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Palliative Use of Noninvasive Ventilation: Navigating Murky Waters

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Abstract

Background: The use of noninvasive positive pressure ventilation (NPPV) as a palliative treatment for respiratory failure and dyspnea has become increasingly common. NPPV has a well-established, evidence-based role in the management of respiratory failure due to acute exacerbations of congestive heart failure and chronic obstructive pulmonary disease, both for patients with and without restrictions on endotracheal intubation. There are emerging uses of NPPV in patients clearly nearing the end-of-life, but the evidence to support these applications is limited. Alongside these emerging applications of NPPV are new ethical dilemmas that should be considered in medical decision-making regarding these therapies.

Discussion: Herein, we describe the use of NPPV in four patients with advanced disease and preexisting treatment-limiting directives. We discuss some of the ethical dilemmas and unintended consequences that may accompany the use of NPPV in such circumstances, and we review the benefits and burdens of palliative NPPV.

Conclusion: Finally, we conclude with a summary of principles that can be used as a guide to decision making regarding palliative NPPV.

Introduction

Dyspnea is a common and often distressing symptom faced by patients near the end of life.[1] Palliative treatment of dyspnea and symptoms of respiratory failure has traditionally focused on the provision of opiates, benzodiazepines, and supplemental oxygen in addition to traditional disease-directed therapies. Current evidence supports the use of opioids as the cornerstone of dyspnea treatment in palliative settings.[2] Oxygen is also a commonly used modality to treat dyspnea, especially in the case of hypoxemic respiratory failure, although it may also be considered life-sustaining when hypoxic respiratory failure is the primary threat to life.[3] Noninvasive positive pressure ventilation (NPPV) has emerged as an additional, although controversial, tool in the management of impending respiratory failure and dyspnea near the end of life. NPPV has a well-established role in the management of respiratory failure due to acute exacerbations of congestive heart failure, chronic obstructive pulmonary disease, and hypoxic respiratory failure in immunocompromised patients.[4] The use of NPPV for patients with do-not-intubate directives and potentially reversible etiologies of respiratory failure is also increasingly common. Additionally, there are circumstances when NPPV may be used in patients who are clearly nearing the end-of-life, either to try to better palliate unrelieved dyspnea or to ''buy time'' until family arrives. The role of NPPV in these later two settings is controversial, and its boundaries have not been established.[4]

To further delineate these boundaries, we describe the potential use of NPPV in four patients, altered to protect anonymity, with very advanced disease, preexisting treatment limiting directives, and differing potential prognostic trajectories. We then discuss the benefits and pitfalls of NPPV and the downstream decisions that may need to be made when NPPV is initiated in patients with expressed wishes to limit some or all other potential life-sustaining therapies. After a discussion, we offer a brief exploration of some of the benefits and burdens of palliative NPPV and conclude with a summary of principles that ought to guide decision making regarding the use of NPPV therapy in this setting.

Case 1: A Time-Limited Trial with Clear End Points for a Patient with DNR/DNI Orders and Potentially Reversible Pulmonary Exacerbation

A 65-year-old male with severe chronic obstructive pulmonary disease (COPD; FEV_1 25% predicted) presents to the

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emergency department with 2 days of increasing dyspnea, productive cough, and fever. He had previously established do-not-intubate (DNI) and do-not-resuscitate (DNR) directives. His baseline quality of life is acceptable to him and he is willing to accept a trial of aggressive treatment, including admission to an intensive care unit (ICU), if there is a significant chance his condition may be reversible. He confirms that he would not permit intubation, even as a trial. After discussion with the patient and his wife, a time-limited trial of 48 hours of NPPV, antibiotics, and corticosteroids is agreed to, after which the goals of care will be revisited. He is admitted to the ICU where his condition rapidly improves and he is weaned from NPPV and discharged home after a 5-day hospitalization.

This relatively straightforward case illustrates the use of NPPV as part of the treatment of a potentially reversible, acute decompensation of a chronic disease in a patient with a preexisting DNR/DNI directive. NPPV is used as a bridge to support ventilatory failure while disease-directed therapy is given a chance to work. Based on the patients expressed goals and values, there is no plan to escalate treatment with regard to intubation and mechanical ventilation if the condition worsens, and the use of NPPV will be regularly reevaluated to see if it is still contributing to the patient's goals. There is a growing literature to support the use of NPPV in such cases.[5–8] In similar circumstances, NPPV would be considered the first line of therapy for patients with no limits on resuscitation if it was likely to help the patient safely avoid being intubated.[4] Of course, some patients may not improve with NPPV (or may not tolerate it), and they then would have to revisit the decision to be DNI or transition to a more ''comfort-oriented'' approach with an escalation of opioids and other adjunctive therapies such as benzodiazepines to treat refractory dyspnea. In this case, NPPV is used as a time-limited trial (TLT)[9] with clear markers of and timelines for improvement or discontinuation. Importantly, the ICU team clearly outlined a time interval for the trial to be reevaluated, and a plan was agreed to with the patient and family for how a ''failed'' trial would be managed. We think most intensivists and palliative care specialists would agree that this is a good, noncontroversial application of and outcome from NPPV in a patient with preexisting treatment limiting decisions.

