MMJ

Malta Medical Journal, 33 (1): Pages (2021)
http://mmsjournals.org/index.php/mmj

REVIEW ARTICLE

The use of high flow nasal oxygen in COPD patients

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High flow nasal oxygen (HFNO) is one of the interventions a physician may opt to prescribe in hypoxemic patients. It involves the delivery of heated and humidified oxygen at rates of up to 60L/min via large bore nasal cannulae in a controlled manner, with variables such as the fraction of inspired oxygen (FiO2) which may be controlled independently. The set-up of HFNO consists of an oxygen generator, a flow meter, a humidifier and wide bore nasal cannulae (figure 1). There are 5 physiologic mechanisms that are believed to be responsible for the efficacy of HFNO. These include physiological dead space washout of waste gases including carbon dioxide (CO2), decreased respiratory rate, positive end-expiratory pressure, increased tidal volume and increased end-expiratory volume. These mechanisms account for the multiple applications of HFNO in hypoxemic patients, both in the acute and chronic settings. The use of HFNO in the management of COPD has risen along the years. It plays a role in both acute and stable COPD patients, however, the present evidence is insufficient for HFNO to be utilised preferentially especially in the acute setting. Larger scale studies are necessary to establish its role especially in these scenarios where NIV is currently recommended as the first line mode of oxygenation and HFNO is reserved for those unable to tolerate NIV.

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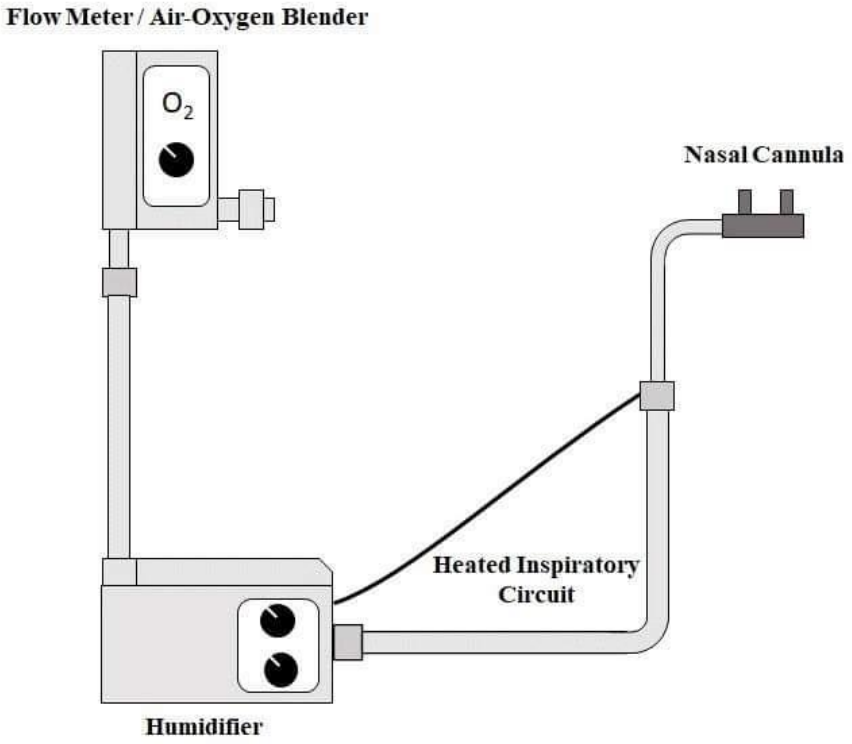
Figure 1 Set-up of high flow nasal oxygen



Introduction

High flow nasal oxygen (HFNO) is one of the interventions a physician may opt to prescribe in hypoxemic patients. It involves the delivery of heated and humidified oxygen at rates of up to 60L/min via large bore nasal cannulae in a controlled manner, with variables such as the fraction of inspired oxygen (FiO2) which may be controlled independently. Unlike low flow nasal oxygen, the FiO2 is not related to the flow rate, and there is the added advantage of less air leaks in HFNO. The set-up of HFNO consists of an oxygen generator, a flow meter, a humidifier and wide bore nasal cannulae.[1] In view of delivering the oxygen in a heated, humidified manner via nasal cannulae, as opposed to cold dry oxygen via a tight fitting mask, HFNO may be better tolerated by patients in comparison to long term oxygen therapy (LTOT) and non-invasive positive pressure ventilation (NIPPV).

