Títle: Efficacy of high-flow oxygen and active humidification in a patient with acute respiratory failure of neuromuscular origin.

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## Abstract

The treatment of choice for patients with respiratory failure of neuromuscular origin, especially in situations of hypercapnic respiratory acidosis, is noninvasive ventilation (NIV). Endotracheal intubation and invasive ventilation are indicated for patients with severe respiratory compromise or failure of NIV. In recent years high-flow oxygen therapy and active humidification devices have been introduced in the medical practice. They are emerging evidence that high-flow may be effective in different clinical settings: such as acute respiratory failure, after cardiac surgery, during sedation and analgesia, in acute heart failure, in hypoxemic respiratory distress, in Do-Not-Intubate patients, in the case of patients with chronic cough and copious secretions, pulmonary fibrosis or cancer, both in critical areas or in the emergency department. We have studied a patient suffering from amyotrophic lateral sclerosis (ALS) who arrived at the emergency department with acute hypercapnic respiratory failure, which was treated successfully with a heated, humidified high-flow oxygen therapy device (HFNC). The patient did not tolerate NIV and we decided to try the HFNC as an alternative to intubation, since the patient had also rejected the application of invasive measures. An ABG performed after an hour of treatment showed a trend for improvement of both the pH, and the PCO2, and also improved the level of awareness of the patient. Respiratory acidosis was corrected and the patient could be discharged after 5 days of hospitalization. The response to HFNC was similar to that expected with NIV. We discuss the mechanisms of action of heated, humidified high-flow oxygen therapy and the need for research on this in the future.

Keywords: High flow oxygen therapy; non-invasive ventilation; amyotrophic lateral sclerosis.

Non invasive ventilation (NIV) is the treatment of choice for patients with respiratory failure of neuromuscular origin, especially in situations of hypercapnic respiratory acidosis (1,2). Endotracheal intubation and invasive ventilation are indicated for patients with severe respiratory compromise or NIV failure. In patients with amyotrophic lateral sclerosis (ALS), respiratory muscle weakness represents the major cause of mortality. As a result, NIV is an important part of disease management (3). Randomized controlled trials have indicated that therapy with long-term NIV improves survival in ALS patients. It can also improve patient symptoms and health-related quality of life (4). NIV has been shown to be effective in correcting respiratory failure, probably by acting to a greater or lesser extent on muscle fatigue, the mechanical properties of the respiratory apparatus, the control of ventilation, the alterations in gas exchange during the night leading to loss of sensitivity of central and peripheral chemoreceptors, and the degree of dysfunction of the upper airways (5).

In recent years heated, humidified high-flow oxygen therapy (HFNC) has been introduced in the medical practice (6). They are emerging evidence that HFNC could be an effective treatment in different clinical settings: such as acute respiratory failure (7-9), after cardiac surgery (10,11), during sedation and analgesia (12), in acute heart failure (13), in hypoxemic respiratory distress, in Do-Not-Intubate patients (14), in the case of patients with chronic cough and copious secretions (15), pulmonary fibrosis (16) or cancer (17), both in critical areas (18) or in the emergency department (19). We have studied a patient suffering from amyotrophic lateral sclerosis (ALS) who arrived at the emergency department with acute hypercapnic respiratory failure, which was treated successfully with HFNC.

Clinical case

A 65 years old woman was diagnosed with ALS 6 months earlier, although she had no other past medical history. Usually she had no dyspnea, decubitus intolerance or other respiratory symptoms. From a functional point of view, the patient had a recent spirometry showing FVC 2450 ml (78 %), FEV1 1420 ml (75 %), FEV1/FVC 0.7. The maximum inspiratory/expiratory pressure was normal, above 80 cm H2O. The patient went to the hospital emergency department, complaining of progressive dyspnea and decreased level of consciousness over two days. She had no fever, cough or expectoration. On physical examination the patient was drowsy, had a blood pressure of 140/70, a heart rate of 110 bpm, a respiratory rate of 13 breaths per minute, and a temperature of 36.8° C, showing an overall of breath sounds at cardiopulmonary auscultation. The remaining physical examination was of irrelevant interest. Laboratory tests showed hemoglobin 16 g/dl, hematocrit 50.6%, WBC 8.7 103/ml with 87% neutrophils, INR 0.9. Biochemistry was normal with a creatinine of 0.59 mg/dl. Arterial blood gases (ABG) performed with 50% oxygen by venturi mask showed: pH 7.27, PCO2 90 mmHg, PO2 88 mmHg, HCO3 40 mmol/l. Chest radiography showed left costophrenic angle obliteration without any other findings of interest. Her husband related the onset of symptoms with a catarrhal process. A hypercapnic respiratory acidosis without infiltrates secondary to a respiratory infection in a patient with ALS was diagnosed. She was treated with antibiotic and steroids. NIV by a bilevel pressure ventilator (Trilogy 100, Philips Respironics, Murrisville, Pensylvania) through an oronasal mask and a passive circuit was then started. The ventilator was adjusted using the following parameters in a ST mode: inspiratory pressure: 16 cm H2O, expiratory pressure: 6 cm H2O; backup rate: 15 breaths per minute; trigger sensitivity: 2; and rise time: 2. Oxygen was added at 5 lpm and the arterial saturation and heart rate was monitored. A severe intolerance was shown by the patient, so NIV was withdrawn after 5 minutes from starting. The patient was agitated, restless, and wanting to remove the mask. Arterial oxygen saturation was of 80 %. Then, a heated, humidified high-flow oxygen therapy device (Optiflow cannula with humidification by an MR880 heated humidifier, both from Fisher & Paykel Healthcare, Auckland, New Zealand) (Figure 1) setting at 45 L/min and a 0.26 fraction of inspired oxygen (FiO2), was applied. After an hour of treatment, the patient showed a clinical improvement and was more awake. ABG showed: pH 7.31, PCO2 74 mmHg, PO2 51 mmHg, HCO3 36 mmol/l. The patient was admitted to the respiratory ward. Three hours later, an ABG showed pH 7.40, PCO2 61 mmHg, PO2 62 mmHg, HCO3 41 mmol/l. The patient gradually improved and was discharged after 5 days of hospital admission. The HFNC device was used during the length of hospitalization. A later chest radiography showed similar left costophrenic angle obliteration without any other findings of interest. On the day of discharge, we put the patient on conventional oxygen therapy by nasal prongs at 1,5 lpm for 5 hours in the morning. An ABG showed pH 7,39, PCO2 48 mmHg, PO2 68 mmHg, CO3H 35 mmol/l. A Domiciliary oxygen therapy by nasal prongs at 1,5 lpm was recommended.

