Myths, Prejudices and Real Problems 10

This chapter focuses, in no particular order, on some common place ideas that positively or negatively often limit the use of NIV or, on the other hand, overestimate its therapeutic properties.

10.1 The Side Effects are Negligible

We must clarify immediately that although the side effects of NIV are much less dramatic than those of intubation, they absolutely must not be underestimated because they sometimes determine whether or not the method is tolerated. They can, therefore, automatically become a cause of failed NIV and intubation, which may sometimes be delayed, is consequently more hazardous.

Intolerance to and poor compliance with the interface are real problems during NIV, but can be mitigated by a careful choice of the mask and mode of ventilation, assuming that the patient is cooperative.

Table 10.1 shows that the most serious and most common side effect is nasal lesions, which are superficially dismissed in numerous studies as "nasal reddening." While it is true that this is the only sign present in most patients, it is well known that some individuals develop much more serious lesions that can lead in some cases to total necrosis of the nasal bridge and, consequently, immediate suspension of the ventilation therapy.

There are scales, such as the one shown in Table 10.2, which can be used to monitor pressure sores, similar to those use for major bedsores (e.g., sacral pressure sores), which we should accustom ourselves to using. These lesions are caused by the excessive pressure exerted by the mask in an attempt to prevent air losses: the lack of an adequate circulation below the mask leads first to reddening and then, in some cases, to necrosis. Prevention consists of applying protections, such as those used around abdominal stoma, on the part of the nose in contact with the mask or of trying to minimize the pressure by applying reinforcements to the masks, which should keep the apex of the device lifted away from the skin.

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Table 10.1 Side effects of NIV described in the literature

• Due to the interface	Frequency (%)
- Discomfort	30–50
- Facial erythema	20–30
- Claustrophobia	5–10
- Nasal ulcers	5–10
- Skin rash	5–10
• Due to the flow of air	
- Nasal congestion	20–50
- Sinusitis	10–30
- Dry mouth	10–20
- Ocular irritation	10–20
- Gastric distension	5–10
• Air leaks	80–100
• Severe complications	
- Aspiration pneumonia	<5
- Hypotension	<5
- Pneumothorax	<5

It is very often believed that fixing the interface very tightly to the patient's face will reduce air losses to a minimum. This is not exactly true, given that in one *in vitro* study it was demonstrated that it is the difference between the pressure applied by the cushion surrounding the structure of the mask and the pressure of insufflation of the ventilator, which determines the amount of air loss. Figure 10.1 shows that, according to this study, there is no point in increasing the difference between these two pressures to over 2 cmH_2O, since above this value the loss remains constant and limited, even though the operator obstinately continues to

Table 10.2 Classification of nasal pressure sores. Adapted from the European pressure ulcer advisory panel, guidelines 1998

GRADE 0: absent
GRADE 1: intact skin with or without erythema. Induration of the skin with slight edema are indicators in dark-skinned individuals
GRADE 2: partial thickness skin loss involving epidermis, dermis, or both. The ulcer is superficial and presents clinically as an abrasion or blister
GRADE 3: substantial loss of tissue with damage to or necrosis of subcutaneous tissue that does not involve the muscle fascia
GRADE 4: extensive tissue destruction with necrosis or direct damage to muscle, cartilage, or supporting structures

increase the pressure against the surface of the nose. We should also remember that NIV is by definition a semi-open system so, when using a good ventilator, small losses are tolerated.

After a few hours of ventilation, patients may also complain of rhinorrhea or, contrariwise, excessive dryness of the nose and throat, which requires the use of a humidification system (see later). Pooled secretions may block the nasal passages, which can interfere with the ventilation, but this problem is easily resolved by nasal lavages with water or by using, with caution, ephedrine drops.

Another side effect of NIV is gastric distension which can be particularly annoying when it prevents correct expansion of the abdomen during inspiration or when the patients is not breathing in harmony with the ventilator. However, this side effect is uncommon, even though North American authors highlight this as one of the most frequent problems occurring during NIV. In some cases, it can be circumvented by reducing the pressure of insufflation or the time of pressurization.