Case 2: Challenges of Using NPPV with a Patient with DNR/DNI Orders but without Other Clear End Points

A 71-year-old female with idiopathic pulmonary fibrosis (IPF), not eligible for lung transplantation, presents to the emergency department with acute worsening of dyspnea. At baseline, she is on 4 liters of oxygen at all times and 6–8 liters with any exertion. A computed tomography (CT) of the chest performed in the emergency department shows progression of the patients underlying pulmonary fibrosis with emergence of ground glass opacities, suggestive of infection, volume overload, hemorrhage, or acute exacerbation of IPF. The patient has preexisting DNR and DNI orders, and she is started on NPPV for management of dyspnea and hypoxemic respiratory failure. At the time of initiation of NPPV, potential end points of therapy or a formal TLT are not discussed with the patient and her family. Her physicians decide against performing bronchoscopy and instead cast a wide net of therapy including broad-spectrum antibiotics, diuretics, and steroids. After 4 days of therapy, she shows little clinical improvement. She is able to come off NPPV for short periods of time, but only to high flow nasal cannula (HFNC) with flow rates of 25–30 L/min and 80% FIO_2. She is relatively comfortable on the NPPV and HFNC and is transferred from the ICU to the inpatient palliative care unit with plans to maintain current treatments and not further escalate them, and with hope that she might stabilize and be able to reduce and even eliminate the NPPV or HFNC in the near future.

After 2 weeks on the inpatient palliative care unit, the patient is unable to tolerate even short intervals off NPPV or HFNC. Despite previously expressed wishes not to die in a hospital, the team is unable to arrange a viable way for her to get home because of the high levels of oxygen required both via NPPV and HFNC. Although the patient is awake and comfortable on NPPV, she understands that her underlying disease is chronic and progressive and, as a result, she is unlikely to be able to improve to a point where she could breathe on her own without NPPV. She expresses a clear and consistent wish to discontinue NPPV with an understanding that this discontinuation will almost certainly precipitate her death. After a long discussion between patient, family, and the palliative care team, a decision is made to discontinue the NPPV, which all agree is ethically and legally permissible. Therapy with opiates and benzodiazepines is initiated and adjusted to minimize her dyspnea and anxiety, and she dies 40 minutes after discontinuation of NPPV and oxygen therapy.

In this case, a patient with a progressive and fatal disease and an established DNI order is treated with NPPV in the hopes of finding a reversible cause of acute respiratory failure. Although NPPV is typically used for ventilatory failure, there is a small evidence base to suggest a role in the treatment of hypoxemic respiratory failure.[10] When she does not respond to targeted therapies, she remains on NPPV and is unable to be weaned due to progressive worsening of her IPF. Because the patient was highly symptomatic at the time NPPV is initiated, and because death was the likely alternative, a fully informed discussion about the boundaries of the intervention from the outset was not initiated. In such cases, the potential end points of a TLT of NPPV are: (1) clinical improvement (hoped for, but often unlikely); (2) clinical worsening and subsequent withdrawal of treatment and death; (3) stabilization on NPPV but inability to live without it followed by a decision to discontinue NPPV with aggressive palliation of terminal dyspnea, or (4) stabilization on NPPV and deciding to extend the therapy as long as possible. We recommend that prolonged NPPV not be offered or endorsed by physicians. However, when a TLT is not explicitly discussed in advance, the likelihood of this fourth endpoint is increased.

Case 3: Postponing Death a Short Time to Allow Additional Time to "Say Goodbye"

A 65-year-old female with widely metastatic small cell lung cancer is hospitalized on the oncology unit for worsening hypoxemia and dyspnea. Her cancer has been unresponsive to treatment, and she has an advance directive declining endotracheal intubation or cardiopulmonary resuscitation (CPR). One evening, she becomes increasingly hypoxemic with significantly increased work of breathing.

She and her family understand and accept that she is dying, but she has a daughter who is flying in from out of town. Her care team decides to offer her a time-limited trial of NPPV in addition to modest increases in her opiate therapy in an attempt to allow the patient a small amount of added time to see and ''say goodbye'' to her daughter. The patient survives until the arrival of her daughter, but she is largely unresponsive and the daughter is upset to find her mother on ''life support, which she never wanted.'' A family meeting is quickly arranged where the family feels guilty and conflicted on two accounts: (1) that they consented to put her on the NPPV, which initially seemed like a good idea but in retrospect seems invasive and ineffective and (2) that they are now being asked to ''pull the plug'' in determining when NPPV should be discontinued. The medical team recommends discontinuing the NPPV, which all agree is ethically permissible, and that the patient would not want continued under these circumstances if she could speak for herself. She dies within 10 minutes of discontinuation. The family is unsettled and angry about the entire process.