## Discussion

In the present case, an ALS patient with hypercapnic acidosis without infiltrates was successfully treated with HFNC. She had not tolerated NIV and also had rejected the application of invasive measures. We decided to try HFNC as an alternative to intubation. Patient management was similar to that of a patient with a COPD exacerbation and respiratory hypercapnic acidosis, using a low FiO2 aimed to maintain an arterial saturation slightly higher than 90 % to prevent greater hypoventilation. We monitored the patient as if she was receiving NIV and an ABG was performed at the first hour of treatment. The ABG showed a trend for improvement of both the pH and

the PCO2, and also improved the level of awareness of the patient. Respiratory acidosis was corrected and the patient was discharged after 5 days of hospitalization. The response to HFNC was similar to that expected with NIV. Basically, we applied the same criteria used for acute COPD patients.

Heated, humidified high flow nasal cannula oxygen is a technique that can deliver up to 100 % heated and humidified oxygen at a maximum flow of 60 L/min of gas via nasal prongs or cannula. The benefits of HFNC are related to a number of physiological properties (20). One of the main effects of delivering high gas flows directly in the nasopharynx is to wash CO2, whereby reducing CO2 rebreathing and providing a reservoir of fresh gas. This reduces dead space and increases the alveolar ventilation over minute ventilation ratio (21). Because high flow devices can generate flows that match or exceed patients peak inspiratory demand, it is thought that high flow nasal oxygen minimizes the nasopharyngeal resistance so decreasing resistive work of breathing. In the same line of reasoning, it was speculated that the use of high flows generated a certain amount of positive airway pressure as have been demonstrated by several authors (22-24). The pressures reached are not very high, estimated in 1 cm H2O of pressure for every 10 L/min of flow. These devices cannot be considered as CPAP devices, but we cannot forget this feature, responsible for some beneficial effects on respiratory mechanics. On the other hand, Corley et al (25) have demonstrated in patients with acute respiratory failure that part at least of the improvement in oxygenation observed is due to alveolar recruitment. Finally, high flow oxygen therapy showed a great tolerance by the patient related to the heat and humidity supplied by the device, the use of nasal prongs instead of face mask and reduction of work of breathing. Correction of hypoxemia may also play a role (26).

Its usefulness in critically ill patients, weaning and as an alternative to intubation, is being investigated and we have promising evidence in the literature (27, 28). The dead space washout, the nasopharyngeal resistance reduction, the positive pharyngeal pressure, the alveolar recruitment, the oxygen dilution reduction, the decreased work of breathing secondary to these mechanisms, the comfort provided by the temperature and humidity the patient receives and an excellent patient tolerance with this technique, may explain the clinical and gasometric improvement in our patient. Respiratory acidosis was corrected and the patient could be discharged from the hospital.

Our experience opens up a field of research in which perhaps some patients with acute respiratory failure and hypercapnic acidosis can be treated with high-flow oxygen therapy and active humidification as an alternative to conventional techniques of NIV. The simplicity of the technique, the lower cost of equipment and greater tolerance by patients, can provide an added benefit to the clinical efficacy of great importance in an era where efficiency should be prioritized. Future research is necessary to clarify these issues.

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## Legend Figure 1

This picture shows the various components of the high-flow oxygen therapy and active humidification device: the platform with the flow source "MaxVenturi" (1) and the humidifier "MR850" (2); the delivery system with the humidification chamber and the breathing circuit (3); and the interface F&P Optiflow TM Nasal Cannula (4).

