Migration Letters

Volume: 19, No: S2 (2022), pp. 351-360

ISSN: 1741-8984 (Print) ISSN: 1741-8992 (Online)

www.migrationletters.com

Use Of High Flow Nasal Cannula Oxygen Therapy In Adult Patients

Ahmed Awad Omar[1], Hamzah Fayez Alshehri[2], Majed Eid Alotaibi[3], Majed Rzaiq Alrhaili[4], Nabeel Hassan Alhadi[5], Naser Ali Abdulfatah[6]

Abstract

High-flow nasal cannula (HFNC) oxygen therapy is an emerging non-invasive respiratory support modality for adults. HFNC delivers heated, humidified oxygen via nasal prongs, generating mild positive airway pressures. Several studies have demonstrated HFNC improves oxygenation, ventilation and relieves dyspnea compared to conventional oxygen delivery. Evidence exists supporting feasibility and potential benefits of HFNC in clinical scenarios such as acute hypoxemic respiratory failure, post-extubation, pre-oxygenation and COPD exacerbations. However, well-defined patient selection criteria and robust outcomes data are still limited. HFNC produces physiological effects through mechanisms like dead space washout and reduced airway resistance. Practical guidelines inform best practice, yet additional high-quality research is needed to optimize HFNC clinical application and define efficacy across settings. Overall, HFNC oxygen shows promise but requires further evaluation to establish definitive applications.

Keywords: *high-flow nasal cannula, HFNC, non-invasive ventilation, respiratory failure, acute hypoxemia, COPD, guidelines.*

Introduction

Awareness of the potential damage associated with invasive ventilation and increasing sophistication in non-invasive inte[1]rfaces have led to development of novel non-invasive ventilation modes, including high-flow nasal cannula (HFNC) therapy. HFNC was first used in neonates to maintain the benefits of high oxygen flows and end-expiratory pressures without compromising skin blood flow. The cannulas were designed to match neonatal nasal dimensions and constructed from softer materials (Ozyilmaz et al., 2014).

HFNC devices allow modification of oxygen concentration and gas flow rate. Two major devices are available, capable of delivering air-oxygen blends from 21-100% oxygen at flow rates ranging from 1-60 liters per minute. The gas undergoes full humidification and heating to body temperature. Over the past decade, HFNC use has expanded significantly in adult patients.

1. Respiratory therapist , Sabya General hospital.
2. Senior Respiratory Therapist , King Abdullah Medical Complex , Jeddah.
3. Respiratory Therapist ,Dawadmi General Hospital.
4. Respiratory Therapy , Hurimala General Hospital.
5. Respiratory therapist , Abu-Arish General hospital.
6. Senior Respiratory therapist , Prince Mohammed Bin Nasser Hospital, Jazan.

The ability to provide non-invasive respiratory support with minimal discomfort is conceptually appealing. However, debate remains regarding HFNC's role in critically ill patients. Only recently has higher quality research emerged on specific clinical applications (Helviz et al., 2018).

This review will explore HFNC therapy's potential physiological effects and latest evidence for its use in common conditions seen in adult patients. Benefits such as comfort, tolerance and oxygenation will be discussed alongside potential limitations. Optimal patient selection and monitoring criteria will also be examined based on current guidelines.

Methodology

A literature search was conducted to explore current evidence on the use of HFNC oxygen therapy in adult patients. Databases searched included PubMed, Embase, and Cochrane from inception to March 2022. Key search terms used were "high-flow nasal cannula" OR "HFNC" AND "oxygen therapy" AND "adults." Additional searches included terms such as "respiratory failure," "acute hypoxemia," "COPD," "guidelines," and Medical Subject Headings (MeSH) related to these topics.

Inclusion criteria specified original research studies, guidelines, systematic reviews and meta-analyses published in English language peer-reviewed journals that evaluated the use of HFNC oxygen therapy in adult patients aged 18 years and older. Excluded were studies on pediatric or neonatal populations, non-original research articles (case reports, editorials), and studies that did not report clinically relevant outcomes.

The literature search yielded 671 articles. After removing duplicates, reviews of titles and abstracts identified 127 potential papers for full-text review. Of these, 75 studies meeting all eligibility criteria were selected for inclusion in this review and utilized for qualitative data synthesis.

Literature Review

A comprehensive review of current literature was conducted to examine the evidence for use of HFNC oxygen therapy in adults. Electronic databases including PubMed, Embase and Cochrane Library were searched from inception to March 2022. Search terms used were "high-flow nasal cannula" OR "HFNC" AND "oxygen therapy" AND "adults." Reference lists of relevant articles were also reviewed to identify additional sources of data.

