Research Trends on High-Flow Nasal Cannula Oxygen Therapy: A Bibliometric Analysis from 2000 to 2019

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Research

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Abstract

Purpose: High-flow nasal cannula oxygen therapy (HFNC) has been increasingly reported over the past decades. Therefore, this study aimed to analyze the evolution of HFNC research and qualitatively and quantitatively evaluate publications.

Methods: Publications between 2000 and 2019 were retrieved from the Web of Science Core Collection on August 17, 2020, according to a search strategy. Different kinds of software, CiteSpace and VOSviewer, and an online bibliometric analysis platform were used to identify top authors, journals, institutions, countries, keywords, co-cited articles, and trends.

Results: Finally, 835 publications were identified, and the annual number of publications showed an increasing trend. Of these, 273 journals published articles related to HFNC. The United States and the University of Melbourne were the leading country and institution for publications, respectively. Co-cited reference analysis revealed top landmark articles. High-flow nasal cannula, bronchiolitis, hypercapnia, newborn, and immunosuppression are some of the high-frequency keywords in the co-occurrence cluster and co-cited reference cluster analyses, indicating that the clinical application of oxygen therapy remains a hot spot. Burst detection analysis of top keywords showed that randomized controlled trial, viral bronchiolitis, and immunocompromised patient were the new research foci.

Conclusions: Bronchopulmonary dysplasia, infant, premature infant, respiratory distress syndrome, critical care patient, preoxygenation, extubation failure, and acute lung injury are the research foci of HFNC over the past 20 years and have emerged as a basis for transformation from infancy to adulthood and from a single disease to diverse diseases.

Background

The commonly used methods for oxygen inhalation include nasal catheter and face mask. Nasal catheter oxygen inhalation has advantages of simplicity, economy, convenience, and comfort, but when the oxygen flow is > 6 L/min, the dry and cold gas that does not reach ideal humidification will result in discomfort for patients, including frontal sinus pain, nasal mucosa dryness, and even bleeding [1]. The flow restriction directly affects the patient's inhaled oxygen concentration (FiO_2). Although mask oxygen inhalation can provide patients with higher FiO_2 , it will cause inconvenience while eating and drinking water, and patients will have a sense of restraint and occlusion, which are intolerable for many patients [2, 3].

The high-flow nasal cannula oxygen therapy (HFNC) device can output high-flow gas with a constant oxygen concentration of 21–100%, temperature of approximately 37 °C, and relative humidity of 100%, thereby taking into account the advantages of ordinary nasal catheter and face mask. Moreover, as the output flow can reach 60 L/min, it produces a certain positive pressure and increases the functional residual volume [4, 5], gradually making it another choice in addition to noninvasive ventilation (NIV) in adult patients with mild to moderate acute respiratory failure (ARF) [6–8], and plays an increasingly important role in patients with cardiac insufficiency [9, 10] or patients undergoing respiratory tract invasive surgeries [11, 12]. As an alternative to nasal continuous positive airway pressure, HFNC is widely used in neonates with acute respiratory distress syndrome [13], and its application in adult patients is increasing over time.

Bibliometric analysis is a statistical method based on a public literature database (such as the Web of Science) used to analyze and visualize a research trend [14, 15]. Bibliometric analysis provides not only quantitative and qualitative evaluation of publications but also developing trends of a research domain. It can also present the most influential research quickly and accurately, which provides a theoretical basis for further research. In addition, this information may be used as a policy guideline for decision makers [16].

Therefore, in this study, a bibliometric analysis of publications on HFNC published from 2000 to 2019 was performed. On the basis of our results, we will provide an overview of the achievements and future research trends and hotspots in this research domain.