There is a risk of hyperventilation, particularly during the night, in neuromuscular patients, in whom the impedance of the system is particularly low and in whom the $PaCO_2$ can drop abruptly, causing acute closure of the glottis to prevent hypocapnia. The mechanism can lead to the onset of episodes of central apnea.

Precisely because patients receiving NIV are rarely sedated, their sleep may be fairly disturbed. One practical tip is to reduce the ventilator's alarms to a minimum and, if the patient is admitted to a subintensive therapy unit, to move him to a traditional ward as soon as his clinical conditions allow.

The side effect of reddened eyes is fairly common, particularly if the insufflation pressures are high; we must remember to take particular care in protecting the eyes when administering nebulized anticholinergics through the NIV circuit, given that phenomena of anisocoria have been observed. As said earlier, all these problems are minor side effects, but can have a substantial influence on the

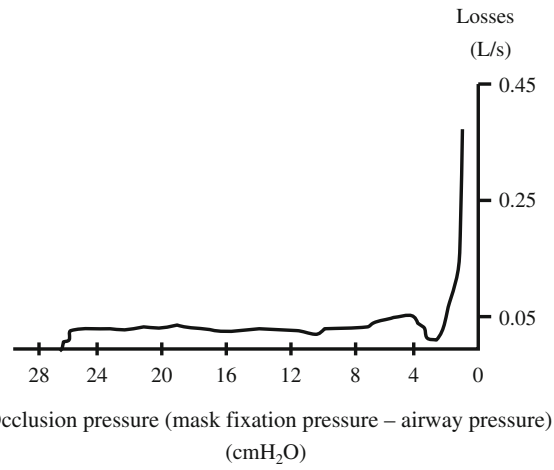

Fig. 10.1 The effect of mask fixation pressure on air leaks. Modified from Schettino et al. (2001)

tolerance to NIV and thereby lead to its failure. This is why the operator must devote great care to minimizing or preventing these problems.

10.2 NIV Does Not Work in Severely Ill Patients

We will deal with the clinical effects of NIV in the specific chapters. Here we will concentrate on the common criticism, raised particularly by our intensive care colleagues, that NIV should be reserved only for less severely ill patients and, therefore, as prevention of intubation rather than as a real alternative. However, 10–15 years ago, it was said that NIV would never enter intensive care, whereas it is now the method used by 50 % of ventilated patients in some countries, such as France.

That said, we do agree with the fact that using NIV in some particularly ill patients, especially if they have acute hypoxic respiratory failure, would definitely be imprudent. For example, it has been demonstrated that sepsis, hemodynamic instability and shock, the presence of ARDS and the lack of improvement in the PaO_2/FiO_2 after <1 h of NIV are inversely correlated with the success of NIV. We should all remember the fundamental concept of medicine, which is "first do no harm," meaning that a brief, judicious trial of NIV can be attempted, but always bearing in mind that the worst problem that we could cause is culpably delaying intubation. One of the key factors for NIV in hypoxic respiratory failure is therefore its early use, when the clinical conditions have still not deteriorated too much. In other words, "the earlier you start, the better are your chances of success".

We must, however, also appreciate that there are conditions, such as exacerbations of COPD and acute pulmonary edema, for which the use of NIV or CPAP is the "first-line" treatment independently of the severity of the patient's clinical condition. It is clear, and we have demonstrated it in the past, that the success of NIV depends on the experience of the team. Indeed, over time, and with a fairly prolonged training period, patients can be treated successfully who would previously have been destined to failure if managed by the same team in the same hospital (Fig. 10.2). In any case, some studies have shown that even in COPD patients with very severe acidosis (pH < 7.22) intubation is not superior to NIV in improving clinical outcome and, indeed, that this latter is associated with fewer side effects and a lesser need for tracheotomy.