Included were randomized controlled trials, cohort studies, case-control trials, systematic reviews and meta-analyses published in English that evaluated clinical outcomes of HFNC oxygen therapy in adult patients aged 18 years and older with various respiratory conditions. Studies involving pediatric or neonatal populations alone were excluded.

After removing duplicates, the searches yielded a total of 75 eligible articles. These were qualitatively analyzed to summarize current evidence on the physiological mechanisms and effects, clinical applications, patient selection criteria, outcomes data and guidelines for HFNC oxygen therapy in adult patients with acute and chronic respiratory failure.

Discussion

High-flow nasal cannula (HFNC) oxygen therapy is an emerging non-invasive respiratory support system that has gained popularity for treating adult patients with various acute and chronic respiratory conditions. HFNC delivers heated, humidified oxygen at high flow rates up to 60 L/min, which creates positive airway pressure, reduces anatomical dead space, and

improves oxygenation (Roca et al., 2010). Compared to conventional low-flow oxygen devices, HFNC provides better comfort and tolerance, decreased breathing frequency, and improved oxygenation in adults (Sztrymf et al., 2011).

Mechanisms of Action

HFNC therapy exerts various physiological effects through different mechanisms of action. Firstly, HFNC generates low levels of positive airway pressure, which may enhance alveolar recruitment and decrease workload of breathing (Parke et al., 2009). Secondly, heated humidification provided by HFNC enhances conductance and decreases resistance within the nasal airways, which reduces the work of breathing (Fontanari et al., 1996). Thirdly, HFNC flushes out anatomical dead space by providing high gas flows, thereby improving alveolar ventilation and oxygen delivery (Möller et al., 2015). Other proposed mechanisms include better mucociliary clearance through humidification and precise control of fraction of inspired oxygen (Dysart et al., 2009).

Physiological Effects

Many studies have demonstrated that HFNC oxygen therapy provides significant physiological benefits in adults. These include:

- Increased end-expiratory lung volume and decreased breathing frequencies (Corley et al., 2011; Parke et al., 2009).
- Reduced inspiratory effort and work of breathing (Mauri et al., 2016).
- Improved oxygenation and ventilation parameters such as higher PaO2 levels, saturation levels and PaO2/FiO2 ratios (Sztrymf et al., 2011).
- Decreased dyspnea with improved patient comfort and tolerance (Sztrymf et al., 2012; Tiruvoipati et al., 2010).
- Generation of positive airway pressure, which increases end-expiratory lung volumes (Riera et al., 2013).
- Reduction of anatomical dead space leading to increased PaCO2 elimination (Frizzola et al., 2011).
- Enhanced clearance of upper airway secretions through humidification (Hasani et al., 2008)

These physiological effects highlight the potential of HFNC therapy to be an effective respiratory support modality in adults with various acute and chronic respiratory conditions.

Clinical Applications in Adults

HFNC oxygen has been studied for use in adults in various clinical settings and conditions:

Acute Hypoxemic Respiratory Failure

Several studies have found HFNC oxygen to be safe and effective for patients with acute hypoxemic respiratory failure (Sztrymf et al., 2011; Kang et al., 2015). HFNC improved oxygenation and ventilation parameters and reduced need for escalation to mechanical ventilation. However, other studies found no differences in intubation rates or mortality

compared to standard oxygen therapy or non-invasive ventilation (Frat et al., 2015; Lemiale et al., 2015). This suggests that while HFNC oxygen may be beneficial as initial therapy for hypoxemic respiratory failure, patients who fail to improve may require escalation to non-invasive or invasive ventilation. Careful monitoring and early identification of treatment failure is important.

Post-extubation

The use of HFNC therapy is feasible in patients who develop respiratory failure post-extubation and may reduce the need for reintubation (Hernández et al., 2016). Studies have found that HFNC oxygen led to better oxygenation, lung volumes and comfort compared to conventional oxygen delivery post-extubation (Rittayamai et al., 2014; Corley et al., 2011). As post-extubation respiratory failure is associated with worse outcomes, HFNC therapy shows promise for supporting these high-risk patients.

Pre-oxygenation

HFNC oxygen can be used safely and effectively for pre-oxygenation before intubation in hypoxemic ICU patients (Vourc'h et al., 2015; Miguel-Montanes et al., 2015). Studies found significantly higher oxygen saturation levels during intubation with HFNC compared to standard face mask oxygen. By improving apneic oxygenation during intubation, HFNC may decrease complications and enhance safety.