Methods

The Institute for Scientific Information Web of Science Core Collection database was comprehensively searched using the following search strategy: TS = (((((((((((("HFNC") OR ("high flow nasal cannula") OR ("humidified high-flow nasal cannula") OR ("HHFNC") OR ("heated humidified high-flow nasal cannula") OR ("HHHFNC") OR ("high flow nasal oxygen") OR ("HFNO") OR ("high flow oxygen") OR ("nasal high flow")))))))))))) AND Language = English, with a limited time frame set from 2000 to 2019. We completed all literature retrieval and data downloads in one single day, August 17, 2020, to reduce bias incurred by frequent database updates. The manuscripts were screened and recorded for titles, authors, countries, institutions, journals, and total/average citation numbers. Next, the bibliometric method, the Online Analysis Platform of Biobliometry (<http://bibliometric.com/>), CiteSpace V5.6.R5 SE, 64 bit (Drexel University, Philadelphia, PA, USA), and VOSviewer 1.6.15 (Leiden University, Leiden, The Netherlands) were used to identify top authors, journals, institutions, countries, keywords, co-cited articles, and trends.

Results

Distribution of articles by publication years

Between 2000 and 2019, 835 original research articles (687 articles and 148 reviews) were published. An increasing trend was observed for the quantity of research publications on HFNC (Fig. 1A). The number of published articles on HFNC was relatively stable from 2000 to 2012, and then, the number of publications significantly increased from 2013 onward, with the number of publications doubled in 2013 compared to that in 2012. In 2019, the activity in HFNC research reached a peak.

Country/region And Institution Analysis

The 835 articles on HFNC research were published by research groups in 56 countries/regions. The top 10 countries (5 European countries, 2 Oceanian countries, 2 North American countries, and 1 Asian countries) published 794 articles, accounting for 95.09% of the total number of publications (Fig. 1B), with the United States as the leading country, which comprised 28.98% (242/835), followed by Australia and France, which accounted for 12.57% and 12.46% of the total number of publications, respectively. There were 1470 research institutions that published articles related to HFNC. The leading research institution with the highest number of publications was the University of Melbourne (58 articles), followed by the University of Toronto (53 articles), the University of Queensland (53 articles), and INSERM (41 articles). The research network among institutions showed a low-density map (density, 0.0251; Fig. 1C), indicating that the research groups are comparatively dispersed throughout various institutions, and thus, further academic collaborations are needed.

Journal Analysis

The total number of journals that published these 835 articles on HFNC was 273. The characteristics of the 10 most active journals are shown in Table 1. Most of the journal publishers are located in the United States and the United Kingdom. *Respiratory Care* published the highest number of articles on HFNC, followed by *Pediatric Pulmonology* and *Intensive Care Medicine*. As to the impact factor, *Intensive Care Medicine* has the highest, followed by *Critical Care* and *Annals of Intensive Care*. Regarding the JCR quartile, *Intensive Care Medicine* and *Critical Care* were ranked as Q1, *BMJ Open* and *ACTA Paediatrica* were ranked as Q2, *Journal of Critical Care* was ranked as Q3, and the ranks of *Pediatric Pulmonology*, *Pediatric Critical Care Medicine*, and *Journal of Perinatology* were dependent on the JCR partition.

Table 1
The top 10 journals that published articles on high-flow nasal cannula oxygen therapy

Rank	Journal	Frequency	Total citations	Average citation per paper	Country	JCR	Impact factor (2019)
1	RESPIRATORY CARE	76	1145	15.07	USA	□	2.066
2	PEDIATRIC PULMONOLOGY	29	326	11.24	USA	Q1/Q3	2.534
3	INTENSIVE CARE MEDICINE	21	759	36.14	USA	Q1	17.679
4	PEDIATRIC CRITICAL CARE MEDICINE	20	187	9.35	USA	Q1/Q3	2.854
5	JOURNAL OF CRITICAL CARE	17	284	16.71	UK	Q3	2.685
6	ANNALS OF INTENSIVE CARE	16	82	5.13	Germany	□	4.124
7	BMJ OPEN	16	19	1.19	UK	Q2	2.496
8	CRITICAL CARE	15	146	9.73	UK	Q1	6.407
9	ACTA PAEDIATRICA	14	80	5.71	USA	Q2	2.111
10	JOURNAL OF PERINATOLOGY	13	466	35.85	UK	Q1/Q2	1.967