10.3 The Work Load Necessary for NIV is Too Onerous

One of the greatest limitations to the generalized use of NIV is the prejudice that this technique is associated with excessive expenditure of human resources. While it is certainly true that one does not become experienced and expert in the field from 1 day to another, it is equally true that after acquiring a bit of theory and

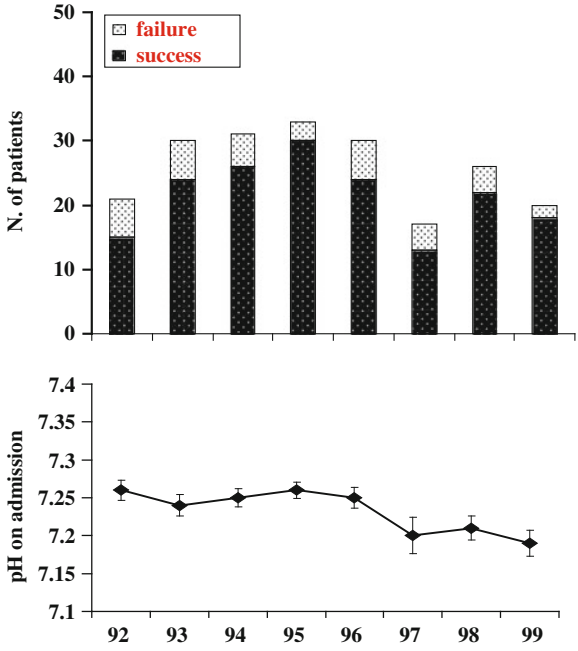

Fig. 10.2 Reduction in the rate of NIV failure over the years, despite increasing severity of respiratory failure. Modified from Carlucci et al. (2003)

practice, using appropriate equipment and being aware of one's own limits, particularly at the beginning, a good NIV service can be established. This is the right place to point out that NIV is never the skill of a single person, but the work of a team whose operative efficacy must always be periodically checked by audits. Let's remember this fact and involve all the members of the team: nurses, physiotherapists, and doctors.

The myth that NIV is onerous in human terms has a very precise origin. In 1991, Chevrolet et al. published one of the most frequently cited papers on NIV in the literature, since it reported the results of the first study designed to determine the human costs of this sort of ventilation therapy. The title itself rings as a warning to anyone who wants to try this technique: "Nasal positive pressure ventilation in patients with acute respiratory failure. Difficult and time-consuming procedure for nurses". The results of this study were surprising given that the authors quantified that the time necessary for the care of COPD patients during NIV was 91 % of the total time of ventilation, whereas this time dropped to 41 % in patients with restrictive airway diseases. The limitations of the study, which were substantial, are well-known: the observational and, therefore, not controlled nature of the study, the small number of patients and, above all, the paucity of the group's training and experience. Indeed, 10 years later, the same authors demonstrated that, with the acquisition of greater confidence and more experience, the previously found unacceptable times and difficulties had been drastically reduced. This is in line with many other studies concordantly stating that while NIV is

indeed more time-consuming than traditional medicine in the first hours of treatment, this effect then disappears, and the patients' clinical outcome is better. The opening of subintensive respiratory care units has certainly helped to overturn the traditional view of the management of ventilated patients, since the medical and paramedical staff in these units are experts in the treatment of both intubated and non invasively ventilated patients.

Since NIV remains not only a method of prevention, but also a real alternative to intubation, it is important to remember that when direct comparisons of human time expenditure for NIV and invasive ventilation are made, the times have been found not to differ greatly. Comparing these two groups of patients, the time of care by the whole hospital staff in the first 24 h was not significantly different between the two groups and remained below 50 % of the total time of ventilation. A detailed analysis of the times, divided according to the type of healthcare professional, showed that the time employed by nurses and rehabilitation therapists decreased significantly after the first 6 h of ventilation, reaching a plateau, whereas the amount of time dedicated to the patient by medical staff remained constant for the first 48 h.

We can, therefore, dismantle the prejudice concerning the difficulties of administering NIV, stating that, at least in specialist environments, this form of ventilation does not seem to affect the time expenditure and workloads of the hospital staff significantly.

