ResMed

CASE STUDY

Six months of high-flow therapy in a COPD patient with frequent exacerbations.

Dr. Salvador Díaz Lobato.
Pulmonology Dept., Hospital Universitario HLA Moncloa.
Prof. of Medicine, Universidad Europea.

High-flow therapy (HFT) has recently become a recognised therapy for hypoxemic COPD patients.[16,17] Its mechanisms of action fit with the pathophysiology of the disease and there is increasing evidence that HFT could be used at home on a long-term basis[16,17], although this practical experience in this area is limited. Evidence[16,17] shows that hypoxemic COPD patients with chronic sputum, recurrent respiratory infections and exacerbations, bronchiectasis or frequent hospital admissions are suitable candidates for HFT.

We present the case of a hypoxemic COPD patient with frequent exacerbations and hospital admissions who was treated successfully with HFT at home. This case is in line with existing evidence[16,17] that shows that HFT could play an important role in the treatment of hypoxemic COPD patients with a "frequent exacerbator" phenotype.

Introduction

High-flow therapy (HFT) is a well-known and recognised therapy for patients with respiratory failure of diverse origins, with greater evidence for patients with acute hypoxemic respiratory failure[1]. In the case of COPD patients, there is increasing evidence that HFT could be used at home on a long-term basis, but this is still very rarely done[2]. This is due to several factors, including limited experience using HFT in patients with chronic respiratory failure, a lack of confidence with using HFT at home, a need for more comprehensive training, an assumption that high-flow is equivalent to high FiO_2 and that high O_2 flows cannot be delivered at home, and a limited evidence base[3].

> From a theoretical point of view, HFT is a treatment that is suitable for hypoxemic COPD patients, especially those with a chronic bronchitis phenotype[4]

Its mechanisms of action fit with the pathophysiology of this disease. **HFT provides sufficient pressure to counteract the patient's autoPEEP,** which is responsible for the air trapping so characteristic of COPD patients[5]. HFT also has effects on ventilatory mechanics, decreasing the inspiratory resistance and reducing respiratory work, so **the patient has less dyspnoea**[6,7]. Moreover, HFT generates a certain degree of expiratory pressure, which contributes to a greater alveolar recruitment and reduces CO_2 in hypercapnic patients due to the CO_2 dead-space washing effect[8,9]. Finally, the warm, humidified gas provides additional benefits: **improving mucociliar clearance, reducing respiratory secretions and infections,** and making this therapy better tolerated and more comfortable than conventional oxygen therapy or non-invasive ventilation[10,11]. These effects are very important, especially in COPD patients with bronchiectasis[12,13].

Moderate to severe hypoxemic COPD patients are characterised by recurrent exacerbations, daily limiting symptoms and frequent hospital admissions which greatly impair their quality of life. These patients are commonly classified as GOLD 3-4 and considered as frequent exacerbators with a chronic bronchitis phenotype. We have some evidence that HFT could clinically improve the condition of these patients, increase QALY and save costs by reducing hospital admissions, so HFT could be an option to consider when treating this kind of patient[14,15].

Case presentation

The patient is a 64-year-old man who is an ex-smoker with a pack-year index of 50 and a personal history of arterial hypertension and hypertensive cardiomyopathy treated with furosemide and amlodipine. A COPD diagnostic was made several years ago and the patient was being treated with a LAMA/LABA inhaler, inhaled steroids, roflumilast and albuterol prn (table 1). He was also on home oxygen therapy, receiving 2 L/min through nasal prongs for 15 hours a day. The patient was very symptomatic with a mMRC 3, a COPD Assessment Test (CAT) 15, coughing almost every day with a productive cough, and had presented three severe exacerbations in the last year requiring hospital admissions and two ED visits. The chest x-ray showed findings of increased bronchovascular markings and cardiomegaly. The FEV1 was 45% in the postbronchodilator spirometry, the arterial oxygen saturation by pulse oximetry (SpO_2) was 85%, and a basal arterial blood gas analysis showed PO_2 around 50 mmHg and normal PCO_2 levels (43 mmHg). **The patient was diagnosed as COPD GOLD 3D with a chronic bronchitis phenotype and hypoxemic chronic respiratory failure.**

Medical Treatment

LABA/LAMA inhaler (indacaterol/glicopirronio)	85/43 mcg/d
Inhaler steroids (Budesonide)	400 mcg/d
Roflumilast	500 mg/d
Albuterol	prn
Oxygen therapy	2 L/min, 15 h/day

Table 1


For illustration purpose only

Patient protocol

After having been discharged from the hospital following a new exacerbation, the patient was evaluated at the pulmonary office where the possibility to treat him with HFT at home was considered. This decision was taken based on previous studies showing that domiciliary high-flow therapy could improve the quality of life and reduce the number of exacerbations in hypoxemic COPD patients, mainly in those who are more symptomatic, with chronic sputum and recurrent visits to ED, and with some evidence of bronchiectasis, even mild bronchiectasis[16,17]. This was the case of this patient, who showed increased bronchovascular markings in the chest x-ray images.

