = 1/V$]. Therefore, during the application of ENPV, a reduction in peri-thoracic (but internal to the ventilator) pressure – as occurs in the inspiratory phase – corresponds to an increase in lung volume; the reverse occurs in the expiratory phase.

chest wall (as the pressure within the ventilator rises to atmospheric levels) (*cyclical negative pressure ventilation).*

Vice versa by using tank (IL) or shell ventilators (cuirass) the *expiration can occur* both *passively* and *mechanically assisted*, as a result of applying positive pressure to the outside of the chest (*negative/positive pressure ventilation*) (Fig. 8.3).

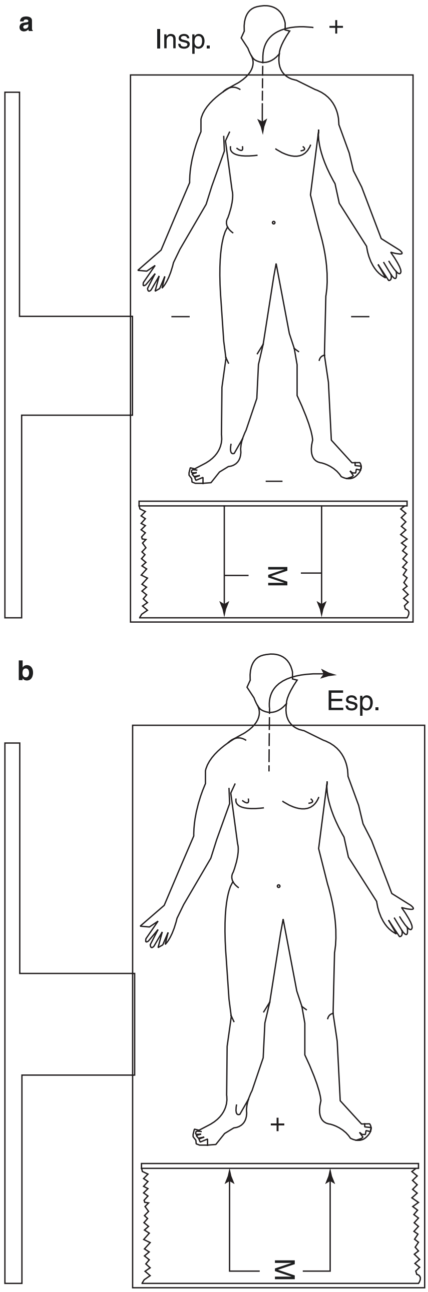

Fig. 8.3 Functional diagram of the "body respirator." The flow is ensured by the pressure difference (ΔP) between the mouth (outside the ventilator) and the alveoli. The pressure variations (ΔP) *inside* the respirator (but *outside* the rib cage) occur thanks to the oscillations of a piston (M); this creates, *at the top*, a negative pressure (–) which assists inspiration (**a**); while *at the bottom*, an area of perithoracic hyper-pressure is created which ensures *expiration* (**b**). *Credits: Del Bufalo C. (1997) Ventilatori agenti per via esterna. In: Del Bufalo C, ed., Intensivologia Respiratoria. Ravenna (Italia): Edizioni Cooperativa Libraria e di Informazione, 1997; 45 (Courtesy of the Author)*

This kind of ventilation mode in patients (pts) with rib-cage (chest wall) disorders increases tidal volume more than cyclical negative pressure alone [4].

Furthermore, a reduction in functional residual capacity (FRC) during the application of continuous positive (extrathoracic) pressure has been described in pts. with moderate airway obstruction [5].

Moreover, while controversial, the application of positive extra-thoracic pressure in expiratory phase in "flow-limited" pts. (chronic obstructive pulmonary disease, COPD) is meant to increase expiratory flow, and the finding in these patients of increased CO_2 concentration in expired air when this kind of ventilation mode is applied might be caused by increased alveolar ventilation [6].

8.1.3 Favorable and Adverse Side Effects of ENPV

The *advantages* include the already mentioned physiological nature of the method, which is preferable when it is necessary to ventilate for a prolonged period of time (sometimes for years) individuals in whom ventilatory autonomy has definitively ceased (like neuromuscular pts.), as well as the finding of an *improvement in hemodynamics* [7]. During ENPV, patient compliance is also reported to be better than the noninvasive positive pressure ventilation (NIPPV), via face mask or helmet [8].

Adverse side effects extend beyond organizational concerns; they also include difficulty of accessing the patient to carry out cardio-respiratory monitoring appropriate to the often very critical condition of patients (pts); this requires skillful ICUs staff trained in handling immobilized pts., as well as in managing arterial and venous lines, chest drains, and urinary catheters. Altogether, such expertise can only be found in a few centers.