Obviously, the management of non invasively ventilated patients is more complicated in hospital wards in which the staff are not familiar with the method of NIV and for this reason it could indeed still be more time-consuming in settings such as intensive care.

10.4 The Helmet is the Interface of Choice

This is the typical statement of some colleagues who have a rather short memory. NIV originated decades ago as a technique that used exclusively nasal or oro-nasal interfaces. The most impressive results from both clinical and scientific points of view were obtained with these masks, such that, to our knowledge, there are no randomized controlled studies on the use of the helmet.

That said, we must all be open to new technology. The helmet has certainly simplified the application of CPAP outside protected environments. Its ease of use avoiding electric sockets, setting the parameters, the irritation of alarms, the good tolerance that patients report when ventilated with this interface and, finally, the low cost due to the possibility of administering a form of NIV without buying a ventilator have made this the interface of choice for the treatment acute pulmonary edema outside hospitals or in unspecialized wards. None of this detracts from the fact that CPAP administered by a helmet can also be used successfully in intensive care.

The huge popularity of this interface during the application of "true" NIV is concentrated particularly in Italy, where it has become the first choice in intensive care. As already specified in the section on interfaces, the helmet is associated with problems of patient-ventilator synchrony (even when particular settings are adopted), difficulty with humidification, and noise but, above all, must be used with extreme care in hypercapnic patients because of the large dead space. Having said this, a helmet can be a valid alternative to face masks in the case that these latter are poorly tolerated, or in the context of rotating different types of interfaces during the daytime hours of ventilation in order to avoid some specific side effects of each of the interfaces.

In our opinion, the helmet is certainly not the interface of first choice and its use in Europe (<10 % of patients ventilated non invasively) shows this.

10.5 It is Better Not to Use an Interface with a Large Dead Space

A large dead space is associated with the concept of a large volume within the interface itself. For this reason, the bulkier masks, such as the total face and the full mask, are often viewed with a certain skepticism. Years ago, we demonstrated that the *in vitro* dead space, that is, the volume measured by filling a mask with water, is not necessarily the same as the *in vitro* dead space, when the mask is applied to a patient's face. The notable difference in dead space found *in vitro* between a nasal mask and a facial mask is not, therefore, present when the measurements are made *in vitro*. Not long ago, Fraticelli et al. (2009) demonstrated that when it came to improving gas exchange, and removal of CO_2 in particular, there was no difference between four interfaces that had considerably different dead spaces, for example, a mouthpiece (dead space of 0 ml) and a total face mask (dead space of 977 ml). However, for the same efficacy, ventilation via a mouthpiece was associated with an increased incidence of asynchrony between the patient and ventilator. One rather particular case is the helmet, which requires a high flow of oxygen to avoid the well-recognized problem of rebreathing. In conclusion, do not be afraid of a dead space effect when using a facial ventilation interface with a large internal volume.

10.6 A Patient Being Non Invasively Ventilated Must Not Be Sedated

The possibility and appropriateness of sedating a patient during NIV is one of the most widely debated problems. Theoretically, NIV should only be applied to subjects who have some minimum residual autonomous respiration and are, therefore, able to trigger the ventilator. Furthermore, one of the presumed advantages of NIV is that of not requiring neuromuscular blockade or profound

sedation. However, in clinical practice, we can find ourselves faced with very anxious and irritable patients who rebel against the interface and often try to remove it. What should we do in these situations? Should we risk further limiting the capacity to breathe spontaneously and end up having to intubate the patient urgently or debunk a little bit the myth that sedatives always and in any case interfere with the respiratory drive? The indications, the preferred drug, and the doses of sedatives to administer are all currently under study.

What is known, however, is that sedation is actually being used in the real world even during NIV. A survey of North Americans and Europeans found that the practice of sedation varied enormously in relation to geography, type of structure in which the NIV was applied and the type of specialist prescribing it. Surprisingly, one of the most widely used methods in North America is that of tying the patients' hands to the bed, a somewhat cruel and ethically debatable practice in our opinion, and fortunately much less used in Europe, except in the most difficult cases.