This case shows how the well-intended use of NPPV to medically micro-manage the last stages of the dying process may backfire. Unless the potential benefits of NPPV in a particular case or circumstance are clear, its very real burdens (precluding eating, difficult communication, need for concomitant symptom management, and the complexity of subsequent decision making) should make clinicians cautious about routinely offering it.

Case 4: NPPV as a Temporizing Palliative Measure to Help Relieve Refractory Terminal Dyspnea

A 47-year-old man with bronchogenic adenocarcinoma with lymphangitic spread that is unresponsive to oncologic treatment is receiving home hospice. He has had refractory pain and dyspnea, and has been on very high doses of subcutaneous opioids with several opioid rotations in the last few weeks to try to better manage his symptoms. Despite rapid dose increases over the last several days and the addition of benzodiazepines, he remains extremely short of breath, and is admitted to an acute palliative care unit for better management of his symptoms. The patient was in extreme respiratory distress, rating his dyspnea and anxiety as 10/10. The palliative care team ordered rapid increases in both the opioids and the benzodiazepines, and the question arose about whether NPPV would provide some temporary relief while they were getting his symptoms under control. The patient was desperate and willing to ''try anything'' to help relieve his suffering. In fact, the NPPV did seem to symptomatically help him in the short run while his palliative medications were adjusted. Propofol was eventually added to his regimen for palliative sedation in addition to the very high doses of opioids and benzodiazepines, and the patient finally appeared more comfortable. The NPPV was then gradually withdrawn, as was his oxygen, and the patient died within 90 minutes.

This case illustrates the potential short term use of NPPV to palliate severe refractory dyspnea in an actively dying patient who was not responding well to usual palliative treatments with opioids and benzodiazepines. In this case, the patient was physiologically tolerant to the usual symptomatic treatments, and was having a crescendo of symptoms that were not responding to a rapid escalation in dosage. NPPV was offered as a temporizing measure to help control symptoms until more effective palliation had been achieved. There was no guarantee that he would tolerate NPPV, or that it would provide symptom relief, but it was tried as a TLT to see if it would help relieve his respiratory distress until adequate palliation could be achieved by other means. In this case, NPPV was tolerated and seemed to help until propofol as palliative sedation was added and the patient appeared much more comfortable. At that point the NPPV was withdrawn without an escalation of symptoms, and the patient died relatively quickly and peacefully.

Discussion

Palliative NPPV encompasses a range of applications, from symptom-based intervention alongside disease-directed treatment to purely palliative treatment delivered at the end of life.[4] Ideally, decisions about all potentially life-sustaining therapies, from endotracheal intubation and CPR to oxygen and NPPV would be carefully considered in the outpatient setting for patients in whom death due to respiratory failure can be anticipated. In patients who decline intubation but are willing to accept NPPV, its status as a potential life-sustaining therapy should be presented as a ''time-limited trial'' with clear end points rather than an end in itself.[9] Anecdotally, NPPV is increasingly being used as a ''last resort'' option in patients dying of respiratory failure,[11] which may frequently have unintended consequences. In patients who can be anticipated to decline as a result of respiratory failure (i.e., those with advanced bronchogenic carcinoma, IPF not eligible for transplantation, and end-stage COPD), the introduction of NPPV as a potentially short-term intervention should be discussed in the outpatient setting but should not be routinely offered to such patients.

However, the realities of outpatient medicine as well as the dynamic nature of chronic illness, prognostic uncertainty and the human desire to avoid such discussions often preclude this ideal. The lack of preparation for decisions surrounding NPPV is further complicated by the fact that these decisions often must be made when a patient is experiencing significant respiratory distress. Even when the option has been discussed in general terms when the patient was stable, it is not uncommon for patients to change their minds in favor of more aggressive interventions during an acute exacerbation when the possibility of death from respiratory failure is looming. To further complicate matters, NPPV may be initiated by EMS or in the emergency department without time for discussion and informed choice A summary of the potential benefits and burdens of NPPV as a palliative measure are presented in Table 1. The clearest benefit of NPPV is in patients with a potentially reversible cause of acute-on-chronic respiratory failure as illustrated the first case above. A recent randomized feasibility trial by Nava and colleagues[12] suggests that NPPV may also be of benefit in patients with advanced solid organ malignancies for treatment of dyspnea. They found that oncology patients randomized to receive NPPV had improved dyspnea scores despite lower doses of narcotics compared to patients who received opiates and oxygen alone. This benefit was most pronounced for patients with hypercapnic respiratory failure. In such cases, lower doses of opiates may allow patients to be more awake and interactive while they are receiving treatment for any