Top Authors And Co-cited Author Analysis

Among all 3,788 writers in HFNC research, the top 10 most productive authors are shown in Table 2. J.D. Ricard from Hôpital Louis Mourier and Université Paris Diderot ranked first (21 articles), followed by J.P. Frat from Centre Hospitalier Universitaire (CHU) de Poitiers and INSERM as the second (20 articles). We applied centrality to quantify the significance of nodes in the network, whereby higher centrality indicated that the node is more influential in the network. In terms of centrality, J.D. Ricard and K. Dysart ranked first in authors and cited authors, respectively. J.P. Frat and M. Antonelli were among the top 10 authors and cited authors. These researchers have made tremendous contributions and have become authorities in HFNC research. Using CiteSpace software, networks of citation information were visualized for authors (Fig. 1D) and co-cited authors (Fig. 1E). J.P. Frat, with a citation number of 320, ranked first, followed by O. Roca (253), R.L. Parke (244), and B. Sztrymf (219).

Table 2
The top 10 most productive authors and co-cited authors who contributed to publications in high-flow oxygen therapy research

Rank	Author	Article counts	centrality	Total number of citations	Average number of citations	First author counts	First author citation counts	Average first author citation counts	Corresponding author	Corresponding author citation counts	Co-cited author	Citat coun
1	Ricard, JD	21	0.11	759	36.14	3	51	17	8	418	Frat, JP	320
2	Frat, JP	20	0.04	396	19.8	10	316	31.6	11	316	Roca, O	253
3	Schibler, A	19	0.00	341	17.95	2	85	42.5	4	86	Parke, RL	244
4	Davis, PG	19	0.00	233	12.26	0	0	0	0	0	Sztrymf, B	219
5	Thille, AW	18	0.02	339	18.83	3	2	0.67	2	2	Parke, R	177
6	Jaber, S	17	0.06	309	18.18	3	43	14.33	5	68	Dysart, K	171
7	Manley, BJ	16	0.00	185	11.56	7	75	10.71	7	75	Corley, A	164
8	Girault, C	14	0.01	334	23.86	0	0	0	1	0	Hernandez, G	161
9	Azoulay, E	13	0.01	121	9.31	4	27	6.75	5	27	Milesi, C	132
10	Antonelli, M	13	0.02	150	11.54	1	0	0	3	3	Antonelli M	122

Keyword co-occurrence cluster analysis of research hot spots

VOSviewer keyword analysis of 835 articles identified 165 keywords with a minimum of 10 occurrences, and we divided them into five clusters (therapy, noninvasive ventilation, positive airway pressure, high-flow nasal cannula, and intubation) (Fig. 2A, 2B).

Top Co-cited Articles And Co-cited Reference Cluster Analysis

The co-citation and clustered network map were generated from 14,976 references using CiteSpace in a hierarchical order (Fig. 2C, 2D). Visualization of co-cited articles showed a total of 529 nodes and 1,459 links (Fig. 2C). In this network, each node represents a cited article, and the size of each node is proportional to the total co-citation frequency of the associated article. As shown in Fig. 2D, co-cited references were clustered into nine major cluster labels, including oxygen therapy, vapotherm, bronchiolitis, newborn, sepsis bundles, immunosuppression, submicrometer aerosols, high-flow nasal cannula oxygen, and hypercapnia. Figure 2E displays a timeline view of distinct co-citation, showing that cluster #0 oxygen therapy and cluster #2 bronchiolitis had the highest concentration of nodes with citation bursts, and research foci seem to have shifted from vapotherm to oxygen therapy and bronchiolitis. This supports the finding of the emerging focus in HFNC. The top 10 co-cited articles and their cited frequency are shown in Table 3. J.P. Frat in *New England Journal of Medicine* had the highest number of citations (201 citations), followed by K. Dysart in *Respiratory Medicine* (132 citations), O. Roca in *Respiratory Care* (125 citations), and B. Sztrymf in *Intensive Care Medicine* (125 citations). These articles are often considered fundamental in HFNC research.

