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Palliative noninvasive ventilation in patients with acute respiratory failure

Received: 21 October 2010
Accepted: 16 April 2011
Published online: 9 June 2011
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ESICM 2011

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Abstract Over the last two decades, the increasing use of noninvasive ventilation (NIV) has diminished the need for endotracheal ventilation, thus decreasing the rate of ventilation-induced complications. Thus, NIV has decreased both intubation rates and mortality rates in specific subsets of patients with acute respiratory failure (e.g., patients with hypercapnia, cardiogenic pulmonary edema, immune deficiencies, or post-transplantation acute respiratory failure). NIV is also increasingly used as a palliative strategy when endotracheal ventilation is deemed inappropriate. In this context, palliative NIV can either be administered to offer a chance for survival, or to alleviate the symptoms of respiratory distress in dying patients. The literature provides information from 10 studies published between 1992 and 2006, in which 458 patients received palliative NIV. The technique was feasible, usually well tolerated, and half of the patients survived. The

objectives of this review article are to define palliative NIV, to delineate the place for palliative NIV among overall indications of NIV, and to define the contribution of NIV to the palliative strategies available for patients with acute respiratory failure. Potential benefits and harm from NIV in patients who are not eligible for endotracheal ventilation are discussed. The appropriateness of palliative NIV should be reported in a study that relies on both quantitative criteria (rate of palliative NIV use and mortality) and qualitative criteria (patient comfort, end-of-life process, family burden, and health-care provider satisfaction).

Keywords ARDS and ALI: clinical studies · Critical care organisation · Ethics · Hematologic–oncologic issues in the ICU · Non-invasive ventilation · Pain management

Introduction

The utilization of intensive care has changed over the last two decades. Patients with AIDS and acute respiratory failure (ARF) requiring mechanical ventilation or septic shock, who had mortality rates greater than 75% in the 1990s, now have far lower mortality rates than patients with other conditions such as New York Heart Association (NYHA) III heart failure, cirrhosis of the liver, or cancer [1]. Similarly,

major survival gains have been achieved in patients with hematological malignancies and ARF. Advances in treatments for hematological malignancies [2–4], a systematic clinical approach [5], and noninvasive management strategies [6] have decreased the mortality rate in these patients from nearly 100% [7, 8] to less than 50% [9].

The radical transformation undergone by intensive care over the last half a century has increased survival rates among patients with the most severe conditions (cancer,

transplantation, advanced AIDS, multiple injuries, burns, or major surgery) to the levels achieved in poliomyelitis patients with ARF in the 1950s [10]. Over the last decade, intensivists have been increasingly asked to admit patients experiencing severe but reversible acute events during the last few months of their lives. These patients are often very elderly and have major comorbidities and/or chronic disabilities (with musculoskeletal, respiratory, cardiac, and neurological impairments). The decision to admit a patient to the intensive care unit (ICU) depends on the wishes of the patient—when they are known—and on the medical data supplied by the professionals caring for the patient [11]. Not infrequently, decisions to limit active treatments (e.g., mechanical ventilation, catecholamines, cardiac massage, and dialysis) are taken immediately upon ICU admission to protect patients from useless interventions that contradict their preferences and values and would deprive them from communicating with their families during the very last moments of their lives [12]. Although intensivists are steeped in a culture of survival, they are now striving to prevent unreasonable therapeutic interventions by introducing palliative care into the ICU, in collaboration with health-care teams that regularly provide palliative care (e.g., in internal medicine, geriatrics, neurology, oncology, hematology, pulmonology, and cardiology) [13]. More recently, palliative care has become the standard of care in patients with inaugural malignancies, limiting side effects of undue chemotherapy, and increasing quality of life as well as duration of life [14].

Outside the palliative care setting, NIV has considerably improved the survival of patients with hypercapnic exacerbations of chronic obstructive pulmonary disease (COPD) [15]. This effect is ascribed to decreased use of endotracheal intubation [16, 17], which results in lower rates of ventilator-associated infection [18, 19]. NIV has also been used successfully in many other situations [20–22] including cardiogenic acute pulmonary edema [23], postoperative ARF [24], particularly in solid organ transplant recipients [25], and ARF in patients with immune deficiencies [26, 27]. However, the effects of NIV or continuous positive airway pressure (CPAP) in hypoxemic ARF remain somewhat controversial [28, 29].

