



High flow nasal therapy in the management of hypoxemic dyspnea at the end of life

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Abstract

Refractory dyspnea is challenging for physicians treating patients near to the end of life. High-flow nasal therapy (HFNT). We report a case in which HFNS was effective in a patient in the last days of life to mitigate dyspnea allowing a minimal quality of life for some days before dying. HFNT may be helpful for severely hypoxemic patients who are unresponsive to common measures adopted in the last weeks–days of life of advanced cancer patients. Future studies should assess an early use of this device in combination with lower doses of opioids or as an alternative.

Keywords Dyspnea · Opioids · Non-invasive ventilation · High-flow nasal therapy · End of life · Advanced cancer

Introduction

Dyspnea is highly prevalent in advanced cancer patients in the last weeks of life [1–3]. It was the most frequent reason for hospital admission on emergency [4], and for hospital admission followed by death [5]. Moreover it was one of the most frequent clinical issues in the last 2 h of life [6], and the most frequent indication for palliative sedation [7].

The main pharmacological option for the management of dyspnea in the last weeks/days of life is the use of opioids. Supplemental oxygen may be considered in hypoxemic patients [1]. However, many patients experience severe dyspnea despite these interventions. High-flow nasal therapy (HFNT) may be considered as an alternative. HFNT is a device that delivers high flows of fully humidified inspired gas driven by a turbine up to 60 L/min, by dedicated nasal prongs. In comparison with other non-invasive ventilation methods, HFNT is less traumatic for the skin, offers less burden for the caregiver, and allows to speak, actively cough, and eat. The mechanisms of action of HFNT include enhanced oxygen pharyngeal concentration, lung mucociliary clearance and humidification, and reduced metabolic

expenditure of gas conditioning, thus impacting carbon dioxide production and attenuation of the inspiratory resistances by splinting nasopharyngeal boundaries. Differently from traditional continuous positive airway pressure (CPAP), HFNT may increase expiratory resistance, by a jet-flow effect, provide a washout of nasopharyngeal dead space, and decrease the inspiratory resistances, leading to an amelioration of dyspnea by reducing the work of breathing due less need for increasing alveolar ventilation [8]. We report a case of a patient with dyspnea poorly responsive to intravenous morphine and oxygen delivered by mask, who was managed by HFNT. Data is reported according to CARE checklist.

A patient, male, over 70 years old, with a history of advanced sarcoma treated with various surgeries and radiotherapy, recently received chemotherapy with doxorubicine 50 mg/mq. He was referred to the main regional center for pain relief and supportive/palliative care (acute unit) for shoulder pain, dyspnea, and progressive general worsening of the clinical conditions. He was previously referred by his home palliative care physician to a local hospital. Due to the poor clinical condition with refractory symptoms, the bed manager asked to admit the patient to our unit.

On admission, the patient was dyspnoic and was receiving oxygen by mask (12 L/min). He was bedridden for weeks and had fever. On ESAS (Edmonton System Assessment Score), the symptoms with higher intensity were pain (6/10), dyspnea (7/10), poor appetite (10/10), and weakness (8/10). He receiving tramadol 200 mg daily and carbamazepine 1200 mg/day. A CT scan showed a large axillary,

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supraclavicular, and retroclavicular mass infiltrating the thoracic wall and the superior lung lobe, and submassive embolism of pulmonary arteries. After a bolus of intravenous morphine titrated up to 8 mg, an intravenous infusion of 30 mg/day was started. The pharmacologic treatment also included carbamazepine 1200 mg/day, fondaparinux 7.5 mg/day, dexamethasone 6 mg/day, furosemide 20 mg/day, ketorolac 60 mg/day, meropenem 3 g/day, haloperidol 2 mg, oxygen therapy 8–10 L/min, and hydration 1200 mL/day. Pain and dyspnea intensity initially came down with increased doses of intravenous morphine up to 60 mg/day, but they worsened again the week after (pain 5/10, dyspnea 8/10), also requiring 7–8 breakthrough boluses/day of intravenous morphine (8 mg) to reduce the peaks of pain and dyspnea intensity. Relatives were informed about the clinical deterioration and the short life expectancy of the patient. Unable to discharge the patient in such conditions, and due to the locations of the patient's home, the team came up with possible alternatives. Due to COVID-19 pandemic, a virtual family meeting was planned. The best shared option was to transfer the patient to the adjacent hospice for end of life care, where relatives could be allowed in the room.