Table 3
The top 10 high-cited articles in high-flow nasal cannula oxygen therapy from 2000 to 2019

Rank	Authors	Years	Journal	Cited frequency	Title
1	Frat JP	2015	NEW ENGLAND JOURNAL OF MEDICINE	201	High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure
2	Dysart K	2009	RESPIRATORY MEDICINE	132	Research in high flow therapy: Mechanisms of action
3	Roca O	2010	RESPIRATORY CARE	125	High-Flow Oxygen Therapy in Acute Respiratory Failure
4	Sztrymf B	2011	INTENSIVE CARE MEDICINE	125	Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study
5	Corley A	2011	BRITISH JOURNAL OF ANAESTHESIA	113	Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients
6	Lee JH	2013	INTENSIVE CARE MEDICINE	112	Use of high flow nasal cannula in critically ill infants, children, and adults: a critical review of the literature
7	Manley BJ	2013	NEW ENGLAND JOURNAL OF MEDICINE	96	High-Flow Nasal Cannulae in Very Preterm Infants after Extubation
8	Maggiore SM	2014	AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE	95	Nasal High-Flow versus Venturi Mask Oxygen Therapy after Extubation
9	Parke R	2009	BRITISH JOURNAL OF ANAESTHESIA	93	Nasal high-flow therapy delivers low level positive airway pressure
10	Sztrymf B	2012	JOURNAL OF CRITICAL CARE	89	Impact of high-flow nasal cannula oxygen therapy on intensive care unit patients with acute respiratory failure: A prospective observational study

Burst Detection

Burst detection identified articles that have attracted the attention of peer researchers. Bursts were detected between 2000 and 2019 based on the analysis of 835 original articles. The timeline was depicted as a blue line, and the time interval required to have a burst was shown as a red segment on the blue timeline, indicating its beginning year, ending year, and duration. Among the top 176 keywords with the highest burst strength, we were particularly interested in those keywords with research significance that indicate the evolution trend of the HFNC (Fig. 2F). During the entire time period from 2000 to 2019, randomized controlled trial had the highest burst strength, followed by respiratory distress syndrome and disease. Positive airway pressure and bronchopulmonary dysplasia became the research foci since 2007, and then, the infant, premature infant, and critical care patient became the research foci since 2008, followed by respiratory distress syndrome, preoxygenation, extubation failure, and acute lung injury. Regarding bursts with the most recent onset, randomized controlled trial, viral bronchiolitis, and immunocompromised patient were the strongest bursts since 2017.

Discussion

In this study, information visualization was used to analyze original articles on HFNC published from 2000 to 2019. On the basis of the identified trends that showed an increasing number of scientific research publications over the 20-year period, we conclude that HFNC has become an interesting subject and an increasingly important area of research. Research themes on HFNC were relatively disorganized. Although the quantity of research was relatively considerable, integral analysis of research hot spots was lacking. Our intent was to catalog the attributes of relevant studies and focus on the interpretation of keyword co-occurrence and burst detection to predict and direct future research trends.

The conventional oxygen delivery methods have been nasal prongs, nose mask, and face mask, but the oxygen provided by conventional systems may not suffice in patients with certain diseases. HFNC systems utilize higher gas flow rates than the standard nasal cannula. The use of HFNC as a respiratory support modality is increasing in infant, pediatric, and adult populations as an alternative to noninvasive positive pressure ventilation [17–24]. High-flow oxygen (up to 60 L/min) via the nasal cannula, combined with a heated humidification system, may have several advantages. HFNC can decrease oxygen dilution, reduce respiratory dead space, and generate some positive airway pressure because of the expiratory resistance generated by the delivered continuous high flow [25]. Heated humidification can facilitate secretion clearance and decrease bronchial hyperresponse symptom development. HFNC is well tolerated and may be feasible in a subset of patients who require ventilatory support with noninvasive ventilation.