Other adverse effects include the finding of a dynamic collapse of upper-airways, such as to determine "flow limitation," as in obstructive sleep apneas syndrome (OSAS), owing to the increased intra-thoracic negative pressure during the inspiratory phase; furthermore this results in the inability to protect the airway and/or high risk of aspiration as well as inability to clear secretions: conditions which altogether require endotracheal intubation (ETI).

8.2 Discussion and Analysis: Main Topic

8.2.1 Why and When ENPV Is to Be Used

ENPV is suitable for patients in need of mechanical ventilation (MV) for ARF who fail to adapt to NIPPV, owing to poor face mask compliance or to abnormal facial morphologies, excessive oropharyngeal secretions, as well as patients who experience anxiety and claustrophobia from a mask or helmet.

8.2.1.1 ENPV in COPD Pts

The role that mechanical ventilation itself plays in COPD exacerbations has long been accepted, both in the reduction of work of breathing (WoB) and in resting respiratory muscles, as shown by the improvement of muscular endurance, defined as muscle ability to carry a load along a given time [9].

In patients with a mild COPD exacerbation (PaO_2 range 49–78 mmHg; $PaCO_2$ range 38–57 mmHg) and chronic respiratory failure, Rochester et al. (*Am J Med 1977*) demonstrated the effectiveness of ENPV – during sleep and for short periods during the day – in WoB reduction and in diaphragm rest [10]; since then mechanical ventilation has been enriched with a further rationale of use.

On the other hand, in a double-blind study on 184 pts. with severe stable COPD treated with ENPV for 12 weeks at home, negative pressure ventilation was found difficult to apply and ineffective when used to let the respiratory muscles rest [11].

Furthermore, ENPV can be applied continuously for a long time although patient familiarization with the ventilator is necessary and improves blood gas exchange both in short [12] and in long-term studies [13]. In short-term studies, ENPV has been shown to improve the respiratory function of COPD pts. with hypercapnic failure and signs of inspiratory muscles dysfunction [14]. The significant fall in $PaCO_2$ is a result both of the increase in alveolar ventilation and in functional reserve of the inspiratory muscles [15] and in resting diaphragm and parasternal muscles [16].

In COPD pts. with acute on chronic respiratory failure (ACRF), ENPV applied by IL is useful in avoiding ETI even when performed on COPD pts. in coma status [17], and can also be considered as effective in avoiding ETI as a conventional approach [18], or as NIPPV [8]. In these pts., other beneficial effects due to ENPV on cardiopulmonary hemodynamics are described [19].

In fact, negative pressure applied to the chest wall increases venous return, thereby improving performance of a right ventricle overloaded by an acute rise in pulmonary artery pressure caused by hypoxic pulmonary vasoconstriction. It may also decrease left ventricular diastolic compliance by displacing the interventricular septum, due to an increase in right ventricular size. It follows that left ventricular ejection is inhibited [19].

On the other hand, in pts. with severe chronic airflow obstruction, a rehabilitation plus ENPV (with pneumowrap) does not result in increased benefit over that achieved by a comprehensive pulmonary rehabilitation program [20].

However, in a recent study of 129 patients with COPD, Hung-Yu Huang et al. (*Medicine, 2016*) showed that long-term (5 years) intermittent application of negative pressure ventilation combined with rehabilitation reduced the decline in lung function, hospitalizations, and healthcare costs [21].

8.2.1.2 ENPV in ARF- Other Than COPD Pts

In etiologies of ACRF other than COPD, such as kyphoscoliosis [22] or neuromuscular respiratory failure [23, 24], ENPV can avoid the need of ETI for the majority of pts.; in these illnesses, NEPV is also effective in weaning pts. from IPPV via ET tube [2].

8.2.2 In ARDS Patients

With some poncho models, it is also possible to maintain continuous negative pressure during CNPV, with physiological effects analogous to those of PEEP (i.e., to keep the pulmonary parenchyma relaxed) and applications in ARDS (*"Adult Respiratory Distress Syndrome"*) as well as in post-transplantation [25].

In the treatment of ARDS pts., the application of CNPV (−20 cm H_2O) increases TPP, thus generating an "*open lung effect*" similar to the one obtained by a PEEP of 15 cm H_2O [26].

Furthermore, CNPV differs from the positive pressure by increasing the venous return and the preload of the heart, and has no negative effects on cardiac performance [26].

As opposed to PEEP, where the increased TPP is associated with increased intrathoracic pressure, CNPV increases TPP by decreasing intrathoracic pressure, rather than by increasing airway pressure. Note that when the negative pressure is applied to the chest and upper abdomen only, as is the case when using a cuirass or a poncho device, the hemodynamic effects of the two approaches (PEEP vs. CNEP) can be expected to be different, due to the different effects on venous return and possibly transmural pressures [27].

