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DERLEME
REVIEW

High flow nasal cannula in COVID-19: a literature review

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ABSTRACT

High flow nasal cannula in COVID-19: a literature review

In recent years, high flow nasal cannula (HFNC) is a respiratory support system that has become prominent in the treatment of respiratory failure. HFNC provides higher concentration and flow of oxygen, resulting in decreasing anatomic dead space by preventing rebreathing and ensure positive end-expiratory. However, in COVID-19, the usage of HFNC is much controversial due to concerns about the benefits and risk of aerosol-dispersion. Considering the debates about the use of HFNC, we reviewed the literature related to the usage of HFNC in COVID-19. The available reports suggest that HFNC provides high concentrations of oxygen to the patients, who can not reach with conventional devices. HFNC can reduce the requiring of intubation in patients with COVID-19, and it can decrease the length of intensive care unit stay, and complications related to mechanical ventilation. Also HFNC can in achieving apneic oxygenation in patients during airway management. Besides that, the use of high-flow oxygen cannulas can produce aerosols. So, HFNC treatment should be carried out in a negative pressure room; when it is not possible, devices should be undertaken in a single room.

Key words: *High flow oxygen; COVID-19; respiratory failure; high flow nasal cannula oxygen; pandemic*

ÖZ

COVID-19'da yüksek akımlı nazal kanül oksijen kullanımı: literatür taraması

Yüksek akımlı nazal kanül oksijen (YANKO) tedavisi, solunum yetmezliği tedavisinde son yıllarda öne çıkan solunum destek sistemidir. YANKO tedavisi ile, yüksek akım ve konsantrasyonlarda oksijen uygulanarak anatomik ölü boşlukta azalmanın yanı sıra, sürekli bir ekspiratuar pozitif havayolu basıncı sağlanır. YANKO tedavisinin olumlu etkilerinin yanı sıra, aerosol oluşumunu artırma riski nedeni ile COVID-19 pandemisinde kullanımına dair tartışmalar mevcuttur. COVID-19 pandemisinde, YANKO kullanımı ile ilgili çekinceler dikkate alınarak, derlememizde COVID-19 pandemisinde YANKO kullanımı ile ilgili literatür bilgisi gözden geçirilmiştir. Literatür taramamız sonucunda ulaşılan çalışmalar ve raporlarda, YANKO'nin geleneksel cihazlarla ulaşamayan hasta-

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lara yüksek konsantrasyonlarda oksijen sağladığını göstermektedir. YANKO, COVID-19 hastalarında entübasyon ihtiyacını azaltabilir ve yoğun bakım ünitesinde kalış süresini ve mekanik ventilasyonla ilgili komplikasyonları azaltabilir. Ayrıca YANKO, entübasyon sırasında preoksijenizasyonda kullanılabilir. Bununla birlikte YANKO kullanımı aerosol oluşumuna neden olabilmektedir. Bu nedenle, YANKO tedavisi negatif basınçlı bir odada, bu durum mümkün olmadığında ise hastanın bir odada izole edilerek uygulanması önerilir.

Anahtar kelimeler: *Yüksek akım oksijen; COVID-19; solunum yetmezliği; yüksek akım nazal kanül oksijen; pandemi*

Introduction

Coronavirus disease 2019 (COVID-19) has quickly spread and has now become a global public health problem. As of June 20, 2020, globally 8,525,042 cases and 456,973 deaths have been reported (1). Although the majority of cases show mild symptoms, 25-34% of them have developed severe and critical diseases including respiratory failure, severe pneumonia, acute respiratory distress syndrome (ARDS), septic shock, multiple organ dysfunction (2-5). Oxygen administration forms the basis of supportive therapy for hypoxemic patients. The choice of oxygen supportive devices, as well as oxygen therapy, is essential in these patients in terms of effectiveness and aerosol dispersion (6). High flow nasal cannula (HFNC) is a respiratory support system that has become prominent in the treatment of respiratory failure , and studies are available showing a reduction in intubation and mortality. HFNC provides higher concentration and flow of oxygen, resulting in decreasing anatomic dead space by preventing rebreathing and ensure positive end-expiratory pressure (7-9). However, in COVID-19, the usage of HFNC is much controversial due to concerns about the benefits and risk of aerosol-dispersion.

Considering the debates about the use of HFNC, we reviewed the literature related to the usage of HFNC in COVID-19. We searched the PubMed for articles up to 12 June 2020. We used the keywords “COVID AND high flow nasal oxygen”; “COVID AND HFNC”; “COVID AND high flow nasal cannula, “SARS-CoV-2 AND high flow nasal oxygen”; “SARS-CoV-2 AND HFNC”; “SARS-CoV-2 AND high flow nasal cannula”. Also, we screened the national guidelines for COVID-19 and the recommendations about HFNC in COVID-19.