Search criteria

The search for publications and abstracts was done electronically on PubMed, the Cochrane database of systematic reviews, using the search terms: 'high flow nasal oxygen in COPD'. The search was limited to articles available in English language, related to human subjects and published within the past five years. A total of fifty- five (55) articles were identified in this search. A single reviewer (myself) screened all potential references for inclusion, which brought the number of articles to thirty-one (31). The last update of the search was performed in May 2020.

Physiological mechanisms

There are 5 physiologic mechanisms that are believed to be responsible for the efficacy of HFNO. These include:

- Physiological dead space washout of waste gases including carbon dioxide (CO2)

- Decreased respiratory rate
- Positive end-expiratory pressure
- Increased tidal volume
- Increased end-expiratory volume

These mechanisms account for the multiple applications of HFNO in hypoxemic patients, both in the acute and chronic settings.

HFNO confers two advantages in relation to the washout of carbon dioxide from the physiological dead space, which is increased in conditions such as emphysema. Firstly, nasal cannulae do not increase the physiological dead space, as happens with masks used in other forms of oxygenation. Secondly, the high flow of oxygen washes out the carbon dioxide in the upper respiratory tract, as has been studied by measuring the CO2 elimination rate using a dynamic CO2 spectroscope with infrared radiation and a gamma camera.[2] The upper respiratory tract is one component of the physiological dead space, and thus the effect on HFNO on the other parts of this dead space, such as the bronchioles, is yet to be ascertained.

Decreased respiratory rate with the use of HFNO has been linked to the first mechanism. Clearance of carbon dioxide from the physiological dead space due to the positive end expiratory effect of HFNO results in better ventilation-perfusion matching, and this decreases the work of breathing and therefore respiratory rate.[2]

A decrease in the work of breathing may also be due to the positive end-expiratory pressure (PEEP) effect of HFNO. This arises from the high flow rate the nasal cannula achieves, which causes resistance against expiratory flow and increases airway pressure. The PEEP effect of HFNO has been compare to the pursed-lip breathing pattern COPD patients often adopt.[2] This effect is related to the size of the nasal prongs, whether the subject's mouth is open or closed, sex, body mass index and is directly proportional to the oxygen flow rate. [3]

Increased end-expiratory lung impedance has been reported with HFNO, suggesting increasing volumes and functional residual capacity which are more pronounced in patients with higher body mass index and not related to body position.[2] This effect was also reported in a small study specifically involving stable COPD patients whereby HFNO was compared to LTOT.[4] This same study reported an increase in tidal volume and a decrease in respiratory rate, thus supporting the above-mentioned mechanisms.

Furthermore, HFNO may improve lung epithelial mucociliary clearance as suggested by in vitro studies, and this was explored in patients with bronchiectasis and COPD with positive results including less acute exacerbations and fewer hospital admissions. However, these studies did not directly link the results to improved mucociliary clearance in COPD patients.[2]

Domiciliary HFNO / HFNO in chronic stable COPD

In 2017, HFNO was deemed safe to use in the short-term in stable COPD patients, where its effects were observed when use for one hour.[5] The Aalborg study in 2018 consisted of 200 COPD patients with chronic hypoxemic respiratory failure on LTOT, who were randomly assigned LTOT only or LTOT and HFNO. The use of HFNO for a daily average of 6-7hours resulted in a statistically significant reduction in acute exacerbations of COPD (AECOPD), as well as an improvement in mMRC grade from 3 months onwards. 138 patients completed the study at twelve months and

despite no significant difference in hospital admission rates, predicted hospital admission rates were lower for the HFNO group compared to the control group using amount of days on HFNO as an explanatory variable.[6] The post-hoc study involving 100 patients with COPD and chronic hypoxic failure confirmed this as there were reductions in the number of AECOPD, the number of hospitalisations and length of stay in patients treated with HFNO and LTOT, particularly in those with two or more exacerbations in the year prior to inclusion in the study. Thus it was concluded that dual treatment with HFNO and LTOT would be more beneficial to patients with frequent exacerbations.[7] Hypercapnic patients were included in this study, however, no correlation between paCO2 and number of exacerbations was identified.

