Setting of High-Flow Nasal Oxygen Post Extubation based on Inspiratory Flow during a Spontaneous Breathing Trial

Sophia Butt

Guy's and Saint Thomas' NHS Foundation Trust <https://orcid.org/0000-0001-5700-7367>

Laura Pistidda

Guy's and Saint Thomas' NHS Foundation Trust

Leda Floris

Guy's and Saint Thomas' NHS Foundation Trust

Corrado Liperi

Universita degli Studi di Sassari

Francesco Vasques

Guy's and Saint Thomas' NHS Foundation Trust

Guy Glover

Guy's and Saint Thomas' NHS Foundation Trust

Nicholas A. Barrett

Guy's and Saint Thomas' NHS Foundation Trust

Barnaby Sanderson

Guy's and Saint Thomas' NHS Foundation Trust

Salvatore Grasso

Universita degli Studi di Bari Aldo Moro

Manu Shankar-Hari

Guy's and Saint Thomas' NHS Foundation Trust

Luigi Camporota (✉ Luigi.Camporota@gstt.nhs.uk)

Department of Adult Critical Care, Guy's and St Thomas' NHS Foundation Trust

Research

Keywords: High-flow, oxygen, intensive care, extubation, spontaneous breathing trial

Posted Date: August 25th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-62281/v1>

Abstract

Background: High flow nasal cannula (HFNC) is commonly used post-extubation in intensive care (ICU). Patients' comfort during HFNC is affected by flow rate: too low flow may limit the beneficial effects of HFNC on gas exchange and work of breathing; whilst excessive flow may reduce comfort and adherence to therapy. Currently, there is no consensus on how to set the flow rate of HFNC post-extubation. The study aims to describe the relationship between pre-extubation inspiratory flow requirements and the post-extubation flow rates on HFNC that maximises patient's level of comfort.

Methods: This was an observational, retrospective, single-site study conducted in a tertiary, university-affiliated ICU. We included all patients extubated following a successful, standardised spontaneous breathing trial (SBT) during a four-month study period. During a 30-minute SBT we recorded haemodynamic and respiratory variables including inspiratory flow, presence of any signs of respiratory distress and level of comfort using a visual analogue scale (VAS). Patients who passed the SBT were extubated onto HFNC – as per standard clinical practice. HFNC was titrated starting from a flow of 20 L/min and increased in steps of 10L/min, up to 60 L/min or maximum tolerated flow. At each step, patient's level of comfort was assessed using a VAS. Fraction of inspired oxygen (FiO_2) was titrated to maintain oxygen saturation measured by pulse oximetry (SpO_2) 92-97%.

Results: Nineteen participants were enrolled in the study with a mean (SD) age of 62.5 ± 13.1 years. There was a significant positive correlation between mean inspiratory flow pre-extubation and the flow setting on HFNC which achieved the best comfort post-extubation (r^2 0.88; $p < 0.001$). The greatest comfort was observed for HFNC flows between 30 and 40 L/min, while above 40 L/min patients' comfort decreased.

Conclusions: Measuring mean inspiratory flow during an SBT allows for individualised setting of HFNC flow rate immediately post-extubation and achieves the greatest comfort and interface tolerance.

Background

High flow nasal cannula (HFNC) is commonly used to administer supplemental oxygen in intensive care (ICU). Clinical trials have shown that the use of HFNC post-extubation decreases the incidence of reintubation, improves gas exchange and reduces the work of breathing^{1,2,3,4}. In contrast with more traditional low-flow systems, which deliver non-heated and non-humidified air/oxygen mixture, HFNC allows the administration of warmed and humidified gas with FiO_2 up to 1 at a flow rate up to 60 L/min⁵ through a nasal interface. The high flow rate presents physiological advantages over low flow⁶, allowing a better matching between the delivered gas flow and patient's spontaneous inspiratory flow, creating a positive end-expiratory pressure (PEEP) effect (generally between 2 and 8 cmH_2O ^{7,8}) and generating a "CO₂ washout" effect from the upper airways^{8,9}. Furthermore, the humidified warm gas favours the mucociliary function and reduces upper airway resistance^{10,11}. The synergistic combination of these

mechanisms leads to improved oxygenation¹⁰, decrease in neuro-ventilatory drive and work of breathing^{3, 12, 13}.