The decision was taken to recommend an HFT device, set at 30 L/min, 34ºC temperature and 100% humidity. The patient was advised to use it during the night, connecting the oxygen at the same flow rate as had been prescribed for long-term oxygen therapy (2 L/min). The air/oxygen flow could be increased if necessary in order to achieve a 92% SpO_2. The patient was initiated to HFT in the pulmonary office and, after this, HFT was started at home. The patient was trained in the use of the device. This protocol was similar to the one described by Storgaard et al[17] (Table 2).

The patient started HFT and a monthly evaluation was planned. During each visit to the pulmonary office, checks were performed on the patient's clinical status, SpO_2 and current oxygen flow, exacerbation symptoms and tolerance to HFT. COPD exacerbation was defined as a worsening of symptoms (worsening of dyspnoea, cough and sputum production) for two consecutive days leading to treatment with systemic glucocorticoids or antibiotics. At each visit, the patient's correct usage of the device was checked.

Storgaard protocol for HFT in COPD at home

Flow	> 20L/min
Targeted temperature	37°C
Targeted level of humidity	100%
Use	At night with the possibility to use during the day
Oxygen	The same flow as prescribed for long-term oxygen therapy. It can be increased if necessary
SaO_2 min	88% leading to flow increase

Table 2

Patient outcomes

> After six months, the patient showed clinical improvement with less cough, sputum and dyspnoea than in the period before starting HFT.

The patient had a mMRC 2 and CAT 8. He coughed less, with a significant reduction in sputum. He didn´t have any exacerbations, visits to the ED or hospital admissions during this period of time. **He felt better and his tolerance of HFT was very good, including sleeping comfortably.**

The patient didn´t complain of adverse events related to HFT. It was not necessary to adjust settings over time, not even the oxygen flow. Table 3 shows the patient´s data over this period.

Follow-up	1st month	2nd month	3rd month	4th month	5th month	6th month
Flow	30 L/min	30 L/min	30 L/min	30 L/min	30 L/min	30 L/min
Temperature	34ºC	34ºC	34ºC	34ºC	34ºC	34ºC
Humidity	100%	100%	100%	100%	100%	100%
Use	8 hours at night	8 hours at night	8 hours at night	8 hours at night	8 hours at night	8 hours at night
Oxygen flow	2 L/min	2 L/min	2 L/min	2 L/min	2 L/min	2 L/min
SpO_2	92%	93%	93%	94%	93%	93%
Clinical status	++	++	++	++	++	++
ED visits	No	No	No	No	No	No
Tolerance to HFT	++	++	++	++	++	++

Table 3

++: improved.

Discussion

Only a few studies investigating the use of long-term HFT in COPD patients have been published. The study from **Rea et al**[16] was conducted in patients with COPD or bronchiectasis. One hundred and eight patients (mean FEV1 45%) were studied in a randomised, controlled study. HFT was administered at a temperature of 37°C and a flow rate of 20-25 L/min and compared with standard care for one year. Although no differences in exacerbation frequency and hospital admissions were observed between the two groups, the number of exacerbation days was significantly lower (18.2 vs. 33.5/patient, p = 0.045) and the median time to first exacerbation (52 vs. 27 days, p = 0.0495) was significantly longer in the HFT group compared to the control group. In addition, differences in lung function and quality of life (QoL) were observed, all in favour of the HFT group. In spite of the limitations of this study, it seems that HFT could be useful in patients with COPD or bronchiectasis.

Another important study is from **Storgaard et al**[17]. This study was conducted in COPD patients with chronic hypoxemic respiratory failure. Two hundred patients with moderately severe COPD (FEV1 ± 31%) who were receiving home oxygen therapy were randomised to receive conventional treatment or HFT. Mean adherence to HFT was 6 hours per day with a recommended flow setting of 20 L/min. Compared to the previous year, patient-reported exacerbations increased from 2.90 to 4.95/patient/year in the control group, while in the HFT group, the exacerbation rate decreased slightly from 3.23 to 3.12/patient/year. Thus, lower rates of acute COPD exacerbation were found in the HFT group during the study period ($p<0.001$). No differences in hospital admissions and all-cause mortality were observed between the groups after one year. However, it appeared that patients who used HFT more hours per day had a reduction in hospital admissions, although these benefits were shown in a post-hoc analysis and not in the intention-to-treat study population. Patients using HFT also showed clinical improvement (symptoms reduction like cough, mucous clearance or dyspnoea) and an improvement in health-related quality of life (HRQOL), $PaCO_2$ and exercise capacity. Moreover, HFT was very well tolerated and the patients found it easy to use.