On the other hand, Nagata et al's cross over trial in patients with stable hypercapnic COPD showed that six weeks of HFNO with LTOT did not improve dyspnoea, yet improved both quality of life and hypercapnia when compared to LTOT alone. The commonest adverse event with HFNO was nocturnal diaphoresis.[8]

Chronic hypercapnic COPD

In a randomised, multi-centre trial in COPD patients with daytime hypercapnia, it was observed that paCO2 decreased with the use of both HFNO and NIV, but decreased more with NIV, thus HFNO should be reserved for those intolerant to NIV.[9] This reduction in paCO2 is flow-dependent.[10]

HFNO in acute exacerbations of COPD

The first trial of HFNO in patients with hypercapnic AECOPD with pH <7.38 who had failed NIV was executed in 2018 by Braunlich et al. A significant improvement in pH and pCO2 was noted, more significantly in those with pH <7.35, and hence HFNO was deemed a promising alternative in the advent of NIV failure.[11] Besides the issue of NIV failure, a case of successful management of an AECOPD was reported in an acidotic, hypercapnic patient who benefitted from HFNO as his facial structure resulted in severe oxygen leaks when using NIV masks.[12]

In 2019, Pisani et al identified five trials about HFNO in relation to COPD exacerbations, which studied a total of 198 subjects with a male predominance and all aged over 70years.[13] Unfortunately, patient severity was not indicated in some trials, yet the FiO2 required to achieve target saturations of 88 to 92% (or 90 to 94% in one study) was accurately recorded. Two trials concerned COPD exacerbations post-extubation and concluded that HFNO, when compared with low flow oxygen therapy, significantly decreases the neuroventilatory drive and the work of breathing in patients with COPD recovering from an episode of acute respiratory failure after a planned extubation.[14] A lower mean arterial pressure was reported with NIV, yet no differences were identified with respect to arterial blood gas values, re-intubation rate, duration of invasive mechanical ventilation, length of stay at the intensive care unit and 28 day-mortality.[15]

The third trial conducted by Longhini et al assessed the effect of HFNO use in patients being weaned off NIV. It was found that whilst 36.7% failed NIV discontinuation, in those with successful discontinuation, NIV was re-started in a lower number of individuals who had received HFNO in comparison to those receiving controlled oxygen therapy (COT). The underlying mechanism for its success was a reduction in work of breathing without a rise in PaCO2, as previously explained.[13]

In patients presenting with severe AECOPD with moderate hypercapnic acute respiratory failure, 30 day intubation and mortality rates were not statistically different with the use of HFNO as opposed to NIV.[16] In this case, severe AECOPD was defined as sudden worsening of resting dyspnea, high respiratory rate (>30 breaths/min), decreased oxygen saturation (6.0 kPa) whilst moderate respiratory failure referred to pH levels between 7.25 and 7.35 on room air. In a similar cohort of patients, HFNO had an acceptable failure rate.[17] Another study noted a slight reduction in pCO2 levels measured transcutaneously when HFNO was used in AECOPD compared with standard nasal prongs, however, this was not statistically significant and there was no specification of the patient's acid-base status.[18]

Besides Pisani et al's analysis of these 5 trials, Sun et al enrolled 82 hypercapnic COPD patients in acute respiratory failure, and noted that HFNO had a lower failure rate than NIV despite this observation not reaching statistical significance. A significant difference was measured with regards to intolerance rate, which was higher for NIV. Despite this, no difference was detected between the two groups in terms of respiratory distress, hypoxemia and carbon dioxide retention. HFNO had less airway care interventions, less dermatological consequences but required a longer time of application compared to NIV. Another end-point that was measured was 28-day mortality, whereby no significant difference was observed between the two groups.[19]

Needless to say, in acute hypoxic respiratory failure it is essential to determine the cause, whilst keeping in mind the patient's co-morbidities, functional status and comfort, with regular evaluation of the clinical status and the need for intubation.[20]