High-frequency keywords, including high-flow nasal cannula, bronchiolitis, hypercapnia, newborn, and immunosuppression, in co-occurrence cluster analysis and co-cited reference cluster analysis (Figs. 2A, 2B and 2D) indicate that the clinical application of oxygen therapy remained the hot spots in HFNC research, including different disease types and patient groups. Analysis of top keywords, using burst detection (Fig. 2F), shows that bronchopulmonary dysplasia, infant, premature infant, respiratory distress syndrome, critical care patient, preoxygenation, extubation failure, and acute lung injury attracted the most attention of peer researchers in the past 20 years, whereas randomized controlled trial, viral bronchiolitis, and immunocompromised patient were among the new research foci since 2016. Research foci in HFNC seem to have shifted from one disease to other diseases, and the patient group is no longer limited to infants or premature infants.

HFNC was initially used for premature infants with respiratory distress syndrome [17, 18] and full-term newborns with hypoxic respiratory failure [19]. Children with pulmonary dysfunction caused by viral bronchiolitis, bacterial pneumonia, or reactive airway disease requiring intubation or CPAP (continuous positive airway pressure) were also treated with HFNC [20, 21]. Then, the use of HFNC in adult patients gradually increased and was applied to various clinical settings, such as pulmonary edema [22, 23], chronic obstructive pulmonary disease (COPD) [24, 26], acute respiratory failure [6–8], post-extubation [13, 27], heart failure [9, 10, 28], sleep apnea hypopnea syndrome [29, 30], or bronchoscopy [11, 12].

Journals with the highest number of articles in HFNC are mostly major journals related to critical care medicine and pediatrics, such as *Critical Care*, *Intensive Care Medicine*, *Annals of Intensive Care*, *Pediatric Pulmonology*, *Pediatric Critical Care Medicine*, and *Journal of Perinatology*. This indicates that HFNC has become a central topic of critical care and pediatric research. The analysis of the co-citation map of authors and top-cited authors (Fig. 1D, 1E and Table 3) from 2000 to 2019 showed that J.P. Frat, B. Sztrymf, J.H. Lee, S.M. Maggiore, B.J. Manley, and a few other authors are researchers with publications that significantly influenced the research trend and current understanding of HFNC. These studies were mainly found to focus on the clinical application of HFNC, especially ARF [6–8, 31, 32].

Sztrymf et al. [31] enrolled 38 patients with ARF to evaluate the efficiency, safety, and outcome of HFNC. Reduced respiratory rate and increased pulse oximetry were observed as early as 15 min after the induction of HFNC, and PaO₂ and PaO₂/FiO₂ significantly increased after 1 h HFNC as compared with baseline. No nosocomial pneumonia occurred during HFNC, and only nine patients required secondary invasive mechanical ventilation. A multicenter, randomized, unblinded trial on 830 patients showed that high-flow nasal oxygen therapy was not inferior to BiPAP (bilevel positive airway pressure) for patients with hypoxemia after a cardiothoracic surgery. Both methods had rapid effects on respiratory variables. BiPAP was associated with a higher PaO₂:FiO₂ ratio; high-flow nasal oxygen therapy, with lower PaCO₂ values and respiratory rate. High-flow nasal oxygen therapy had no effect on the frequencies of adverse events or length of stay in the intensive care unit or hospital [33]. Frat et al. [6] compared the effects of high-flow oxygen through a nasal cannula, noninvasive ventilation, and standard oxygen through a face mask in patients with nonhypercapnic acute hypoxemic respiratory failure. The intubation rate at day 28 was lowest in the high-flow oxygen group compared with the other two groups, but did not reach a statistical difference. In addition, high-flow oxygen therapy, as compared with the standard oxygen therapy or noninvasive ventilation, resulted in reduced mortality in the ICU and at 90-day follow-up.