Our patient results are in line with the studies by Storgaard and Rea, which have shown us that patients with moderate-severe hypoxemic COPD with a bronchiectasis component are good candidates for HFT. Our patient met these criteria. He was a severe hypoxemic COPD patient with a history of chronic pulmonary secretions and indirect data of mild bronchiectasis in the chest x-ray images that showed an increased bronchovascular markings. He had presented three severe exacerbations in the previous year requiring hospital admissions. The Storgaard and Rea studies have also shown us the impact of HFT in the reduction in exacerbation days and lower rates of COPD exacerbation. For these reasons, the possibility of treating him with HFT at home was considered. The patient did not present any exacerbation in the study period and showed significant symptomatic improvement

A recommended 20 L/min flow rate was decided in the Storgaard study[17] after an unpublished pilot test determined that this was comfortable and allowed high compliance during sleep. Starting at 15 L/min, flow was titrated over 30 minutes at the baseline visit. In our patient, **we recommended 30 L/min in order to satisfy inspiratory peak flow demand** and on the basis of our personal experience and protocols[18]. We also set a temperature of 34ºC due to the fact that HFT temperature seems to significantly impact the comfort of patients: a lower temperature could be more comfortable[19]. Based on this, we think **it could be a reasonable option to start HFT with a temperature of 34ºC** and increase it or decrease it depending on the patient's tolerance. Our patient showed a good tolerance and did not need any temperature modification.

In the Storgaard study[17], patients were instructed in the use of the device, received a written quick guide to the device and were recommended to use HFT for 8 hours/day, preferably at night. However, there were no restrictions on the duration of use or the time of day. In this study, HFT was used at night by 53% of the patients, during the day by 32%, and during both night and day by 15%. On average, HFT was used 6 hours/day throughout the study period. Patients using HFT at night, or both night and day, used the device significantly longer than those using only during the day time. Based on this data, **we recommended that our patient should use HFT for 8 hours at night.** The patient showed a good adherence to this protocol, used HFT while he was asleep and did not complain about quality of sleep. Lately, Storgaard et al[20] have analysed the patients' experience and have found that it improves thanks to a reduction in symptoms and an increase in activities of daily life. Furthermore, they have substantiated the necessity of perceived usefulness and ease of use as important factors for adherence to treatment.

In the Storgaard study[17], the supplementary oxygen flow was kept unaltered during HFT therapy unless a SpO_2 < 88% was detected. Mean oxygen flow during long-term oxygen therapy remained unaltered at 12 months in both groups, as was the case for our patient: a flow of 2 L/min was able to maintain a stable SpO_2 of around 93-94% throughout the follow-up.

> In summary, our patient showed a good response to HFT and improvements in both symptoms and the number of exacerbations.

The patient adapted to HFT without problems, showing a good tolerance of and comfort with the therapy. The ease of usage of the device was highlighted by the patient and it was not necessary to change HFT settings. As in our case, in hypoxemic COPD patients with frequent exacerbations, particularly if they have bronchiectasis, HFT as an add-on therapy to long-term oxygen therapy may be particularly beneficial in terms of reduction of exacerbations, improvement of symptoms and quality of life, and therapy comfort and tolerability. Data from published studies tell us that HFT could be included as a new approach to treat hypoxemic COPD patients with recurrent exacerbations or bronchiectasis. Studies comparing HFT with other strategies and recruiting larger numbers of patients are needed.