Despite growing evidence supporting the benefits of HFNC therapy, it is still unclear how to set the flow rate to achieve the optimal comfort and efficacy. Some authors, such as Hernandez⁴, Corley¹⁵ and Parke¹⁶, suggested titrating the flow in order to reach good level of oxygenation ($\text{SpO}_2 > 92-95\%$) or 'titrate to comfort', but in practice a fixed flow is often used for every patient, and titrations are not dictated by physiological parameters¹⁷. Titrating the flow rate according to measures of comfort and respiratory mechanics may increase tolerance and minimise the premature discontinuation of HFNC.

We hypothesised that the "optimal" post-extubation HFNC flow rate may be correlated to the inspiratory flow measured during a spontaneous breathing trial (SBT), and therefore may allow rapid establishment of the best HFNC setting immediately post-extubation.

Methods

Study design

This is was an observational, retrospective single-centre study conducted at Guy's & St Thomas' NHS Foundation Trust ICU, London (UK).

Patients

We collected data from all consecutive mechanically ventilated adult patients who underwent a SBT using a 'T-piece' (i.e., using PEEP and pressure support both set at 0 cmH₂O), and who then underwent tracheal tube extubation onto HFNC from 01 January through 01 April 2017. We did not include patients ventilated for <24 hours, those who did not undergo formal SBT and patients who received non-invasive ventilation (NIV) post extubation. All data were retrospectively collected, fully anonymised from our database and from the ICU electronic patient record (CareVue, Philips Medical Systems UK Limited). The study had institutional approval. The need for individual informed consent was waived as this was an analysis of data collected as part of a prospective audit for usual clinical care, with no breach of privacy or anonymity. The study qualified as a service evaluation as defined by the UK NHS Health Research Authority and therefore did not require review by the Research Ethics Committee (<http://www.hra.nhs.uk>).

Study protocol

Pre-extubation

The protocol was based on the Departmental guidelines at Guy's & St Thomas' NHS Foundation Trust. After successful pre-extubation assessment (*Online Supplement 1*), patients underwent an SBT using 0 cmH₂O pressure support and 0 cmH₂O positive end expiratory pressure (PEEP) and no automatic tube compensation. During the SBT, the mechanical ventilator (Drager V500) records all parameters including peak inspiratory flow (PIF) and mean inspiratory flow (MIF), respiratory drive (P0.1), negative inspiratory force (NIF), rapid shallow breathing index (RSBI), P0.1/NIF ratio (online supplement ETables 1 and 2). Comfort was assessed using a visual analogue scale (VAS), ranging from 0-10, immediately prior to extubation (online supplement *EFigure 1*).

Post-extubation

Post-extubation, all patients were commenced on HFNC therapy as per our standard of care and FiO₂ was adjusted in order to maintain SpO₂ 92-97%. The HFNC device included an air-oxygen blender, which allowed the accurate adjustment of FiO₂ between 0.21 and 1.0 and delivery of gas flow up to 60 L/min through a heated humidifier (MR850, Fisher & Paykel Healthcare). The gas mixture was routed through a circuit to the subject at a temperature of 37°C and an absolute humidity of 44 mgH₂O/L via large-bore nasal prongs. HFNC was initially administered at a gas flow of 20 L/min and then increased every 10-15 minutes by 10 L/min up to 60 L/min or maximum tolerated rate. At each step, patient's comfort was assessed using a VAS. The HFNC final flow was set according to patient's best comfort (online supplement *EFigure 2*).

For every day of HFNC therapy post-extubation (from day 0 to the end of therapy), HFNC setting (flow rate and FiO₂) was titrated and recorded in the patients' electronic medical record. VAS of comfort was re-assessed and final flow rates set accordingly.

Statistical analysis

Comparisons between pre-extubation ventilatory parameters and SBT-related variables versus post-extubation HFNC flow at optimum VAS were performed using multiple comparisons ANOVA with pairwise *post-hoc* comparisons. Correlation between PIF on SBT and best comfort HFNC flow rate, and MIF on SBT and best comfort HFNC flow rate were performed using Spearman's Rank correlation test. A p-value <0.05 was considered statistically significant. All analyses were performed using GraphPad Prism version 7.0 (GraphPad Software, La Jolla California, USA) and STATA v16.1 (StataCorp – USA).

Results

Baseline and pre-extubation variables

A total of 19 patients were included in the study. Baseline and demographic characteristics, reason for ICU admission and mechanical intubation are shown in the Table 1. Pre-extubation ventilatory setting and

SBT-related variables are shown in Table 2. All patients were in a supported spontaneous breathing mode of ventilation before extubation: nine patients were ventilated on CPAP (47.3%), ten on CPAP/PS (52.7%).