The most widely used drugs in North America are benzodiazepines alone, followed by opioids (morphine and fentanyl), while exactly the opposite is the case in Europe. Our experience with benzodiazepines has not always been positive since, although there are specific antidotes, side effects (e.g., hemodynamic decompensation) are not uncommon in the elderly and are not always easily neutralized by the antagonists. Haloperidol is also used with a certain frequency, although in intensive care it tends to be reserved particularly for delirious patients taking into account its possible side effects, which may be severe, such a *torsades de pointes*. Dexemetomidine, on the other hand, is rarely used, perhaps because of its high costs, despite being probably the only compound that has been found not to have side effects on the central nervous system even when given for more than 24 h. The use of sedation is almost never based on specific protocols but rather on the physician's experience; the preferred route of administration is extemporaneous boluses. One of the most interesting findings of the survey was that the frequency of use of sedatives and analgesics was proportional to the use of NIV in a given setting, as if more expert staff had fewer qualms about giving drugs. All things considered, the most widely used doses for NIV are within the safe range, since there are no published studies demonstrating a clear effect of benzodiazepines and opioids on respiratory drive at these doses. Our advice is to record the patient's level of sedation using the Ramsey scale (Table 10.3).

Table 10.3 Ramsay sedation score. Modified from Hansen-Flaschen et al. (1994)

1	Patient anxious and agitated
2	Patient cooperative, oriented and calm
3	Patient responsive to commands only
4	Patient responds briskly to glabellar compression
5	Patient responds sluggishly to glabellar compression
6	Patient unresponsive to glabellar compression

Interesting pilot studies can help us to give some clinical advice. In two studies in patients who had failed an initial trial of NIV because of intolerance, it was demonstrated that the use of a new opioid based on anilidopiperidine (rimifentanil) was able to avoid the need for intubation in nine of them (69 %). The starting dose used was 0.025 μg/kg/min, given intravenously, and then the dose was increased up to a maximum of 0.15 μg/kg, until reaching a sedation score between two and three on the Ramsey scale. In three patients in whom the maximum dose was reached, propofol had to be added.

In conclusion, our advice is that "judicious" sedation should not be denied before declaring NIV a total failure in an agitated patient and, therefore, intubating the patient immediately.

10.7 It is (Almost) Impossible to Use NIV in a Comatose Patient

As a joke to disprove this statement, it could be said that it is easier to ventilate comatose patients, particularly if their sensorial dulling is based on hypercapnia, than it is to ventilate to over-agitated patients. If anything, the problems could start later, when the patient wakes up!

An altered sensorium has always been considered an absolute or relative contraindication to NIV in guidelines and state-of-the-art conferences. What do we mean by sensorial dulling? The classical scales used in neurological settings, such as the Glasgow Coma Scale, are of little help in patients with respiratory disorders, whereas the Kelly scale for monitoring the state of consciousness is certainly more appropriate for our patients. This simple instrument, presented in Table 5.2, enables the level of consciousness to be classified with sufficient precision. In most of the studies carried out, only patients with a score of 1 or 2 were ventilated with NIV. A series of case-controlled studies compared the outcomes of patients with COPD and an intact sensorium with those of a group of stuporous patients who could only carry out simple commands after "vigorous" attempts at arousal (grade > 2). The probability of failure of NIV was undoubtedly higher in this latter group of patients, but certainly better than could have been expected and over 50 %. With due caution it is, therefore, advisable not to exclude patients with sensorial dulling *a priori* from a trial with NIV, taking into account that this should only be performed in a protected environment in which intubation can be performed promptly and, in particular, focusing on those patients whose encephalopathy is due to severe hypercapnia.