Several studies provide evidence that denial of ICU admission is high, especially among older patients and those with chronic respiratory disorders and cancer [11, 30–34]. Implementing palliative NIV in the ICU or in the wards remains a controversial issue. Even though it is regularly performed [35], quantitative and qualitative data are scarce.

ARF and dyspnea are extremely common in patients receiving palliative care

Together with pain, dyspnea is among the most common symptoms in palliative care patients [36, 37]. The

symptomatic treatment of dyspnea related to hypoxemia in a patient with ARF relies on supplemental oxygen [38]. Two situations can be distinguished according to whether the dyspnea is related to a reversible factor (e.g., pulmonary edema, infection, or drug overdose) or is a manifestation of an irreversible process (terminal dyspnea, due for instance to progression of a malignant or neurological disease such as carcinomatous lymphangitis, nerve compression, amyotrophic lateral sclerosis, or other advanced degenerative neuromuscular diseases).

When dyspnea is related to a reversible event, symptomatic treatment is combined with interventions that target the cause (e.g., diuretics, antibiotics, antidotes, or physical therapy). NIV has been evaluated in this situation. Terminal dyspnea, in contrast, is a symptom of the end of life and requires comfort care [38]. Opiates in subanalgesic dosages relieve the subjective sensation of dyspnea without improving ventilation or oxygenation [37, 38]. Anxiolytic agents may be required [39], but this is matter of debate [40, 41]. The use of NIV in patients with terminal dyspnea is controversial. NIV for terminal dyspnea has been described both as an example of futile care and as a tool for improving patient comfort at the end of life.

Palliative NIV in patients for whom endotracheal ventilation is not an option

The appropriateness of palliative NIV in patients with decisions to forego endotracheal mechanical ventilation has been a matter of debate for nearly 15 years (Table 1). The first published study was conducted in France in 30 elderly patients [42]. NIV was successful in 60% of these patients and well tolerated in 75%. All the survivors recovered their previous level of function [42]. A 1994 report describes the results of NIV in 11 patients with ARF during terminal illnesses [43]. Among them, four patients failed to benefit from NIV and died; NIV discontinuation in these four patients was not perceived as traumatic by the patients or families. In addition, palliative NIV relieved the sensation of dyspnea while allowing patients to communicate with their loved ones. Although the authors of this study concluded that NIV improved patient comfort and dignity, the sample size was small and the potential benefits of NIV were not measured rigorously using a questionnaire or a qualitative method. At the same time, palliative NIV was challenged on ethical and economic grounds [44, 45]. In addition to the two above-mentioned studies [42, 43], ten studies evaluated palliative NIV in patients with do-not-intubate decisions. Table 1 lists the main results from these ten studies in 458 patients. Five main conclusions can be drawn: NIV is often offered to patients receiving palliative care; among patients given palliative NIV for ARF related to reversible

Table 1 Studies of palliative NIV (10 studies, 458 patients)

| Authors | Year of publication | N patients | Type of patients | Hospital mortality | Additional results |
|---|---------------------|------------|----------------------------------|-----------------------------------|---|
| Benhamou et al. [42] | 1992 | 30 | Elderly | 12 (40%) | 18 (60%) survivors, all of whom returned to their previous level of respiratory function. Clinical tolerance was poor in 7 (23%) patients |
| Meduri et al. [43] | 1994 | 11 | Unselected | 4 (36.4%) | Removal of the ventilator was not a traumatic experience for the patients or families ($n = 4$). NIV offered comfort and dignity, lessened dyspnea, and allowed verbal communication |
| Chu et al. [57] | 2004 | 37 | COPD | ND | 1-year survival was 30% and 1-year event-free survival was 16% |
| Levy et al. [58] | 2004 | 114 | Mixed (unselected) population | 65 (57%) | Patients with heart failure had significantly better survival rates than patients with other conditions (COPD, cancer, pneumonia). A stronger cough and being awake were associated with increased survival |
| Schettino et al. [59] | 2005 | 131 | Unselected | Mortality ranged from 37.5 to 86% | Advanced cancer was associated with 85% mortality Mortality was less than 40% in COPD or cardiogenic pulmonary edema, 68% in non-COPD hypercapnic ARF, 77% in postextubation ARF, and 86% in hypoxemic ARF |
| Cuomo et al. [60] | 2004 | 23 | Cancer only | 10 (43%) | A higher SAPS II score and a lower PaO ₂ /FiO ₂ were associated with a lower probability of survival |
| Meert et al. [61] Bulow and Thorsager [62] | 2006 2009 | 18 38 | Cancer only COPD or pneumonia | 8 (44.4%) 27 (71%) | 6-month mortality was 84.3%. 10% survived for 5 years or more. Survival was highest in the COPD patients |
| Corral-Gudino et al. [63] | 2010 | 44 | COPD or heart failure | 18 (41%) | 1-year survival was 43.5% Worst outcomes in cancer patients |
| Duchateau et al. [64] | 2010 | 12 | Emergency medical service | ND | All patients improved their respiratory distress. In one, NIV was stopped because of discomfort and deterioration of consciousness |
| Total (10 studies) | 1992–2006 | 458 | Unselected | About 50% | Overall, palliative NIV is feasible, successful in 50 to 70% of patients, and usually well tolerated |