On hospice admission, doses of corticosteroids were increased (dexamethasone 12 mg/day) and oxygen saturation was > 90%. In the subsequent days, however, there was a progressive oxygen desaturation, ranging 83–88%, and dyspnea increased in intensity, despite oxygen delivered at 12 L/min, the increased doses of morphine up to 120 mg/day, and several intravenous morphine boluses as breakthrough medication. HFNT was started. The machine was set at 40 L/min and 60% of oxygen. Oxygen saturation and dyspnea improved significantly (92%, dyspnea on ESAS 3/10). The patient was able to talk on WhatsApp with relatives, eat, and chat with the team. Midazolam was added during night hours to facilitate the sleep. We tried to wean him from HFNT to oxygen therapy by mask, but this was unsuccessful, as dyspnea and oxygen saturation worsened in a few minutes (SO₂ 84%). The restoration of HFNT was immediately effective and the patient had to keep it on as he felt that he was highly dependent on it in order to enjoy the little things that he could still do. Three days after he becomes agitated, palliative sedation with midazolam infusion 30 mg/day was started. He died 24 h after.

Discussion

Refractory dyspnea is challenging for physicians treating patients near to the end of life [1, 2]. This case shows that HFNT can improve oxygen saturation and dyspnea in a very compromised patient, albeit in the last days of life. The patient could maintain a minimal level of quality of life that was not guaranteed by a relatively high flow

of oxygen given by mask and morphine. HFNT discontinuation, even for few minutes, immediately caused rapid deterioration, while its restoration produced an immediate improvement lasting for some days, when the development of agitation required palliative sedation for the last 24 h of life.

HFNT seems to offer advantageous properties, particularly for patient's compliance and acceptability, and should precede NIV application. HFNT offers a less traumatic interface in terms of skin breakdown and less burden for the caregiver. The patient is able to speak and eat (that may occur with nasal mask BiPAP). This would make HFNT also suitable as a first-line therapy to relieve severe dyspnea in many conditions [8].

Information about the use of ventilator support at end of life is lacking. Indeed, with the COVID pandemic, many palliative care physicians have gained experience with HFNT and literature on this kind of ventilatory support has expanded significantly during the pandemic. In Wuhan population, HFNT was an effective way of respiratory support in the treatment of COVID-19 patients [9]. In a review commissioned by the World Health Organization, HFNT was found to reduce the need for invasive ventilation and escalation of therapy compared with conventional oxygen therapy in COVID-19 patients with acute hypoxemic respiratory failure, although this benefit must be balanced against the unknown risk of airborne transmission [10]. Thus, HFNT was a useful treatment in order to avoid intubation or as a bridge therapy, and no increased mortality was observed due to the delay in intubation.

Some experimental pilot studies of short duration have shown the positive effect of HFNS in advanced cancer patients, reducing either exertional dyspnea (incident) or dyspnea at rest in non-hypoxemic cancer patients. In a four-arm (HFNT, high-flow air, low-flow oxygen, or low-flow air), double-blind randomized clinical trial examining the role of HFNT on exertional dyspnea in cancer patients without hypoxemia, HFNT, but not high-flow air, resulted in significantly lower dyspnea scores and longer exercise time, even in non-hypoxemic cancer patients [11]. In a double-blind, 4 × 4 crossover clinical trial, hospitalized patients with cancer who were dyspneic at rest and non-hypoxemic were randomized to 10 min of HFNT (oxygen), HFAir, low-flow oxygen, and low-flow air in different orders. The flow rate was titrated between 20 and 60 L/min in the high-flow interventions and 2 L/min in the low-flow interventions. HFNT (oxygen) and HFAir provided a rapid and clinically significant reduction of dyspnea at rest in hospitalized non-hypoxemic cancer patients [12]. In hospitalized patients with advanced cancer and persistent dyspnea, both HFNT and BiPAP for 2 h provided improvements in dyspnea intensity and respiratory parameters. No significant adverse effects were observed [13].

The case presented showed a real clinical condition of an advanced hypoxemic patient not responsive to increased doses of morphine and oxygen given by mask. This was a spontaneous “n of 1” study, as the patient was tested with two treatments in a short time with a clear indication for a favorable effect of HFNT that was strongly preferred by the patient.

Conclusion

HFNT may be helpful for severely hypoxemic patients who are unresponsive to common measured adopted in the last weeks–days of life of advanced cancer patients. Future studies should assess an early use of this device in combination with lower doses of opioids or as an alternative.

Author contribution Authors shared equally in the paper.

Code availability Words.

Declarations

Ethics approval Not necessary.

Consent to participate and consent for publication Permission to publish the case anonymously was obtained from patient’s relatives.

Conflict of interest The authors declare no competing interests.

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