Table 1
Characteristic of patients at enrolment. IBW, ideal body weight; BMI, body mass index; GI, gastro-intestinal.

Demographics	
N = 19	
Age (years)	62.5 ± 13.1
Height (m)	1.7 ± 0.1
Weight (kg)	78.9 ± 15.1
IBW (kg)	62.9 ± 12.6
BMI (kg/m ²)	28.9 ± 6.4
Admission	
Medical	8
- Respiratory failure	4
- Cardiac arrest	1
- Septic shock	2
- Status Epilepticus	1
SURGERY	11
<i>Scheduled</i>	2
<i>Unscheduled</i>	9
- Cardiac surgery	3
- Vascular Surgery	6
- GI surgery	2
Duration of MV prior to extubation (days)	7.3 ± 6.7

Table 2
Ventilation parameters during mechanical ventilation prior to extubation

Ventilation parameters during mechanical ventilation					
	MAX	MIN	Δ	SD	Mean
Vt (L)	0.76	0.25	0.51	0.14	0.48
T insp (s)	0.02	0.01	0.02	0.00	0.01
RR (s)	25	9	16	4.92	17.74
FiO ₂	0.40	0.21	0.19	0.07	0.29
PEEP (cmH ₂ O)	8	5	3	0.81	5.26
PS (cmH ₂ O)	12	0	12	3.65	2.74

Table 3
Weaning criteria. Pre-extubation assessment.

Pre- extubation assessment					
	MAX	MIN	Δ	SD	Mean
P 0.1 (cmH ₂ O)	6.00	0.90	5.10	1.52	3.01
NIF (cmH ₂ O)	-11	-40	29	7.76	-31.79
RSBI (breaths/min/L)	80	14	66	18.71	42.00
P0.1/NIF	0.19	-0.19	0.38	0.08	-0.08
VAS	10	8	2	0.77	9.53

HFNC settings, comfort and pre-extubation inspiratory flow

The highest mean VAS of comfort was 8.58 seen for HFNC flow rates of both 30L/min (SD 1.57) and 40L/min (SD 1.35). Above 50 L/min of HFNC flow rate, average patients' comfort decreased significantly (Fig. 1). We found a significant, positive correlation between both pre-extubation PIF (r^2 0.53, $p < 0.001$; Fig. 2A) and MIF (r^2 0.88, $p < 0.001$; Fig. 2B), and the post-extubation HFNC flow rate associated with the patient's greatest level of comfort as defined by the highest VAS of each individual patient.

HFNC flow settings over time

All the 19 patients enrolled in the study were followed up until the discontinuation of HFNC therapy. The duration of the HFNC therapy ranged between 1 day and 7 days post-extubation. During this time, VAS for comfort and HFNC settings (flow and FiO₂) were collected and flow re-adjusted according to the level of comfort. Flow setting ranged from a 20 L/min to 50 L/min. Flow requirement was not always stable during the day, with variations of 0–20 L/min (Fig. 3).

Discussion

This study showed that the “optimal” post-extubation HFNC flow rate could be predicted by the inspiratory flow measured during the pre-extubation SBT. We found that the pre-extubation variable that best correlated with HFNC flow rate setting at which the patient was most comfortable (i.e. “optimal” post-extubation HFNC flow rate), was the mean inspiratory flow (MIF). In our study, HFNC flow rate setting associated with highest mean VAS of comfort was 30–40 L/min (Fig. 1). Comfort significantly and progressively decreased at flow setting on HFNC of 50 and 60 L/min.

The majority of studies on HFNC chose flow settings of 30–50 L/min, that were associated in our study with a mean VAS of comfort 8.02 (SD 1.64). An exception was the OPERA trial, where Futier et al¹⁸ chose flow settings post-extubation between 50 and 60 L/min. In our patients, at these relatively high flow rates, we reported a lower mean VAS of comfort compared with a flow rate of 30–40 L/min (Fig. 3). It is possible that this could explain the 7.4% premature discontinuation of HFNC in the OPERA trial. Moreover, the OPERA trial did not show improved pulmonary outcomes in patients who received HFNC compared with standard oxygen therapy. The choice of flow setting associated with lower comfort may have contributed to this outcome.