Dynamic CT-scan showed that CNPV improved oxygenation compared to continuous positive pressure ventilation (CPPV) in patients with ARDS. This improved oxygenation due to CNPV, compared to CPPV, was not related to better lung perfusion, but to greater lung distension and better alveolar recruitment throughout the ventilatory cycle, as reflected by greater portions of the lung being ventilated and less lung atelectasis [27].

Analogous results have been obtained in pts. with ARDS by comparing 2 h CNPV in IL with 2 h CPPV. Tank pressures were −32.5 cm H_2O (minimum–maximum −30 to −43) at end inspiration and −15 cm H_2O (minimum-maximum −15 to −19 cm H_2O) at end expiration. CNPV improved gas exchange at lower transpulmonary airway and intra-abdominal pressures and, at least initially, improved hemodynamics [28].

In experimental lung injury[2] induced in Yorkshire pigs, continuous negative abdominal pressure ventilation (CNAPV) was applied to the external abdominal wall at constant negative pressure (−5 cm H_2O), to examine the effects on regional lung recruitment, gas exchange, and lung injury [30].

It is important to mention that the vertical gradient of pleural pressure is measured from the anterior to the dorsal part of the thorax in the supine position. In ARDS pts., the pressure gradient is increased; this is due to the greater presence of atelectasis and tissue imbibition in the dorsal part of the thorax. In this case, the poorly ventilated or atelectatic part of the lung is referred to as the "dependent lung," while the part of the lung that can still be ventilated, which is higher up, is

[2] In experimental lung injury, lung lavage is usually applied until the ratio of arterial partial pressure of oxygen (PaO_2) to fraction of inspired oxygen (FiO_2) was <100 for 10 min, at PEEP of 5 cm H_2O [29].

referred to as the "non-dependent lung" [31]. Being reduced in ARDS, the total ventilable lung volume is called "baby lung" [32].

PEEP increases transpulmonary pressure in all lung regions, increasing pressure in the free airways and expanding the thorax non-selectively. This leads to increased pressures in the baby lung with possible damage. CNAPV, on the other hand, lowers pleural pressure in the "dependent" part, but not in the "non-dependent" part, leading to an expansion of the thorax without adversely affecting the well-ventilated part. Thus, CNAPV, in ARDS, reduces the vertical gradient of pleural pressure (i.e., the difference between dependent and non-dependent pleural pressure), improving oxygenation and lung compliance [33–35].

8.2.3 As a Bridge to Lung Transplant

For a select group of patients, ENPV applied by biphasic cuirass ventilator offers a less invasive respiratory support strategy as a bridge to lung transplant. ENPV applies alternate sub-atmospheric (negative) and atmospheric (zero) pressures on a control mode with an initial set of −15 cm H_2O synchronized to the patient's inspiration and +5 cm H_2O synchronized for expiration. Frequency, as well as inspiratory-to-expiratory ratio, was adjusted to synchronize patient efforts around the thorax and the abdomen facilitating airflow into the lung [36, 37]. Moreover, after total cavopulmonary anastomosis the application of negative extrathoracic pressure is described to be associated with large increases in pulmonary blood flow, which suggests that ENPV may be of particular benefit in patients subject to severe right heart overload [38]. In the context of hemodynamics, much is expected from the application of double positive + negative synchronized ventilation, in which two ventilators are applied simultaneously, synchronized with each other, one acting internally (at positive pressure) and one acting externally (at negative pressure). The most relevant effect found, due to the compensation of opposing pressures acting on the thorax, is that, during the entire inspiratory act created by the ventilators, the pressure in the airways and at alveolar level is equal to zero. This is also the case if the pressures delivered by the two machines are added together, i.e., if the transpulmonary pressure is doubled. Compensation of intrathoracic pressures should also allow, although this has not yet been demonstrated, an improvement in venous return, systolic output [39].

8.3 Conclusions and Take Home

- ENPV reduce diaphragm "fatigue" in patients with chronic respiratory failure; therefore, its use is reserved for the weaning from IPPV or the "long-term" treatment of ventilator-dependent patients;
- Its use is limited by difficulties in patient's monitoring, and when in the presence of "flow limitation" (that is in O.S.A.S. and in asthma patients);

- ENPV applications in ARDS and in post-transplantation patients are interesting, especially in terms of reducing side effects in the context of hemodynamics;
- The application of double positive + negative synchronized ventilation seems to be very promising in this respect.

Quiz

[Note: only 1 answer is correct: one in italics].

External ventilation using body ventilators (poncho, cuirasse, iron lung) is indicated:

1. In all forms of respiratory failure, even in hemodynamically unstable patients;
2. In patients with obstructive sleep apnoea or bronchial asthma;
3. *In the treatment of respiratory insufficiency due to COPD in patients who are hemodynamically stable and do not have obstructive sleep apnea or bronchial asthma*.

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