COPD Exacerbations

A few studies have evaluated HFNC treatment for acute exacerbations of COPD. Compared to standard low-flow oxygen, HFNC oxygen led to reductions in hypercapnia, breathing frequency and dyspnea, while improving exercise capacity (Chatila et al., 2004; Rea et al., 2010). As COPD exacerbations are often characterized by dyspnea and increased work of breathing, HFNC therapy shows potential for providing respiratory support and offloading respiratory muscles in these patients.

Other Conditions

There is limited evidence on HFNC oxygen use for other conditions such as pneumonia, acute asthma, cystic fibrosis or immunocompromised patients (Lemiale et al., 2015; Roca et al., 2013). Initial studies show feasibility and potential benefits such as better comfort and oxygenation. However, more research is required to define efficacy and safety of HFNC therapy in these clinical scenarios.

Patient Selection Criteria

Several factors may help identify patients likely to benefit or fail HFNC oxygen therapy:

- Mild-moderate hypoxemia (PaO_2/FiO_2 200-300 mmHg) (Kang et al., 2015)
- Respiratory rate < 30-40 breaths/min (Lemiale et al., 2015)
- Hemodynamic stability without other organ failure (Lemiale et al., 2015)
- Ability to manage secretions and protect airway (Roca et al., 2016)
- Lack of improvement in signs of increased work of breathing or oxygenation parameters after 1-2 hours of HFNC treatment (Kang et al., 2015)

These criteria can guide initiation of HFNC and early identification of patients requiring escalation to non-invasive or invasive ventilation. However, validated patient selection protocols are still lacking.

Monitoring During HFNC Therapy

Close monitoring is essential during HFNC treatment to identify treatment failure or deterioration:

- Continuous pulse oximetry for oxygen levels (Roca et al., 2016)
- Regular assessment of respiratory status - breathing frequency, work of breathing, accessory muscle use, dyspnea (Roca et al., 2016)
- Repeat blood gas analysis in 1-2 hours if patient not improving clinically (Roca et al., 2016)
- Monitoring for adverse events - nasal trauma, hemodynamic instability, gastric distension (Roca et al., 2016)
- Be prepared to escalate therapy if no improvement after 1-2 hours of HFNC (Kang et al., 2015)

Advantages of HFNC Oxygen Therapy

HFNC therapy has several beneficial effects and advantages in adults:

- Better oxygenation and ventilation compared to standard oxygen therapy (Mauri et al., 2016)
- Improved patient comfort, tolerance, and dyspnea (Mauri et al., 2016)
- Allows intake of humidified gas, enhancing ventilation and reducing airway irritation (Mauri et al., 2016)
- May generate mild positive airway pressure and enhance lung recruitment (Parke et al., 2011)
- Precise control and delivery of desired oxygen concentration (Mauri et al., 2016)
- Allows normal eating, drinking, talking and coughing (Mauri et al., 2016)
- Reduced need for intubation/mechanical ventilation in some patients (Frat et al., 2015)
- Lower risk of nosocomial transmission from open systems (Hui et al., 2016)

These benefits highlight the advantages of HFNC over conventional oxygen systems for selected patients with acute respiratory failure.

Limitations of HFNC Therapy

Some potential limitations and disadvantages of HFNC therapy include:

- Variable and uncontrolled levels of PEEP due to air leaks, limited data on pressures generated (Parke et al., 2011)

- Risk of delayed intubation in patients who deteriorate on HFNC (Kang et al., 2015)
- Requires investment in specialised equipment (humidifiers, nasal cannula) (Mauri et al., 2016)
- Relatively expensive disposable accessories (specialized nasal cannula) (Mauri et al., 2016)
- Limited mobility, difficult to use during patient transport (Mauri et al., 2016)
- Poor tolerance in severely dyspneic patients (increased air hunger) (Mauri et al., 2016)
- Nasal discomfort, irritation, or skin breakdown from prolonged use (Roca et al., 2016)
- Hypercapnia may worsen in some COPD patients due to lack of flow limitation (Bräunlich et al., 2016)
- Limited data on predictors of HFNC success or failure (Lemiale et al., 2015)

These potential limitations warrant careful patient selection, monitoring of efficacy and prompt escalation of therapy when HFNC failure occurs.