HFNO AT THE EMERGENCY DEPARTMENT

HFNO causes less dyspnea and is more comfortable compared to COT in patients at the emergency department with acute dyspnea and hypoxemia, which may be attributed to COPD. However, there are currently no trials specific to COPD emergency presentations, and furthermore, this study did not measure FiO2 in COT subjects which is important to compare gas exchange especially in COPD patients.[21]

AEROSOL DELIVERY VIA HFNO

COPD management may involve the use of aerosolised treatment such as salbutamol. Inhalation of salbutamol/ipratropium bromide solutions via the oral route and HFNO route was studied in a population on separate days, and no significant post-inhalational differences were measured on spirometry.[22] However, HFNO confers the advantage of delivering medications without interruption of the oxygen supply. A comparison of the different modes of medication administration via HFNO cannulae at low flow rates of oxygen was drawn by measuring urinary salbutamol excretion. Vibrating mesh nebulisers were superior to jet nebulisers, and no additional benefit was derived from additionally using a spacer with the HFNO cannulae set-up.[23]

HFNO POST-EXTUBATION

Besides Jing and Di Mussi's observations explored above as AECOPD post- extubation, Zhang et al studied HFNO safety in COPD patients post-extubation. HFNO was deemed safe to use as it reduced length of stay at ITU, did not alter mortality and re-intubation rate, and had a similar side-effect incidence when compared to NIV. The only adverse finding was that of a higher oxygenation index in the

NIV group at twelve hours post-extubation, however, this observation did not hold at 24 and 72hours after extubation.[24]

HFNO DURING SLEEP

A small prospective study in 2017 assessed the effect of oxygen and HFNO on sleep in COPD patients with FEV1 >30% predicted and smokers as the control. HFNO was found to be advantageous in that it not only reduced the work of breathing, but also reduced paCO2, an effect not seen when using conventional oxygen.[25]

In 2018, the above findings were confirmed separately by directly measuring CO2 production using a metabolic hood and polysomnography. Two conclusions were derived, the first one being that responses in ventilation to HFNO during sleep were similar in COPD patients and controls. Secondly, the physiological mechanisms of HFNO were confirmed as the use of HFNO caused a substantial decline in minute ventilation due to a reduction in dead space ventilation without a major change in alveolar ventilation, CO2 production, energy expenditure or transcutaneous CO2.[26]

Later that year, the effect of HFNO on sympathetic activity during sleep was researched using finger pulse wave amplitude. HFNO reduced sympathetic activity in COPD patients especially during REM sleep, whilst supplemental oxygen did not. This effect was not observed in the control group, and was observed to a lesser degree in COPD patients with forced expiratory volume of greater than 1.65L.[27]

HFNO AND EXERCISE TOLERANCE

Exercise intolerance in COPD may be attributed to the dead space volume in the upper airways, and thus HFNO might play a role in this regard. In a small trial involving severe COPD patients with ventilatory limitation, the subjects experienced less dyspnoea during exercise when using HFNO. Other findings were those of increased oxygen partial pressure, however, the mechanism for these results was not studied.[28]

HFNO IN PALLIATIVE COPD PATIENTS

In his review of end-of-life respiratory support, Davies concludes that in spite of a wide evidence base for the use of NIV in this context, there is no evidence yet to support the use of HFNO, and this lack of evidence is not restricted to its use in COPD palliation, but also in other conditions.[29]

CONCLUSION

The use of HFNO in the management of COPD has risen along the years.[30] It plays a role in both acute and stable COPD patients, however, the present evidence is insufficient for HFNO to be utilised preferentially especially in the acute setting.[31] Larger scale studies are necessary to establish its role especially in these scenarios where NIV is currently recommended as the first line mode of oxygenation and HFNO is reserved for those unable to tolerate NIV.