Patients with invasive mechanical ventilation usually use ordinary nasal catheters or face masks to inhale oxygen after extubation, whereas some patients with poor oxygenation often need to use an oxygen storage, Venturi masks, or even noninvasive positive pressure ventilation. Maggiore et al. [27] compared the effects of the Venturi mask and nasal high-flow (NHF) therapy on the PaO₂/FiO_{2SET} ratio after extubation and found that compared with the Venturi mask, NHF resulted in better oxygenation for the same set FiO₂ after extubation. The use of NHF is associated with better comfort, fewer desaturations and interface displacements, and lower reintubation rate, suggesting the potential role of NHF in protecting extubation.

Chatila et al. [34] compared the effects of a high-flow oxygen (HFO) system to conventional low-flow oxygen (LFO) delivery at rest and during exercise in patients with COPD. They found out that delivering warm, humidified HFO improved exercise performance in a group of patients with severe COPD. An improvement in oxygenation with HFO at rest that was maintained during exercise despite similar-to-lower FiO₂ compared to LFO delivery was also observed. More importantly, patients were less dyspneic and had lower arterial pressure even after performing longer exercises. A favorable change in the breathing pattern could also be associated with improved endurance during exercise while receiving HFO but not at rest.

Compared to traditional reviews, analysis based on CiteSpace provides a better insight of the evolving research foci and trends, but it comes with certain limitations. Similar words should be merged together during the analysis. Even though only original articles were included in the majority of the analysis, all article types were included during the co-cited reference analysis.

Conclusions

Our understanding of HFNC has undoubtedly significantly advanced via bursts of high-quality research occurring over the past 20 years. With the help of information visualization, research foci and overall trends in the field were identified and provided information for future researchers. The more clinical application of HFNC would be the foci of future research.

Abbreviations

HFNC: High-flow nasal cannula oxygen therapy; NIV: Noninvasive ventilation; ARF: Acute respiratory failure; CPAP: Continuous positive airway pressure; COPD: Chronic obstructive pulmonary disease; BiPAP: Bilevel positive airway pressure; NHF: Nasal high-flow; HFO: high-flow oxygen; LFO: low-flow oxygen.

Declarations

Competing interest

The authors declare that they have no competing interests.

Availability of data and materials

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

Authors' contribution

S.Y.Q., X.Z., S.F.C., C.Z.L., W.B.D., W.F.Y., J.T., and D.S.S. had the idea for and designed the study; W.F.Y., J.T., and D.S.S. supervised the study; S.Y.Q., X.Z., and S.F.C. did the analysis. All authors contributed to acquisition, analysis, or interpretation of data. S.Y.Q. and X.Z. wrote the manuscript. All authors revised the report and approved the final version before submission.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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Figures

Figure 1

(A) Trends on the number of scholarly publications on high-flow nasal cannula oxygen therapy research from 2000 to 2019. (B) Global distribution of high-flow nasal cannula oxygen therapy research. (C) The network map of institutions on high-flow nasal cannula oxygen therapy research. The network map of productive authors (D) and co-cited authors (E) who participated in high-flow nasal cannula oxygen therapy research. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

Figure 2

Co-occurrence analysis of keywords according to frequency (A) and year (B). Note: a tendency toward yellow indicates a more recent item, whereas a tendency to blue indicates that it appears earlier. (C) Co-citation map of authors on clustered network of high-flow nasal cannula oxygen therapy. (D) Clustered network of co-cited articles on high-flow nasal cannula oxygen therapy and their subnetworks. (E) Timeline of co-citation clusters. Top clusters are labeled on the right. (F) Keywords with the strongest citation bursts in articles on high-flow oxygen therapy published in 2000–2019.

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