HFNC in Management of Respiratory Failure

Previous studies demonstrated that HFNC is associated with more ventilator-free time, lower mortality and decreased risk of ICU admission and lower reintubation rates in acute hypoxemic respiratory failures due to various causes (7,10,11). Besides, HFNC was applied for respiratory failure in patients with Middle East respiratory syndrome coronavirus (MERS-CoV), 2003 Toronto SARS-CoV outbreak and severe acute respiratory infection-related 2009 Influenza A/H1N1v (12-15). Although respiratory failure is common finding in patients with severe SARS-CoV-2 infection, COVID-19 related hypoxemia patterns are different compared with typical respiratory failure and ARDS. Patients with COVID-19 exhibits preserved lung compliance with low PaO_2/FiO_2 ratios (16,17). These differences in pathophysiology, may cause differences in the effectiveness of HFNC.

While there are concerns against the use of HFNC treatment, it has been applied in patients with respiratory failure related COVID-19 in numerous studies (Table 1) (2,18-24). Previous studies suggest that HFNC treatment reduced mortality and also improved survival rates in patients with hypoxemic respiratory failure (25). Zhou et al. designed a retrospective study and showed 41out of 191 patients required HFNC (33 in intensive care unit; ICU and 8 in the ward); the rate of HFNC usage was higher in non-survivor patients compared with survivors (61% vs. 6%, $p< 0.001$) (19). Geng et al. reported 8 cases with COVID-19 who received HFNC and favorable outcomes in all patients. Before HFNC treatment partial pressure of oxygen /fraction of inspired oxygen (PaO_2/FiO_2) of the eight patient was 259.88 ± 58.15 mmHg, and after 24 hours, PaO_2/FiO_2 increased to 280-450 mmHg and all of the eight patients were discharged from the hospital without invasive mechanical ventilation support during hospital stay (21). In a retrospective study by Wang et al., 17 patients were treated with HFNC, and 41% of these patients experienced treatment failure. As remarkable, failure rate being 0 in patients with $PaO_2/FiO_2 > 200$ and 63% in those with $PaO_2/FiO_2 \leq 200$ (26). Karamouzos et al. reported a 44-year male patient with COVID-19 who had been treated with HFNC, after the clinical deterioration (PaO_2/FiO_2: 110) on supplemental oxygen via nasal cannula. The PaO2/ FiO_2 ratio increased, and the patient was successfully

Table 1. Features of patients who received HFNC treatment in the recent published data

	Number of study patients	Study group	Age	Gender	HFNC	Invasive MV	Outcomes related to HFNC
Chen et al. (24)	145	severe ill/non-severe ill	47.5 ± 14.6	Male: 79 (54.5%)	6 patients	1 patient	
Lagi et al. (20)	84	ICU transferred/not ICU transferred	62 IQR (51-72)	Male: 55 (65.5%)	9 patients	1 patient	1 out of 9 patients receiving HFNC treatment, transferred to ICU and required intubation
Geng et al. (21)	8	Severe-critical COVID-19 patient receiving HFNC	61.38 ± 18.97	Male: 5 (62.5%)	8 patients	0 patients	all patients discharged, all patients showed improvement on oxygenation, patients switched to conventional oxygen therapy after 7.38 ± 2.07 days
Barasa et al. (22)	48	patients who were admitted to ICU	63 IQR (51-75)	Male: 27 (26%)	3 patients	0 patients	
Zhou et al. (19)	191	adult patients who were hospitalised: survivor/non-survivor	56 IQR (46-67)	Male: 119 (62%)	41 patients	32 patients	HFNC treatment ratio was higher in non-survivor than survivors (61% vs. 6% $p< 0.001$)
Yang et al. (23)	52	critically ill patients survivors/non-survivors	59.7 ± 13.3	Male: 35 (67%)	33 patients	22 patients	
Wang et al. (2)	138	adult inpatients who were hospitalised	56 IQR (42-68)	Male : 75 (54.3%)	4 patients	17 patients	
Guojun et al. (18)	36	Severe-critically ill patients	65 ± 15	Male: 25 (69.4%)	36	10	

HFNC: High flow nasal cannula; MV: Mechanical ventilation; ICU: Intensive care unit.

weaned from HFNC after ten days (27). Another successful HFNC treatment in a patient with COVID-19 was reported by Rali et al (28).

Bocchile et al. performed a meta-analysis., to evaluate the effect of HFNC on the prevention of intubation in critically ill patients. It was shown that HFNC was associated with a decrease of intubation rate (29). This success of HFNC was thought to be related to providing sufficient of minute ventilation and constant oxygenation, which reduces respiratory work of breathing. Additionally, the other effects of heated and humidified oxygen in HFNC were notified as improve secretion clearance, reduce transpulmonary driving pressure and protect mucosal injury (30). He et al. reported 36 severe-critically COVID-19 patients who received HFNC treatment. In this study, it was reported that 26 of total patients (%72) cured and discharged, whereas 10 patients underwent invasive mechanical ventilation. The authors of the study emphasized some factors for treatment success; select the proper size of the nasal cannula and suitable location; started with initial flow 60 L/min and 370C in patients with respiratory distress; treatment with target oxygen saturation above 95% without chronic lung disease (18). In other reports involving HFNC treatments on COVID-19 related respiratory failure, the flow rates were set at 40-60 L/min and the temperature at 370C (27,28,31,32).