FUTURE DEVELOPMENTS

Keeping in mind the body of evidence for the applications of HFNO in COPD patients which was explored in this article, there are still applications that need to be addressed or that necessitate larger trials to be conducted. One such query is posed by Mansfield regarding HFNO preceding the use of NIV in AECOPD, as well as its use when NIV is not tolerated.[32]

References

1. Nishimura M. High-Flow Nasal Cannula Oxygen Therapy Devices. Respir Care. 2019 Jun;64(6):735–42.
2. Pisani L, Vega ML. Use of Nasal High Flow in Stable COPD: Rationale and Physiology. COPD. 2017 Jun;14(3):346–50.
3. Nishimura M. High-Flow Nasal Cannula Oxygen Therapy in Adults: Physiological Benefits, Indication, Clinical Benefits, and Adverse Effects. Respir Care. 2016 Apr;61(4):529–41.
4. Fraser JF, Spooner AJ, Dunster KR, Anstey CM, Corley A. Nasal high flow oxygen therapy in patients with COPD reduces respiratory rate and tissue carbon dioxide while increasing tidal and end-expiratory lung volumes: a randomised crossover trial. Vol. 71, Thorax. 2016. p. 759–61.
5. Vogelsinger H, Halank M, Braun S, Wilkens H, Geiser T, Ott S, et al. Efficacy and safety of nasal high-flow oxygen in COPD patients. BMC Pulm Med. 2017 Nov;17(1):143.
6. 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. Int J Chron Obstruct Pulmon Dis. 2018;13:1195–205.
7. Weinreich UM. Domiciliary high-flow treatment in patients with COPD and chronic hypoxic failure: In whom can we reduce exacerbations and hospitalizations? PLoS One. 2019;14(12):e0227221.
8. Nagata K, Kikuchi T, Horie T, Shiraki A, Kitajima T, Kadowaki T, et al. Domiciliary High-Flow Nasal Cannula Oxygen Therapy for Patients with Stable Hypercapnic Chronic Obstructive Pulmonary Disease. A Multicenter Randomized Crossover Trial. Ann Am Thorac Soc. 2018 Apr;15(4):432–9.
9. Bräunlich J, Dellweg D, Bastian A, Budweiser S, Randerath W, Triché D, et al. Nasal high-flow versus noninvasive ventilation in patients with chronic hypercapnic COPD. Int J Chron Obstruct Pulmon Dis. 2019;14:1411–21.
10. McKinstry S, Pilcher J, Bardsley G, Berry J, Van de Hei S, Braithwaite I, et al. Nasal high flow therapy and PtCO(2) in stable COPD: A randomized controlled cross-over trial. Respirology. 2018 Apr;23(4):378–84.
11. Bräunlich J, Wirtz H. Nasal high-flow in acute hypercapnic exacerbation of COPD. Vol. 13, International journal of chronic obstructive pulmonary disease. 2018. p. 3895–7.
12. Plotnikow G, Thille AW, Vasquez D, Pratto R, Desmery P. High-flow nasal cannula oxygen for reverting severe acute exacerbation of chronic obstructive pulmonary disease: A case report. Vol. 41, Medicina intensiva. Spain; 2017. p. 571–2.
13. Pisani L, Astuto M, Prediletto I, Longhini F. High flow through nasal cannula in exacerbated COPD patients: a systematic review. Pulmonology. 2019;25(6):348–54.
14. Di Mussi R, Spadaro S, Stripoli T, Volta CA, Trerotoli P, Pierucci P, et al. High-flow nasal cannula oxygen therapy decreases postextubation neuroventilatory drive and work of breathing in patients with chronic obstructive pulmonary disease. Crit Care. 2018 Aug;22(1):180.
15. Jing G, Li J, Hao D, Wang T, Sun Y, Tian H, et al. Comparison of high flow nasal cannula with noninvasive ventilation in chronic obstructive pulmonary disease patients with hypercapnia in preventing postextubation respiratory failure: A pilot randomized controlled trial. Res Nurs Health. 2019 Jun;42(3):217–25.
16. Lee MK, Choi J, Park B, Kim B, Lee SJ, Kim S-H, et al. High flow nasal cannulae oxygen therapy in acute-moderate hypercapnic respiratory failure. Clin Respir J. 2018 Jun;12(6):2046–56.
17. Yuste ME, Moreno O, Narbona S, Acosta F, Peñas L, Colmenero M. Efficacy and safety of high-flow nasal cannula oxygen therapy in moderate acute hypercapnic respiratory failure. Rev Bras Ter intensiva. 2019 May;31(2):156–63.
18. Pilcher J, Eastlake L, Richards M, Power S, Cripps T, Bibby S, et al. Physiological effects of titrated oxygen via nasal high-flow cannulae in COPD exacerbations: A randomized controlled cross-over trial. Respirology. 2017 Aug;22(6):1149–55.