NIV noninvasive ventilation, COPD chronic obstructive pulmonary disease, ND not determined, ARF acute respiratory failure, SAPS II Simplified Acute Physiology Score version II

events, nearly half survive and can return home; survival varies with the underlying condition (being higher in patients with COPD or acute pulmonary edema than in patients with cancer) and with the cause of ARF; survival is lower in patients with a coma at NIV initiation or with an ineffective cough; and patient comfort and family satisfaction, although not specifically measured, are not described as poor.

Interestingly, two practice surveys have evaluated whether palliative NIV is widely used in patients for whom endotracheal ventilation is not an option. In the UK, among 38 physicians specialized in Duchenne's muscular dystrophy, nearly 80% reported discussing palliative NIV with the patients and families, and the same proportion had already used palliative NIV for their patients [46]. The other survey was done in Canada and

the USA in intensivists, pulmonologists, and physical therapists [47]. The vast majority of respondents felt that NIV should be offered to patients with ARF and decisions to forego endotracheal ventilation. Nearly half the respondents perceived palliative NIV as a component of comfort care, and nearly 80% had used palliative NIV in patients with end-stage COPD or heart failure. Palliative NIV was less often used in patients with cancer and in those who had chosen comfort care only (60 and 50%, respectively). Table 2 lists the main advantages and disadvantages of palliative NIV. It is still controversial to consider that the ICU is the best place to offer NIV as a palliative tool or to state that the ICU is a good place to die. Along this line, a very recent paper has shown that cancer patients and their relatives considered that the ICU was a very bad place to die [48]. Studies are needed to

compare palliative NIV in both places, because we know that in real life it is administrated in both the ICU and the wards [49].

Despite this evidence that palliative NIV is widely used, further studies are needed, for several reasons. No accurate data are available on the rate of palliative NIV use in patients for whom endotracheal ventilation is not an option. The impact of palliative NIV has been measured in terms of overall survival but not quality of life. Qualitative assessments via interviews or questionnaires have not been performed, although a qualitative approach is crucial to assess the risk/benefit ratio of palliative NIV. The impact of palliative NIV has been evaluated in patients with a variety of underlying conditions (e.g., heart failure, COPD, and cancer) but has not been measured according to the cause of the respiratory deterioration. Finally, the perceptions of the health-care professionals along the chain of care (nurses and physicians in wards and ICUs) have not been reported. To date, a single qualitative study reported beneficial effects of palliative NIV in patients with amyotrophic lateral sclerosis in the absence of acute events [50]. Promising improvements in quality of life were obtained. However, none of these patients had ARF. Instead, they experienced a gradual deterioration in their respiratory status, and their quality of life and respiratory function were evaluated every 2 months.