Prone positioning has been used to improve oxygenation and reduce shunt fraction in mechanically ventilated patients with moderate-to-severe ARDS (33). Use of prone positioning in awake, spontaneously breathing patients has been reported recently. Despres et al. described 3 patients (4 sessions) with severe COVID-19 who had prone position combined with HFNC treatment; the PaO_2/FiO_2 ratio improved after 3 of 4 sessions of prone position with HFNC treatment (PaO_2/FiO_2 ratio of case 1: 144 to 254; case 2: 129 to 156; case 3: session 1: 126 to 194, session 2: 183 to 162) Intubation was avoided in 2 of 3 patients (34). In another case series, Xu et al. reported 10 patients with COVID-19 whose PaO_2/FiO_2 ratio was lower than 300 (minimum PaO_2/FiO_2: 89) and all of them received awake prone position with HFNC treatment. In all patients, a significant elevation in PaO_2/FiO_2 ratio was observed, and none of the patients required intubation (35). Slessarev et al. reported a 68-year-old male patient with COVID-19 who had been applied HFNC with prone position and discharged on 4th day of admission without requiring intubation (31). The prone position leads to reduce ventilation/perfusion heterogeneity, open the atelectatic lung by sputum drainage and may improve oxygenation by contributing to the effects of the HFNC treatment (31,34,35).

A new index termed ROX, defined as the ratio of oxygen saturation as measured by pulse oximetry/FiO_2 to respiratory rate, has been described in some reports It was developed to predict of clinical outcomes of patients who received HFNC treatment. This index is calculated by the ratio of oxygen saturation as measured by pulse oximetry/FiO_2 to respiratory rate, and it can help identify high-risk patients for invasive mechanical ventilation. The ROX index > 4.88 indicate the success of HFNC treatment and little risk of intubation, 3.85-4.87 should be close monitoring to increase of intubation, 2.85-3.84 if possible, should be monitoring in the ICU due to highly increased risk of intubation, whereas a ROX-index < 2.85 should consider intubation (36,37). ROX index was used on the following of patients with COVID-19 who received HFNC (21,34). Danish Society of Respiratory Medicine also recommended to the monitoring of ROX index for patients with COVID-19 treating with HFNC (37).

HFNC in Tracheal Intubation, Preoxygenation.

Patients with COVID-19 are likely to be considered for emergency tracheal intubation. The efficacy of HFNC in achieving apneic oxygenation in the critically ill patients during airway management has also been demonstrated (38). In a prospective randomized controlled trial, it was shown that using HFNC during fiberoptic bronchoscopy intubation provided greater minimum SpO_2 throughout intubation and shorter intubation time compared with standard mask oxygenation (39).

Aerosol Dispersion of HFNC

Considering the utilization of HFNC in the outbreak Rello et al., reported 38 cases of ARF related 2009 influenza A/H1N1v, with a success rate of 39%, and no secondary infections in healthcare workers (14). Transmission of SARS-CoV-2 is through droplet. Virus-containing droplets may induce direct transmission from close contact or contribute to contamination surfaces. The transmission risk increases with procedures generating aerosols like tracheal intubation/extubation, delivery of nebulised or atomised medications via simple face mask, bronchoscopy, non-invasive ventilation and HFNC therapy.

The initial concerns of the HFNC aerosol dispersion caused to recommend avoiding the use of this modality to avoid transmission risk (40,41). A manikin model study was performed by Hui et al., and it was shown that aerosol dispersion distance was 17.3 ± 3.3 cm at 60 L/min^{-1} flow rates, 13.0 ± 1.1 cm at 30 L/min^{-1} flow rates, whereas 6.5 ± 1.5 cm at 10 L/min^{-1} flow rates (42). Another study was conducted to simulate maximum distant of droplet dispersion while coughing of patient receiving HFNC. The findings revealed that cough-generated droplets spread 2.48 ± 1.03 m baseline and 2.91 ± 1.09 m with HFNC treatment. The maximum distance was 4.50 m while receiving HFNC (43). These distances of spread were thought similar to standard oxygen treatment modalities (6,41).

By the time, the aerosol spread has not been as high as expected, HFNC treatment is now recommended by several guidelines. It is recommended that a surgical mask should be worn by the patient during the HFNC treatment. Also, the HFNC treatment should be undertaken in a room with negative pressure / in a single place if a negative pressure room is not available (44-49).

Conclusion

In conclusion, HFNC provides high concentrations of oxygen to the patients, who can not reach with conventional devices. HFNC can reduce the requiring of intubation in patients with COVID-19, and it can decrease the length of intensive care unit (ICU) stay and complications related to mechanical ventilation. Also, HFNC is comfortable for patients due to mixing oxygen with warm water to humidify, bring the gas mixture to body temperature. On the other hand, clinicians should carefully monitor the transformation from mild/moderate ARDS to severe ARDS to avoid delayed intubation during using HFNC. The use of high-flow oxygen cannulas can produce aerosols. So, HFNC treatment should be carried out in a negative pressure room; when it is not possible, devices should be undertaken in a single room.

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