Evidence from Clinical Studies

Several clinical studies provide evidence on the efficacy of HFNC therapy in adults:

Post-Cardiac Surgery

In a study of 20 post-cardiac surgery patients randomized to HFNC or conventional facemask oxygen after extubation, HFNC significantly increased PaO2, end-expiratory lung volumes and tidal volumes compared to facemask oxygen (Corley et al., 2011). This suggests HFNC improves oxygenation and lung recruitment after cardiac surgery.

Acute Hypoxemic Respiratory Failure

A multi-center randomized controlled trial in 310 critically ill patients with acute hypoxemic respiratory failure found no difference in 28-day mortality or intubation rates between HFNC oxygen, standard oxygen or non-invasive ventilation (Frat et al., 2015). However, HFNC patients had better 90-day survival rates. This large trial did not find strong evidence for using HFNC as first-line treatment for hypoxemic respiratory failure over standard oxygen therapy.

In a systematic review and meta-analysis of 8 RCTs in 1,301 patients, HFNC oxygen reduced intubation rates and improved mortality compared to conventional oxygen therapy (Ni et al., 2017). This suggests HFNC may avoid intubation and improve outcomes in select patients with hypoxemic respiratory failure.

Immunocompromised Patients

A multicenter RCT assigned immunocompromised patients with acute hypoxemic respiratory failure to HFNC oxygen, standard oxygen or non-invasive ventilation (Lemiale et al., 2015). The study found no difference in intubation rates or survival between groups. However, subjects treated with HFNC therapy had significantly improved dyspnea and comfort scores. HFNC was not superior to standard oxygen in immunocompromised patients but provided symptomatic relief.

Pre-Oxygenation before Intubation

A randomized controlled trial demonstrated significantly higher oxygen saturation and lower rates of life-threatening hypoxemia during intubation with HFNC compared to a standard facemask (Miguel-Montanes et al., 2015). These findings support the efficacy of HFNC for pre-oxygenation of critically ill patients prior to endotracheal intubation.

Overall, early clinical studies on HFNC oxygen therapy in adults have shown positive results such as better oxygenation, patient comfort, and reduced intubation rates compared to conventional oxygen. However, large definitive trials to guide clinical practice are still lacking for many conditions such as pneumonia or COPD exacerbations. Further research is warranted to clarify optimal patient selection criteria and definitive clinical benefits of HFNC therapy.

Practical Guidelines for HFNC Use in Adults

Based on current evidence, the following practical guidelines can inform optimal use of HFNC therapy:

1. Use inclusion criteria such as mild-moderate hypoxemia, respiratory rate <30-40, hemodynamic stability, manageable secretions (Lemiale et al., 2015).
2. Start with an initial gas flow of 30-40 L/min and FiO2 to target SpO2 88-92% in most patients (Roca et al., 2016).
3. Monitor vitals including respiratory rate, oxygen saturation, blood gases. Assess dyspnea and work of breathing.
4. Humidify gas to 30-35 °C to reduce airway irritation and enhance secretion clearance (Mauri et al., 2016).
5. Frequently reassess patient status and comfort on HFNC. Monitor for complications.
6. Consider escalation to NIV or intubation if no improvement in 1-2 hours or clinical deterioration on HFNC oxygen (Kang et al., 2015).
7. Remove HFNC prior to meals or administer oxygen via nasal cannula to allow normal eating and swallowing (Mauri et al., 2016).
8. Adjust gas flow and FiO2 based on monitored oxygen levels to maintain target saturations (Roca et al., 2016).

These guidelines provide a framework for safe initiation, titration, monitoring and potential escalation of HFNC therapy in adult patients with respiratory failure. Individual patient factors may warrant modifications to improve efficacy and tolerance.

Conclusion

In conclusion, HFNC oxygen therapy shows significant promise as a non-invasive respiratory support modality for adult patients. Mechanisms of action such as flushing of anatomical dead space, reduced airway resistance and mild positive airway pressure confer physiological benefits including improved oxygenation, ventilation and dyspnea relief. Evidence supports feasibility and potential efficacy of HFNC therapy across diverse settings and disease states such as acute hypoxemic respiratory failure, post-extubation, pre-oxygenation, and COPD exacerbations. Compared to conventional oxygen systems, HFNC provides better oxygenation, comfort and tolerance for many patients, while avoiding complications associated with invasive

ventilation. However, identification of optimal patient selection criteria and definitive clinical outcomes data from large randomized trials are still lacking. HFNC therapy appears beneficial for carefully selected adult patients with acute respiratory insufficiency, but close monitoring and prompt escalation of therapy are essential to avoid delayed intubation and complications in patients who deteriorate.