19. Sun J, Li Y, Ling B, Zhu Q, Hu Y, Tan D, et al. High flow nasal cannula oxygen therapy versus non-invasive ventilation for chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: an observational cohort study. Int J Chron Obstruct Pulmon Dis. 2019;14:1229–37.
20. Pisani I, Comellini V, Nava S. Noninvasive ventilation versus oxygen therapy for the treatment of acute respiratory failure. Expert Rev Respir Med. 2016 Jul;10(7):813–21.
21. Rittayamai N, Tscheikuna J, Praphruetkit N, Kijpinyochai S. Use of High-Flow Nasal Cannula for Acute Dyspnea and Hypoxemia in the Emergency Department. Respir Care. 2015 Oct;60(10):1377–82.
22. Bräunlich J, Wirtz H. Oral Versus Nasal High-Flow Bronchodilator Inhalation in Chronic Obstructive Pulmonary Disease. J Aerosol Med Pulm Drug Deliv. 2018 Aug;31(4):248–54.
23. Madney YM, Fathy M, Elberry AA, Rabea H, Abdelrahim ME. Aerosol Delivery Through an Adult High-Flow Nasal Cannula Circuit Using Low-Flow Oxygen. Respir Care. 2019 Apr;64(4):453–61.
24. Zhang JC, Wu FX, Meng LL, Zeng CY, Lu YQ. [A study on the effects and safety of sequential humidified high flow nasal cannula oxygenation therapy on the COPD patients after extubation]. Zhonghua Yi Xue Za Zhi. 2018 Jan;98(2):109–12.
25. Biselli PJC, Kirkness JP, Grote L, Fricke K, Schwartz AR, Smith P, et al. Nasal high-flow therapy reduces work of breathing compared with oxygen during sleep in COPD and smoking controls: a prospective observational study. J Appl Physiol. 2017 Jan;122(1):82–8.
26. Biselli P, Fricke K, Grote L, Braun AT, Kirkness J, Smith P, et al. Reductions in dead space ventilation with nasal high flow depend on physiological dead space volume: metabolic hood measurements during sleep in patients with COPD and controls. Eur Respir J. 2018 May;51(5).
27. Fricke K, Schneider H, Biselli P, Hansel NN, Zhang ZG, Sowho MO, et al. Nasal high flow, but not supplemental O(2), reduces peripheral vascular sympathetic activity during sleep in COPD patients. Int J Chron Obstruct Pulmon Dis. 2018;13:3635–43.
28. Cirio S, Piran M, Vitacca M, Piaggi G, Ceriana P, Prazzoli M, et al. Effects of heated and humidified high flow gases during high-intensity constant-load exercise on severe COPD patients with ventilatory limitation. Respir Med. 2016 Sep;118:128–32.
29. Davies JD. Noninvasive Respiratory Support at the End of Life. Respir Care. 2019 Jun;64(6):701–11.
30. Stefan MS, Eckert P, Tiru B, Friderici J, Lindenauer PK, Steingrub JS. High flow nasal oxygen therapy utilization: 7-year experience at a community teaching hospital. Hosp Pract (1995). 2018 Apr;46(2):73–6.
31. Bruni A, Garofalo E, Cammarota G, Murabito P, Astuto M, Navalesi P, et al. High Flow Through Nasal Cannula in Stable and Exacerbated Chronic Obstructive Pulmonary Disease Patients. Rev Recent Clin Trials. 2019;14(4):247–60.
32. Mansfield DR. Nasal high-flow therapy: Established roles and emerging opportunities. Vol. 24, Respirology (Carlton, Vic.). Australia; 2019. p. 1039–41.