Table 2 Possible advantages and disadvantages of palliative NIV in the ICU

| Advantages | Disadvantages |
|--|---|
| Improves survival in some patients | Unreasonable persistence in curative treatment with the generation of false hopes and lack of understanding of side effects (facial necrosis) |
| Can be incorporated into a strategy of continuous care for the patient | Mediocre results, unnecessarily prolongs the dying process |
| Palliation: relieves the subjective sensation of dyspnea | Patient comfort and family satisfaction have not been evaluated |
| Enables the patient to communicate verbally | No study has systematically evaluated the results of palliative NIV along the entire chain of care, using qualitative and quantitative approaches |
| The ICU could be one of the best places for using palliative NIV when indicated (presence of physicians and other health-care professionals). When palliative NIV fails, the 24-h presence of the ICU staff enables the prompt initiation of opiates and anxiolytic agents | High mortality rate. The process for deciding whether to use palliative NIV is complex, possibly suboptimal, and a potential source of confusion, ambiguity, conflict, and burnout not only in the staff, but also in the patients and families |

Position of learned societies regarding NIV use in patients with decisions to forego intubation

Palliative care specialists have expressed concern about the increasing use of palliative NIV [51], and most surveyed physicians request that learned societies issue recommendations about palliative NIV [46]. Physicians worry that patients may perceive palliative NIV as a highly technical, uncomfortable, and aggressive procedure that conflicts with their preferences and values. The term "noninvasive" may not be fully justified. The non-invasiveness of NIV has never been qualitatively established from a patient or proxy perspective. Actually, recommendations have been issued for patients with degenerative neurological diseases in the absence of acute events [52].

According to the consensus statement on NIV for ARF issued in 2001 [American Thoracic Society (ATS), the European Society of Intensive Care Medicine (ESICM), Société de Réanimation de Langue Française (SRLF), the European Respiratory Society (ERS)], palliative NIV is appropriate in selected patients for whom endotracheal ventilation is not an option provided the cause of ARF is reversible and NIV improves patient comfort [53, 54]. Palliative NIV is not discussed in the 2002 recommendations issued by the British Thoracic Society [55]. A European survey coordinated by the ERS indicated that palliative NIV was used in a large proportion (31%) of patients with decisions to limit active treatments [35]. The authors concluded that a qualitative evaluation of palliative NIV was needed. In 2007, a Society for Critical Care Medicine (SCCM) task force suggested an approach for deciding when to offer NIV to patients for whom endotracheal ventilation is not an option [56]. This approach involves a daily evaluation of NIV objectives, which are classified into three categories (Tables 3, 4), among which patients may move from day to day: NIV as life support for patients without treatment-limitation decisions; NIV as life support for patients with do-not-intubate decisions, under the rationale that the adverse effects of NIV (e.g., some degree of patient discomfort, leaks, and alarms) are acceptable given the expected survival benefits; and NIV as a palliative measure in patients receiving comfort care only. The last two categories define palliative NIV. Preserved communication between the patient and family is considered one of the main benefits of NIV. NIV for comfort care is intended to relieve the sensation of dyspnea. In this situation, recovery is not a treatment objective and adverse effects of NIV are consequently unacceptable. This classification scheme can be expected to improve communication among physicians, other health-care professionals, patients, and families. It rests on an ethical scaffold involving clarification of treatment goals, respect for patient preferences and values, and communication with and between the patient and family.

A 2006 consensus statement on NIV in ARF [Société Française d'Anesthésie et de Réanimation (SFAR), Société de Pneumologie de Langue Française (SPLF), and SRLF with contributions from the Association des Anesthésistes Réanimateurs Pédiatriques d'Expression Française (ADARPEF), Groupe Francophone de Réanimationet Urgences Pédiatriques(GFRUP), Services d'Aide Médicale Urgente (SAMU) de France, and Société Française de Médecine d'Urgence (SFMU)] describes the indications for palliative NIV as follows: "NIV can be used in patients who choose to forego endotracheal ventilation or whose prognosis is too poor to warrant endotracheal intubation (Grade 2+). In patients at the end of life, NIV is warranted only when it improves patient comfort." This consensus conference did not specifically recommend the use of a code status such as "Do Not Perform NIV."

Among the important issues not addressed by the current literature, studies are warranted to find answers to the three following points: (1) we do not know whether palliative ventilation increases duration of life or if it extends the dying process. Similarly, objective data are needed to guide the optimal duration of trial of palliative NIV so as to avoid extending non-beneficial care in patients who will inexorably die. (2) Qualitative observational data are also required to list actual benefits from palliative NIV, such as improvement of family experience, patient's well-being, quality of end-of-life care, family satisfaction, global clinician's perspective. (3) Should palliative NIV be performed in incapacitated patients in order to either get a chance of survival (SCCM 2 type) or to alleviate symptoms of respiratory distress?

