Fig. 1. A simplified scheme of the cellular immune response to M. tuberculosis. The (+) and (−) signs indicate the positive or negative feedback induced by each cell or cytokine under normal circumstances. The main sites where glatiramer acetate (GA) directly participates are marked with a black dot (•) and arrow to indicate the induced effect (increase or decrease). It directly affects macrophage activation (M act) by inhibiting T-helper 1 (Th1) response and thus, reducing levels of circulating interferon (IFN) γ, which plays an important role in their activation. It inhibits production of interleukin (IL) 12 which amplifies the Th1 response. IL-10 production is increased, directly inhibiting macrophage activation, and blocking the effects of dendritic cells (DC) and the differentiation of naive T cells into Th1 cells. It blocks the migration of Th1 cells from lymph nodes back to the lungs, and inhibits the expression and release of tumor necrosis factor (TNF)-α. Finally, it stimulates T-regulatory (T-reg) cells which also block the Th1 response.

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**References**


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**High-flow Nasal Cannula Oxygen Therapy: Preliminary Study in Hospitalized Patients**

Oxigenoterapia de alto flujo con cánula nasal: estudio preliminar en pacientes hospitalizados

To the Editor,

High flow nasal cannula (HFNC) oxygen therapy is a recently introduced alternative to conventional oxygen therapy. It uses a system that mixes oxygen and air to administer an FIO2 of 21%–100% at flow velocities of up to 60 lpm. To avoid condensation, the mixture of oxygen and air passes through a humidifier to a heated inspiratory circuit. This mixture is then administered to the patient by way of wide-bore nasal cannulae. The most important feature of HFNC is that it can be used to administer a humidified flow higher than the maximum inspiratory flow, and, moreover, the real FIO2 can be more reliably assessed.

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We report 3 patients with acute respiratory failure despite conventional oxygen therapy, who received HFNC in a hospital ward using an Optiflow® device, AIRVO 2® model (Fisher & Paykel).

Patient 1 was a 71-year-old man with a history of stage IIIA epidermoid lung cancer, treated with right upper lobectomy, hilar and mediastinal lymphadenectomy, chemotherapy and radiation therapy. Areas of honeycombing indicative of radiation-induced fibrosis were seen on successive tomography follow-ups. The patient was admitted for an episode of respiratory infection. He received conventional oxygen therapy (COT) via nasal prongs, antibiotics, nebulized bronchodilators and intravenous corticosteroid therapy. On day 10 of admission, the patient’s respiratory status declined, and he developed heart failure with hypoxemic respiratory failure (Table 1). Treatment began with high flow oxygen therapy at an initial FiO2 of 100% and a flow of 50 lpm. The patient tolerated the device well, and reported greater comfort compared with nasal prongs (9/10 compared to 6/10, respectively) and an absence of mouth dryness. His respiratory situation improved significantly, and the device was withdrawn 48 hours later.

Patient 2 was an 85-year-old woman with a history of obesity, cardiac hypertension and Dana Point group 2 pulmonary hypertension, receiving home oxygen therapy. She was admitted for a clinical picture of fever, cough with greenish expectoration, increased basal dyspnea, and signs of decompensated heart failure. Treatment began with oxygen therapy using a Ventimask® face mask with an FiO2 of 50%, antibiotics, diuretics, nebulized bronchodilators, and systemic corticosteroid therapy. Twenty-four hours after admission, she continued to show increased work of breathing and developed hypoxemic respiratory failure (Table 1), so HFNC was introduced at an initial FiO2 of 100% and a flow of 50 lpm. The patient tolerated the device well, and reported greater comfort compared with the face mask (8/10 compared to 2/10, respectively) and an absence of mouth dryness. Her clinical progress and blood gas parameters were favorable, and the patient was switched to COT via nasal prongs 72 hours later.

Patient 3 was a 74-year-old woman, former smoker, with a history of idiopathic pulmonary fibrosis. She had been diagnosed with lung cancer 7 months previously, treated with chemotherapy and radiation therapy. She was admitted for an episode of progressive dyspnea, until breathing difficulties were present at rest, in addition to fever and symptoms of lower respiratory tract infection. Treatment began with antibiotics, bronchodilators and a corticosteroid, plus concomitant oxygen therapy via a Ventimask® face mask at an initial FiO2 of 50%. Respiratory failure worsened, and the patient developed marked hypoxemic respiratory failure (Table 1) despite the use of a reservoir mask, so on day 8 of admission, HFNC was introduced, at an initial FiO2 of 95% and a flow of 40 lpm. The patient tolerated the device well, and reported greater comfort compared with the reservoir mask (9/10 compared to 1/10, respectively) and an absence of mouth dryness. The device was used for 7 days, after which the patient was switched to COT via nasal prongs.