We also found a wide variation in the HFNC flow settings criteria among the previous studies. Most of the time a fixed flow was used for every patient, whilst some authors decided to titrate flow to reach good level of oxygenation with SpO₂ 92–95%. Those who decided to use a fixed flow had a higher rate of discontinuation than those who opted for a titration of flow. Stephan³, Tiruvoipati¹⁷ and Maggiore² chose a fixed flow with 1.45%, 6% and 7.4% of HFNC premature discontinuation, respectively (online supplement ETable 3. Hernandez^{4,19,20}, who titrated HFNC flow to comfort, using clinical criteria had no discontinuation. These criteria are not specified and therefore not reproducible in all settings. In this context, more standardised criteria based on physiological parameters may lead to more consistent application of optimal settings in the immediate post-extubation period. Establishing comfort immediately post extubation may improve early extubation success rate and increase patient acceptance of the interface.

Overtime, titration will require clinical assessment of comfort and respiratory effort. Indeed, in our cohort, measurements of comfort throughout the duration of HFNC therapy showed that most of the patients required changes in flow rate to achieve the optimal comfort. Variations of flow rate up to 20L/min were

required. These data suggest, that frequent flow rate adjustments could be required to optimize and maintain patient comfort during the HFNC therapy.

Limitations of these findings include that our sample size was relatively small and may not give an indication of the relationship for values outside our range of PIF and MIF. Furthermore, we have not directly considered the impact on efficacy of HFNC and respiratory function when titrating flow to best comfort.

Conclusion

We found a significant correlation between the pre-extubation MIF and the post-extubation HFNC flow rate associated with the greatest level of patient comfort. Our data suggest that the mean patient's inspiratory flow rate could be a convenient parameter for individual titration of HFNC flow rate to match patients' best comfort.

List Of Abbreviations

HFNC - High-flow nasal canulae

SBT- spontaneous breathing trial

ICU - Intensive care unit

VAS - visual analogue scale

NIV - non-invasive ventilation

PEEP - positive end expiratory pressure

PIF - peak inspiratory flow

MIF - mean inspiratory flow (MIF)

P0.1 - respiratory drive

NIF - negative inspiratory force

RSBI - rapid shallow breathing index

Declarations

Ethics approval and consent to participate

The study had institutional approval. The need for individual informed consent was waived as this was an analysis of data collected as part of a prospective audit for usual clinical care, with no breach of privacy or anonymity. The study qualified as a service evaluation as defined by the UK NHS Health Research Authority and therefore did not require review by the Research Ethics Committee (<http://www.hra.nhs.uk>).

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

Funding

Not applicable

Authors' contributions

SB made substantial contributions to the design of the project, analysed and interpreted the data, and drafted the manuscript. LP made substantial contributions to the design of the project, analysed and interpreted the data, and drafted the manuscript. LF made substantial contributions to the design of the project, analysed and interpreted the data, and contributed to revising the final manuscript. CL made substantial contributions to the design of the project, analysed and interpreted the data, and contributed to revising the final manuscript. FV made substantial contributions to the design of the project, analysed and interpreted the data, and contributed to revising the final manuscript. GG made substantial contributions to the design of the project, analysed and interpreted the data, and contributed to revising the final manuscript. NB made substantial contributions to the design of the project, analysed and interpreted the data, and contributed to revising the final manuscript. BS made substantial contributions to the design of the project, analysed and interpreted the data, and contributed to revising the final manuscript. SG made substantial contributions to the design of the project, analysed and interpreted the data, and contributed to revising the final manuscript. MS-H made substantial contributions to the design

of the project, analysed and interpreted the data, and contributed to revising the final manuscript. LC made substantial contributions to the design of the project, analysed and interpreted the data, and contributed to revising the final manuscript. The authors read and approved the final manuscript.

Acknowledgements

MSH is supported by the National Institute for Health Research Clinician Scientist Award (CS-2016-16-011). The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health and Social Care.