Table 1. Benefits and Burdens of NPPV as a Palliative Intervention

Benefits	*Burdens*
Treatment of potentially reversible respiratory illness without intubation and mechanical ventilation in patients who are ''full code'' as well as those who are DNR/DNI	Potential to medically prolong the dying process
May postpone death a small amount to allow the patient to achieve some short-term goals	May be uncomfortable in itself, and adding to suffering rather than alleviating it
When combined with opiates, may improve dyspnea compared to oxygen and opiates	Added burden of decision making for patients and families, including potentially having to withdraw life prolonging therapy
Provide temporary relief of dyspnea while other palliative treatments are being initiated	Introduction of technology at the end of life may prevent communication and intimacy at the end of life

NPPV, noninvasive positive pressure ventilation; DNR/DNI, do-not-rescuscitate/do-not-intubate.

potentially reversible aspects of their disease. One of the challenges of allowing this ''option'' is uncertainty about how to proceed if the patient is not improving. If clear end points are not established upfront, as illustrated in case 2, then there is risk of the patient being indefinitely sustained with NPPV with no prospect of getting off and no agreement with regard to the parameters for discontinuation. The patient and/or family then have to make another major decision about stopping life support, with all of its emotional and clinical challenges.

Case 3 similarly illustrates a patient hoping to prolong her life a small amount to ''say goodbye'' to an out-of-town family member only to have her not be alert enough to interact with the family member. Because the patient is no longer capable of making medical decisions, the family now has the burden of consenting to stopping a treatment that is almost immediately associated with the patient's death. Case 4 illustrates using NPPV as a purely palliative measure at the very end of life to help relieve refractory dyspnea while the clinicians were trying to find effective palliative treatment alternatives in a patient very tolerant to opioids and benzodiazepines.

While palliative NPPV may have some utility in patients truly at the end stage of disease, it also has the potential to further medicalize death and have the dying process be even more dominated by technology, machines, and medical decision-making. The mask interface may be uncomfortable and often creates a barrier to communication and intimacy between patients and loved ones. Initiation of NPPV near the end-of-life creates a therapy that will likely be withdrawn prior to death, thus adding decisional burden to families and surrogates for marginal benefit. Although ethically equivalent, not starting a therapy is often psychologically easier on patients, families and medical staff than discontinuing it,[13–16] and even offering such a near futile treatment toward the very end of life may shift focus away from the appropriate and necessary sadness of ''saying good-bye'' to a further emphasis on medical decision making and intervening. In many cases, psychosocial costs of NPPV at the end-of-life may outweigh marginal benefit without even considering unfavorable economic cost-benefit analysis.

In general, we feel that NPPV may have a role in selected cases as part of a TLT to give potentially effective treatments (antibiotics, diuretics, steroids) a chance to work in patients with preexisting DNR/DNI directives, especially when clear parameters of the trial working or not are spelled out upfront. The introduction of technology such as NPPV should generally be avoided at the very end of life when a patient is actively dying unless it is a potential bridge to short-term goals such as achieving more effective symptom management. NPPV has considerable burdens in that it may cause patient discomfort, typically precludes eating, and makes verbal communication challenging. Upfront communication with patient and surrogates is of paramount importance. When NPPV is being considered as a means of treating unrelieved dyspnea, physicians should first consider whether opiates, anxiolytics, and oxygen are adequately dosed.

Principles of the Use of Palliative NPPV

In conclusion, we offer several principles to guide clinicians as they consider the role of palliative NPPV. First, clarify among the treating teams whether NPPV is potentially indicated for the particular patient under their clinical and psychosocial circumstances. Before burdening patients and families with yet another major medical decision, clarify the real odds of NPPV being temporary, and/or that the desired objectives are achievable. Second, if the decision to offer NPPV is made, clearly describe the objectives of therapy as well as its potential burdens. Include the best estimate of the intervention achieving the desired effects as well as the odds of it not achieving them.[17] Given what is known medically about the patient's condition and their values, try to make a recommendation based on your best medical judgment.[18] Third, if NPPV is being seriously considered, consider framing it in terms of a ''time limited trial (TLT)'' from the outset with clear timeframes and markers of success or failure.[9] The TLT frame would have been appropriate in each of the cases discussed above. Fourth, when palliative NPPV is used, ensure that pharmacologic treatment of dyspnea and anxiety is maximized both during the course of therapy and if/when therapy is withdrawn.[15] NPPV should not be used to palliate dyspnea because opiates and/or benzodiazepines are underdosed.

With these caveats, a TLT of NPPV may be appropriate with well-defined, patient- and family-centered, short-term goals. Future research is needed to investigate the impact of palliative NPPV on patients and surrogates, and also to better understand provider motivations for offering (or not offering) this therapy.

Author Disclosure Statement

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