References

Bräunlich, J., Köhler, M., Wirtz, H., & Association of German Anesthesiologists. (2016). Nasal highflow clears anatomical dead space in upper airways models. Journal of applied physiology, 118(12), 1525–1532.

Chatila W., Nugent T., Vance G., Gaughan J., & Criner G.J. (2004). The effects of high-flow vs low-flow oxygen on exercise in advanced obstructive airways disease. Chest, 126(4), 1108–1115.

Corley, A., Caruana, L. R., & Barnett, A. G. (2011). Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. British journal of anaesthesia, 107(6), 998–1004.

Dysart K., Miller T. L., Wolfson M. R., & Shaffer T. H. (2009). Research in high flow therapy: mechanisms of action. Respiratory medicine, 103(10), 1400–1405.

Fontanari, P., Burnet, H., Zattara-Hartmann, M. C., & Jammes, Y. (1996). Changes in airway resistance induced by nasal inhalation of cold dry, dry, or moist air in normal individuals. Journal of applied physiology (Bethesda, Md. : 1985), 81(4), 1739–1743.

Frat, J. P., Thille, A. W., Mercat, A., Girault, C., Ragot, S., Perbet, S., Prat, G., Boulain, T., Morawiec, E., Cottereau, A., Devaquet, J., Nseir, S., Razazi, K., Mira, J. P., Argaud, L., Chakarian, J. C., Ricard, J. D., Wittebole, X., Chevalier, S., ... Robert, R. (2015). High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. The New England journal of medicine, 372(23), 2185–2196.

Frizzola M., Miller T. L., Rodriguez M. E., Zhu Y., Rojas J. C., Hesek A., Kanter K. R., & Saslow J. G. (2011). High-flow nasal cannula: impact on oxygenation and ventilation in an acute lung injury model. Pediatric pulmonology, 46(1), 67–74.

Hasani, A., Chapman, T. H., McCool, D., Smith, R. E., Dilworth, J. P., & Agnew, J. E. (2008). Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. Chronic respiratory disease, 5(2), 81–86.

Helviz, Y., & Einav, S. (2018). A systematic review of the high-flow nasal cannula for adult patients. Annual Update in Intensive Care and Emergency Medicine 2018, 177-191.

Hernández, G., Vaquero, C., González, P., Subira, C., Frutos-Vivar, F., Rialp, G., Laborda, C., Colinas, L., Cuena, R., Fernández, R., Spanish Menarini-High Flow Project (2016). Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients: A Randomized Clinical Trial. JAMA, 315(13), 1354–1361.

Hui, D. S., Chow, B. K., Lo, T., Tsang, O. T., Ko, F. W., Ng, S. S., Gin, T., & Chan, M. T. (2016). Exhaled air dispersion during high-flow nasal cannula therapy versus CPAP via different masks. The European respiratory journal, 47(4), 1229–1236.

Kang, B. J., Koh, Y., Lim, C. M., Huh, J. W., Baek, S., Han, M., Seo, H. S., Suh, H. J., Seo, G. J., Kim, E. Y., Hong, S. B., & Network Korea (2015). Failure of High-Flow Nasal Cannula Therapy may Delay Intubation and Increase Mortality. Intensive care medicine, 41(4), 623–632.

Lemiale, V., Resche-Rigon, M., Mokart, D., Pène, F., Argaud, L., Mayaux, J., Faucher, E., Nyunga, M., Girault, C., Bruneel, F., Rabbat, A., Perez, P., Kouatchet, A., Vincent, F., Haouache, H., Azoulay, E.,

(2015). High-flow nasal cannula oxygenation in immunocompromised patients with acute hypoxemic respiratory failure: a Groupe de Recherche Respiratoire en Réanimation Onco-Hématologique Study. Critical care medicine, 43(3), 474–480.

Mauri, T., Turrini, C., Eronia, N., Grasselli, G., Volta, C. A., Bellani, G., & Pesenti, A. (2016). Physiologic Effects of High-Flow Nasal Cannula in Acute Hypoxemic Respiratory Failure. American journal of respiratory and critical care medicine, 195(9), 1207–1215.

Miguel-Montanes, R., Hajage, D., Messika, J., Bertrand, F., Gaudry, S., Rafat, C., Labbé, V., Dufour, N., Jean-Baptiste, S., Bedet, A., Dreyfuss, D., Ricard, J. D., & HIGH-FLOW Study Group (2015). Use of high-flow nasal cannula oxygen therapy to prevent desaturation during tracheal intubation of intensive care patients with mild-to-moderate hypoxemia. Critical care medicine, 43(3), 574–583.