References

1. Frat J, Thille A, Mercat A, Girault C, Ragot S, Perbet S, et al. High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure. *N Engl J Med*. 2015;372:2185–96.
2. Maggiore S, Idone F, Vaschetto R, Festa R, Cataldo A, Antonicelli F, et al. Nasal High-Flow versus Venturi Mask Oxygen Therapy after Extubation. Effects on Oxygenation, Comfort, and Clinical Outcome. *Am J Respir Crit Care Med*. 2014;190:282–8.
3. Stéphan F, Barrucand B, Petit P, Rézaiguia-Delclaux S, Médard A, Delannoy B, et al. High-Flow Nasal Oxygen vs Noninvasive Positive Airway Pressure in Hypoxemic Patients After Cardiothoracic Surgery. *JAMA*. 2015;313:2331.
4. Hernández G, Vaquero C, González P, Subira C, Frutos-Vivar F, Rialp G, et al. Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients. *JAMA*. 2016;315:1354.
5. Kallstrom T. Oxygen Therapy for Adults in the Acute Care Facility — 2002 Revision & Update. *Respir Care*. 2002;47:717–20.
6. Spence C, Buchmann N, Jermy M, Moore S. Stereoscopic PIV measurements of flow in the nasal cavity with high flow therapy. *Exp Fluids*. 2010;50:1005–17.
7. Frizzola M, Miller T, Rodriguez M, Zhu Y, Rojas J, Hesek A, et al. High-flow nasal cannula: Impact on oxygenation and ventilation in an acute lung injury model. *Pediatr Pulmonol*. 2010;46:67–74.
8. Möller W, Celik G, Feng S, Bartenstein P, Meyer G, Eickelberg O, et al. Nasal high flow clears anatomical dead space in upper airway models. *J Appl Physiol*. 2015;118:1525–32.
9. Mauri T, Turrini C, Eronia N, Grasselli G, Volta C, Bellani G, et al. Physiologic Effects of High-Flow Nasal Cannula in Acute Hypoxemic Respiratory Failure. *American Journal of Respiratory Critical Care Med*. 2017;195:1207–15.
10. Shapiro B. Clinical application of respiratory care. St. Louis: Mosby Year Book; 1991.
11. Rittayamai N, Tscheikuna J, Rujiwit P. High-Flow Nasal Cannula Versus Conventional Oxygen Therapy After Endotracheal Extubation: A Randomized Crossover Physiologic Study. *Respir Care*. 2013;59:485–90.

12. Hasani A, Chapman T, McCool D, Smith R, Dilworth J, Agnew J. Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. *Chron Respir Dis*. 2008;5:81–6.
13. Williams R, Rankin N, Smith T, Galler D, Seakins P. Relationship between the humidity and temperature of inspired gas and the function of the airway mucosa. *Critical Care Med*. 1996;24:1920–9.
14. 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. *Crit Care*. 2018;22:120.
15. Corley A, Caruana L, Barnett A, Tronstad O, Fraser J. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. *Br J Anaesth*. 2011;107:998–1004.
16. Parke R, McGuinness S, Eccleston M. A Preliminary Randomized Controlled Trial to Assess Effectiveness of Nasal High-Flow Oxygen in Intensive Care Patients. *Respir Care*. 2011;56:265–70.
17. Tiruvoipati R, Lewis D, Haji K, Botha J. High-flow nasal oxygen vs high-flow face mask: A randomized crossover trial in extubated patients. *J Crit Care*. 2010;25:463–8.
18. Futier E, Paugam-Burtz C, Godet T, Khoy-Ear L, Rozencwajg S, Delay J, et al. Effect of early postextubation high-flow nasal cannula vs conventional oxygen therapy on hypoxaemia in patients after major abdominal surgery: a French multicentre randomised controlled trial (OPERA). *Intensive Care Med*. 2016;42:1888–98.
19. Hernández G, Vaquero C, Colinas L, Cuenca R, González P, Canabal A, et al. Effect of Postextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High-Risk Patients. *JAMA*. 2016;316:1565.
20. Fernandez R, Subira C, Frutos-Vivar F, Rialp G, Laborda C, Masclans J, et al. High-flow nasal cannula to prevent postextubation respiratory failure in high-risk non-hypercapnic patients: a randomized multicenter trial. *Ann Intensive Care*. 2017;7:47.

Figures

Figure 1

Relationship between mean VAS and HFNC flow setting during post-extubation HFNC. Line represents the mean and shaded area the 95% CI based on a fractional polynomial prediction model

Figure 2

Graph of relationship between peak inspiratory flow (A) and mean inspiratory flow (B) and HFNC setting which achieved best comfort. The regression line is shown with shaded area representing the 95% CI

Figure 3

Variation of flow during the therapy for each patient over 7 days post extubation (A) and inter-patients daily variations in HFNC (B).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [HFNCPaperSupplement15.8.20.docx](#)