In adults, HFNC has been studied in many situations, including bronchoscopies, weaning from intubation, patients who are not candidates for invasive ventilation, acute respiratory failure in emergency settings or intensive care, etc. However, this evidence is based largely on observational studies and case series. Lenglet et al. found a significant reduction in respiratory rate, less dyspnea on the Borg scale, and increased PaO2 in a group of patients with acute respiratory failure treated in an emergency department. The same group (Sztrymf et al.) found similar results in patients with acute respiratory failure refractory to oxygen therapy in an intensive care unit.

Our patients tolerated the device better than conventional oxygen therapy. The heated humidification provided by the HFNC appears to improve patient comfort and tolerance, compared to face masks, as shown in recent studies. This may benefit patients with borderline respiratory capacity, whose hypoxemia levels can fall when the mask is removed for eating, drinking or expectorating. Comparative studies have focused on patients with hypoxemic respiratory failure, while excluding those with hypercapnic respiratory failure. Although the results from preliminary studies appear promising, with no significant increases in PCO2 or pH, the use of HFNC is not approved in these patients, so more research is needed.

To conclude, we report our initial experience with the use of high-flow nasal cannula with heated humidification in an acute hospitalization unit. To date, most publications in adults have focused on emergency departments and intensive care units, but no data are available on the use of these devices in hospitalized patients.

References

Paraneoplastic cerebellar degeneration associated with small cell neuroendocrine mediastinal carcinoma

Degeneración cerebelosa paraneoplásica asociada a carcinoma neuroendocrino mediastínico de células pequeñas

To the Editor,

We report the case of a 69-year-old woman admitted with a 7-month history of anorexia and asthenia, along with unsteadiness, vomiting, tremor and double vision. She also reported a 1-month history of dyspnea and voice changes. On examination, she presented a bitonal voice, ataxic gait and dysmetria, with intention tremor in the left arm. Magnetic resonance imaging (MRI) of the head revealed a small lacunar infarction, which did not explain the clinical symptoms. Blood work, biochemistry, proteins, immunoglobulins, thyroid profile, vitamin B12, vitamin E and folate were normal, and serologies for HIV, hepatitis, cytomegalovirus, Epstein-Barr virus, syphilis and Borrelia were all negative. Cerebrospinal fluid cytochemistry was also normal. Carcinoembryonic antigen and neurospecific enolase tumor markers were elevated at 30.4 ng/ml (0–5 ng/ml) and 21.7 ng/ml (0–16 ng/ml), respectively. Computed tomography (CT) of the chest and abdomen revealed a mass in the upper mediastinum, measuring 70 mm × 40 mm, suggestive of clustered lymphadenopathy. An immune-mediated process was suspected, so antinuclear antibodies and onconeural antibodies were tested, but these were negative, with anti-glutamic acid decarboxylase antibodies (anti-GAD) 2.4 U/ml (0–5 U/ml) and anti-acetylcholine receptor antibodies 0.01 nmol/l (0–0.1 nmol/l). F-18 fluorodeoxyglucose uptake on a positron emission tomography scan suggested malignancy, so a biopsy was obtained by mediastinoscopy. The pathology report confirmed small cell neuroendocrine carcinoma of the thymus, positive for chromogranin and synaptophysin (Fig. 1). A scintigraphy (octreoscan) was then performed to complete the examination, showing 111In-pentetreotide uptake in the tumor and supraclavicular lymph node metastases. The patient underwent surgical resection and received chemotherapy with carboplatin and etoposide. She achieved full remission of the cancer and almost complete resolution of her neurological symptoms, although tremor at rest did persist.

Neuroendocrine tumors (NET) are rare cancers, generally found in the gastrointestinal tract, although they may occur in the lung, thymus, ovaries and non-parenchymatous tissue. Thymic NETs account for less than 5% of mediastinal tumors.1 Approximately 30% are malignant, although this rate rises to 82% if they are located in the thymus.1 They present as a mediastinal mass mainly in patients aged 30–50 years, and are 3 times more common in men.2 Local clinical manifestations can range from dysphonia or dyspnea to superior vena cava syndrome, and one-third of patients have endocrine symptoms associated with multiple endocrine neoplasia syndrome. CT, MRI and 123I-metaiodobenzylguanidine scintigraphy are useful, but the octreoscan is the most sensitive procedure (71%–100%) for detecting NETs, depending on the somatostatin receptors expressed by the tumors. Histology examination shows cell nests with fibrovascular tracts, positive for neuroendocrine markers such as chromogranin, synaptophysin and neuroenolase. Paraneoplastic cerebellar degeneration (PCD) is the most common paraneoplastic neurological syndrome. In 18%–50% of cases, no antibodies are identified,1 and in early stages of the disease, MRI is normal.3 It is associated with several neoplastic processes, including thymic NETs.5 In view of the favorable response to specific cancer treatment, we classified our case as seronegative PCD associated with thymic NET.

Fig. 1. Histology slide at 30× amplification with chromogranin immune staining, showing tumor cell nests separated by fibrovascular tracts.

References