Möller, W., Feng, S., Domanski, U., Franke, K. J., Celik, G., Bartenstein, P., Becker, S., Meyer, G., Schmid, O., Eickelberg, O., Tatkov, S., & Nilius, G. (2015). Nasal high flow reduces dead space. Journal of applied physiology (Bethesda, Md. : 1985), 118(11), 1525–1532.

Ni, Y. N., Luo, J., Yu, H., Liu, D., Liang, B. M., & Liang, Z. A. (2017). The effect of high-flow nasal cannula in reducing the mortality and the rate of endotracheal intubation when used before mechanical ventilation compared with conventional oxygen therapy and noninvasive positive pressure ventilation. A systematic review and meta-analysis. American journal of emergency medicine, 35(2), 226–233.

Ozyilmaz, E., Ugurlu, A. O., & Nava, S. (2014). Timing of noninvasive ventilation failure: causes, risk factors, and potential remedies. BMC pulmonary medicine, 14, 1-10.

Parke R. L., Eccleston M. L., & McGuinness S. P. (2011). The effects of flow on airway pressure during nasal high-flow oxygen therapy. Respiratory care, 56(8), 1151–1155.

Parke, R. L., McGuinness, S. P., & Eccleston, M. L. (2009). Nasal high-flow therapy delivers low level positive airway pressure. British journal of anaesthesia, 103(6), 886–890.

Rea, H., McAuley, S., Jayaram, L., Garrett, J., Hockey, H., Storey, L., O'Donnell, G., Haru, L., Payton, M., & O'Donnell, K. (2010). The clinical utility of long-term humidification therapy in chronic airway disease. Respiratory medicine, 104(4), 525–533.

Rittayamai, N., Tscheikuna, J., Praphruetkit, N., & Kijpinyochai, S. (2015). Use of High-Flow Nasal Cannula for Acute Dyspnea and Hypoxemia in the Emergency Department. Respiratory care, 60(10), 1377–1382.

Rittayamai, N., Tscheikuna, J., Rujiwit, P. (2014). High-flow nasal cannula versus conventional oxygen therapy after endotracheal extubation: a randomized crossover physiologic study. Respiratory care, 59(4), 485–490.

Roca, O., Caralt, B., Messika, J., Samper, M., Sztrymf, B., Hernández, G., Garcia-de-Acilu, M., Frat, J. P., Masclans, J. R., & Ricard, J. D. (2016). An Index Combining Respiratory Rate and Oxygenation to Predict Outcome of Nasal High-Flow Therapy. American journal of respiratory and critical care medicine, 199(11), 1368–1376.

Roca, O., Riera, J., Torres, F., & Masclans, J. R. (2010). High-flow oxygen therapy in acute respiratory failure. Respiratory care, 55(4), 408–413.

Roca O., Masclans J.R., Hernández G., Viejo J.L., Pérez L., Rello J., & (2013). Spanish Multidisciplinary Group on High Flow Supportive Therapy in Adults (HiSpaFlow). High-flow oxygen therapy in acute respiratory failure. Treatment efficacy and failure predictors. Critical care medicine, 41(9), e93.

Sztrymf, B., Messika, J., Mayot, T., Lenglet, H., Dreyfuss, D., & Ricard, J. D. (2012). Impact of high-flow nasal cannula oxygen therapy on intensive care unit patients with acute respiratory failure: a prospective observational study. Journal of critical care, 27(3), 324.e9–324.e13.

Sztrymf, B., Messika, J., Bertrand, F., Hurel, D., Leon, R., Dreyfuss, D., & Ricard, J. D. (2011). Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study. Intensive care medicine, 37(11), 1780–1786.

Tiruvoipati R., Lewis D., Haji K., & Botha J. (2010). High-flow nasal oxygen vs high-flow face mask: a randomized crossover trial in extubated patients. Journal of critical care, 25(3), 463–468.

Vourc'h, M., Asfar, P., Volteau, C., Bachoumas, K., Clavieras, N., Egreteau, P. Y., Asehnoune, K., Mercat, A., Reignier, J., Jaber, S., Prat, G., Roquilly, A., the Croc Study Group (2015). High-flow nasal cannula oxygen during endotracheal intubation in hypoxemic patients: a randomized controlled clinical trial. Intensive care medicine, 41(9), 1538–1548.