Description of the OVNI study

OVNI is a longitudinal observational multicenter study performed between November 2010 and April 2011. All patients given NIV were monitored daily until hospital discharge to determine survival, treatment-limitation decisions (if any), and treatment intensity. In the ICUs, patients were classified daily according to SCCM task force criteria (Tables 3, 4) as receiving NIV as life support without treatment-limitation decisions, receiving NIV as life support with do-not-intubate orders, or receiving NIV as comfort care. The last two categories define palliative NIV. The patients and families will be followed up for 1 year, with phone calls on days 90, 180, and 365 to collect data on survival, quality of life, and self-sufficiency. Information will be obtained on family burden (symptoms of anxiety, depression, and stress). The nurses, intensivists, and referring physicians will be asked about their satisfaction with treatment-limitation decisions and with the results of palliative NIV. This study should provide qualitative and quantitative information on the results of NIV at the end-of-life.

Conclusion

Palliative NIV is regularly performed in the ICU as well as in the medical wards or the emergency department. The technique is perceived as feasible and provides survival benefits in hypercapnic patients and those with cardiac pulmonary edema. In cancer patients, benefit seems dismal. Current recommendations from

Table 3 Classification of situations for NIV use established by the SCCM (from [56])

| Primary goals of care | Determination of success | Response to failure | What is said to the family |
|--|---|--|---|
| Category 1: life support without preset limits | | | |
| Assist ventilation and/or oxygenation | Improved oxygenation and/or ventilation | Intubation and mechanical ventilation | Goals are to restore health and use intubation if necessary and indicated |
| Alleviate dyspnea | | | |
| Achieve comfort | | | |
| Reduce risk of intubation | | | |
| Reduce risk of mortality | | | |
| Avoidance of intubation | | | |
| Category 2: life support with preset limit (do not intubate) | | | |
| Includes same as category 1 except intubation declined | Improved oxygenation and/or ventilation | Change to comfort measures only and palliate symptoms without NPPV | Goal is to restore health without using endotracheal intubation and without causing unacceptable discomfort |
| Also could include briefly prolonging life for a specific purpose (e.g., arrival of family member) | Tolerance of NPPV or minor discomfort that is outweighed by potential benefit | | |
| Category 3: comfort measures only | | | |
| Palliation of symptoms (relief of dyspnea) | Improved symptoms Tolerance of NPPV | Palliate symptoms without NPPV | Goal is to maximize comfort while minimizing adverse effects of opiates |

NPPV noninvasive positive pressure ventilation

Table 4 Data on situations for NIV use as established by the SCCM [56]

| Approach definition | Category 1: life support without preset limits | Category 2: life support with preset limit (do not intubate) | Category 3: comfort measures only |
|--|--|--|-----------------------------------|
| Acute exacerbation of COPD | Multiple randomized trials and several meta-analyses showing benefit | Observational studies suggesting benefit | No data supporting use |
| Hypoxic respiratory failure in immunocompromised patient | Several randomized trials and one meta-analysis showing benefit | Observational studies suggesting benefit | No data supporting use |
| Acute respiratory failure with cardiogenic pulmonary edema | Two randomized trials and one meta-analysis suggesting benefit | Observational studies suggesting benefit | No data supporting use |
| Neuromuscular diseases | Two small uncontrolled observational studies suggesting possible benefit | No data supporting use in acute setting | No data supporting use |

teaching societies recognize the use of palliative NIV. However, no qualitative data are available to date. For instance, studies are needed to identify actual benefits from palliative NIV that are not related to survival. In patients who survive, quality of life data may convince clinicians that palliative NIV actually extends duration of life and does not merely extend the dying process. In patients who die, studies reporting quality of dying and

death for patients and post-ICU burden in relatives (e.g., complicated grief, post-traumatic stress disorder, anxiety, and depression) are warranted. Further recommendations should help to increase the use of palliative NIV in patients who may benefit, but also highlight those patients in whom the technique provides no survival and no qualitative benefits.

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