10.8 Reimbursement for NIV Through the DRG System

More than a myth or a prejudice, reimbursement for NIV through the DRG System is a real problem. But how much does NIV cost? The direct costs are defined as the expenses necessary to evaluate and treat the individual patient and, therefore,

include functional studies and tests (for example, X-rays, blood-gas analyses), the costs of drugs and disposable equipment (for example, masks and tubes), and salaries of the medical and paramedical staff. The cost of the staff per patient is usually derived by multiplying the number of days in hospital by the daily wage for each component of the staff involved in the care of the patient. For example, if the doctor–patient ratio in an intensive respiratory unit is 1:3, the cost for a patient admitted for 10 days is calculated by multiplying the daily wage (gross) of a doctor by 10 and dividing by three. The costs of the disposable equipment used by the staff to treat the patients (masks, gloves, etc.) must then be added to the previously calculated direct costs.

Indirect hospital costs are those costs necessary to cover the institute's services, such as heating, laundry, transport, administrative staff, amortization of equipment (ventilators, monitoring systems), and many others.

A study by Kramer et al. demonstrated that in the 1990s the daily cost of NIV was USA dollars (USD) 1,850, equivalent to about €1,500, for an average period of admission of 20 days, while the daily cost of traditional medical therapy was USD 1,800, equivalent to about €1,450, for an average admission of 18 days (Kramer et al. 1995).

Criner and colleagues designed an *ad hoc* study to analyze costs, although the study did not include a control group. The daily cost of each of the patients treated with NIV was USD 1,570 (about €1,200) for a mean time of 20 days spent in hospital, thus essentially replicating the results obtained by Kramer (Criner et al. 1995).

In the study that we carried out to quantify medical and paramedical activity during NIV and invasive ventilation treatment, we analyzed overall costs using the same scheme as that used in the previously cited North American studies. The costs of the two ventilatory techniques were comparable, although considerably lower than those in the previously cited studies. The daily costs in the first 48 h of NIV were quantified as USD 806, equivalent to about €600, while those for invasive ventilation were USD 865, equivalent to €650 (Nava et al. 1997). Some years later, we calculated that the average daily cost could be reduced if the less severely ill patients (i.e., with a pH $>$ 7.28) were treated in a ward. For example, compared with a daily cost of €558 of non invasively ventilating a patient with an exacerbation of COPD in a subintensive therapy unit, the same method used in a ward cost €470. These costs were calculated in a single structure, in which the medical ward considered was "physically" connected to the subintensive therapy unit (Carlucci et al. 2003).

It is clear that the impact of the diagnostic procedures, the drugs and equipment are similar in absolute terms, in either euros or dollars; what differed significantly was the salary of the staff, whether medical or paramedical.

The DRG reimbursement system is very punitive. Criner et al. calculated the loss due to this system of payment for 27 patients treated acutely in an intensive care unit. The mean time spent in hospital was about 20 days and the financial loss per patient was USD 9,700, with 82 % of the cases being under-reimbursed (Criner et al. 1995). In Italy too, the introduction of the DRG reimburesement

system has clearly favored some practices (e.g., tracheotomy), but penalized others. At this point, if we have given scientific and clinical dignity to NIV as an alternative to invasive ventilation, we must now try to make it considered equivalent also from an economic point of view. It is ventilation in any case, simply with a different interface.

As far as concerns the cost-effectiveness ratio of NIV, there is no longer any doubt that this treatment drastically reduces expenses, at least for the treatment of patients with exacerbations of COPD. For example, Plant et al. demonstrated that about £54,000 could be saved annually by treating 56 patients in this way in a year in typical hospital in the United Kingdom (Plant et al. 2003).

Furthermore, the fact that infectious complications are less common with NIV than with invasive ventilation is another indirect cause of saving. A study published in *Public Health Report* (Klevens et al. 2007) showed that the total cost of a case of ventilator-associated pneumonia is more than USD 100,000 per patient. In the light of this, it was thought in the USA to consider ventilator-associated pneumonia as an avoidable complication and not, therefore, reimbursable by the agency responsible for hospital reimbursements. So here in another good occasion to use NIV, but also to sensitize the people pulling the wires of the national health system to consider a different form of reimbursement.

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