Références

1. Roca O, Hernández G, Díaz Lobato S, Carratalá JM, Gutierrez R, Masclans JR. Current evidence for the effectiveness of heated and humidified high flow nasal cannula supportive therapy in adult patients with respiratory failure. Crit Care 2016;20:109. DOI: 10.1186/s13054-016-1263-z
2. Bonnevie T, Elkins M, Paumier C, Medrinal C, Combret Y, Patout M et al. Nasal high flow for stable patients with chronic obstructive pulmonary disease: A systematic review and meta-analysis. COPD: Journal of Chronic Obstructive Pulmonary Disease 2019. DOI: 10.1080/15412555.2019.1672637
3. Spicuzza L, Schisano M. High-flow nasal cannula oxygen therapy as an emerging option for respiratory failure: the present and the future. Ther Adv Chron Dis 2020;11:1-15. DOI: 10.1177/2040622320920106
4. Zantah M, Pandya A, Jacobs MR, Criner GJ. The mechanisms of benefit of high-flow nasal therapy in stable COPD. J Clin Med 2020;9:3832. DOI: 10.3390/jcm9123832
5. Nava, S., Ambrosino, N., Rubini, F., Fracchia, C., Rampulla, C., Torri, G., & Calderini, E. (1993). Effect of nasal pressure support ventilation and external PEEP on diaphragmatic activity in patients with severe stable COPD. Chest, 103(1), 143–150. DOI: 10.1378/chest.103.1.143
6. Atwood CW, Camhi S, Little KC et al. Impact of heated humidified high flow air via nasal cannula on respiratory effort in patients with chronic obstructive pulmonary disease. Chron Obstr Pulm Dis 2017;4:279-286. DOI: 10.15326/jcopdf.4.4.2016.0169
7. Cortegiani A, Crimi C, Noto A, Helviz Y, Giarratano A, Gregoretti C et al. Effect of high-flow nasal therapy on dyspnea, comfort and respiratory rate. Crit Care 2019;23:201. DOI: 10.1186/s13054-019-2473-y
8. Elshof J, Duiverman ML. Clinical evidence of nasal high-flow therapy in chronic obstructive pulmonary disease patients. Respiration 2020;99:140-153. DOI: 10.1159/000505583
9. Fricke K, Tatkov S, Domanski U, Franke KJ, Nilius G, Schneider H. Nasal high flow reduces hypercapnia by clearance of anatomical dead space in a COPD patient. Respir Med Case Report 2016;19:115-117. DOI: 10.1016/j.rmcr.2016.08.010
10. Gotera C, Díaz Lobato S, Pinto T, Winck J. Clinical evidence on high flow oxygen therapy and active humidification in adults. Pulmonology J 2013;19:217-227. DOI: 10.1016/j.rppneu.2013.03.005
11. Pandya A, Criner G, So J, Jacobs MR, Tomas J, Criner H. Tolerance and safety of humidified high-flow nasal cannula oxygen therapy in patients hospitalized with an acute exacerbation of chronic obstructive pulmonary disease (COPD). AJRCCM 2020:201:A3327. DOI: 10.1164/ajrccm-conference.2019.199.1
12. Good WR, Garrett J, Hockey HUP, Jayaram L, Wong C, Rea H. The role of high flow nasal therapy in bronchiectasis. A post-hoc analysis. ERJ Open Res 2020. DOI: 10.1183/23120541.00711-2020
13. Crimi C, Noto A, Cortegiani A, et al. High flow nasal therapy use in patients with acute exacerbation of COPD and bronchiectasis: a feasibility study. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2020;17(2):184-190. DOI: 10.1080/15412555.2020.1728736
14. Storgaard S, Møller U, Storgaard LH. Assessment of health-related quality of life and hospital admission costs of domiciliary High-Flow nasal cannula treatment for severe COPD with chronic hypoxic failure. Eur Respir J 2020:56:1661. DOI: 10.2147/CEOR.S312523
15. Dolidon S, Dupuis J, Molano LC, Salaün M, Thiberville L, Muir JF et al. Characteristics and outcome of patients set up on high-flow oxygen therapy at home. Ther Adv Respir Dis 2019;13:1-8. DOI: 10.1177/1753466619879794
16. Rea H, McAuley S, Jayaram L, et al. The clinical utility of long-term humidification therapy in chronic airway disease. Respiratory Medicine. 2010;104(4):525-533. DOI: 10.1016/j.rmed.2009.12.016
17. Storgaard LH, Hockey H-U, Laursen BS, Weinreich UM. Long-term effects of oxygen-enriched high-flow nasal cannula treatment in COPD patients with chronic hypoxemic respiratory failure. International Journal of Chronic Obstructive Pulmonary Disease. 2018;13:1195. DOI: 10.2147/COPD.S159666
18. Díaz Lobato S, Carratalá JM, Alonso JM, Mayoralas S, Segovia B, Escalier N et al. Things to keep in mind in high flow therapy: As usual the devil is in the detail. Int J Crit Care Emerg Med 2018;4:048. DOI: 10.23937/2474-3674/1510048
19. Mauri T, Galazzi A, Binda F, Masciopinto L, Corcione N, Carlesso E et al. Impact of flow and temperature on patient comfort during respiratory support by high-flow nasal cannula. Critical Care 2018;22:120. DOI: 10.1186/s13054-018-2039-4
20. Storgaard L, Weinreich U, Laursen BS. COPD patients experience of long-term domestic oxygen-enriched nasal high flow treatment: A qualitative study. COPD: Journal of Chronic Obstructive Pulmonary Disease 2020;17:175-183. DOI: 10.1080/15412555.2020.1736998

The writing of the case study was financed by ResMed. Please refer to the user guides for relevant information related to any warnings and precautions to be considered before and during use of the product.
This content is intended for health professionals only.