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Respiratory Medicine 187 (2021) 106554

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

High-flow nasal oxygen (HFNO) for patients with Covid-19 outside intensive care units

Issa Issa [a,*], Mårten Söderberg [a,b]

[a] Department of Internal Medicine, Södersjukhuset, Stockholm, Sweden
[b] Karolinska Institutet, Department of Clinical Science and Education, Södersjukhuset, Stockholm, Sweden

ARTICLE INFO

Keywords:
High-flow nasal oxygen
Covid-19
ICU
ARDS

ABSTRACT

Introduction: High-flow nasal oxygen (HFNO) has traditionally only been used in intensive care units (ICU) especially in acute respiratory distress syndrome (ARDS).
Methods: We studied the use of HFNO at Södersjukhuset, Stockholm, in patients with moderate to severe ARDS related to Covid-19 as well as its benefits both for patients and to offload the ICU. The patients were observed with frequent controls to assess the need of ICU in case of deterioration.
Results: We studied 41 patients with HFNO treatment either as primarily treatment (Step-Up) or after stabilizing in the ICU (Step-Down). The average duration for treatment with HFNO was 5.6 days. Of these patients 55% were discharged home or to geriatric rehabilitation and 10% avoided ICU completely. The usage of HFNO saved in total 229 days in the ICU. Mortality was higher among elderly patients, and patients with comorbidities (mainly hypertension and obesity).
Discussion and conclusion: HFNO treatment is feasible and efficient for patients with Covid-19, saving resources in the ICU and offering additional advantages as waken proning and fewer complications compared to traditional ICU care. It requires however frequent controls as deterioration is recurrent.

1. Introduction

With millions of people affected, the novel Covid-19 pandemic is among the most severe and widespread pandemics in modern history. A challenge is how to manage space in hospitals and increase the capacity of intensive care units to parallel the increasing need. Sweden has fewer intensive care beds in comparison to other European countries [1]. Previous studies have shown that the usage of HFNO (high-flow nasal oxygen therapy) has helped patients with Covid-19-infection to both skip the ICU and receive better outcomes than ordinary oxygen treatment [2]. HFNO is a technique whereby heated and humidified oxygen is delivered to the nose by using small nasal prongs, which patients describe as generally soft and pliable. When compared to traditional oxygen therapy, HFNC (high-flow nasal cannula) has improved patient comfort [3–5] and generates positive pressure in the upper airways, permitting a higher fraction of minute ventilation to participate in alveolar gas exchange, and decreasing physiological dead space by flushing expired carbon dioxide from the upper airway [3–5], which potentially decrease the work of breathing and enhance oxygenation in patients with ARDS (acute respiratory distress syndrome). The usage of HFNO can be aerosol-generating (i.e. more contagious) but the evidence is scarce.

The aim of the study is to investigate the efficacy of HFNO in Covid-19 patients outside the ICU and its role in offloading the ICU.

2. Methods

At Södersjukhuset, Stockholm, HFNO treatment (AIRVO2 or Optiflow, Fisher & Paykel Health Care Ltd., Auckland, New Zealand) was initiated at the department of infectious diseases, with modern ventilation and negative suction pressure, which is preferable according to current guidelines [2]. PF ratio (PaO2/FIO2) was used to determine the need of mechanical respiration inclusive of HFNO. Severe ARDS is defined as PaO2/FIO2 $\leq$100 mm Hg while moderate is defined as PaO2/FIO2 $\leq$200 mm Hg. Normal PaO2/FIO2 is $>$ 300 mm Hg [6]. Patients who were stabilized with HFNO in the ICU or in need of assessment regarding the necessity of intensive care were candidates for this treatment.

HFNO was initiated at 50 L/min with the temperature set at 34 C°. Nasal cannula size was determined by the patient's nostril size. FIO2 was

* Corresponding author.
E-mail address: issa.issa@sll.se (I. Issa).

https://doi.org/10.1016/j.rmed.2021.106554
Received 13 May 2021; Received in revised form 23 July 2021; Accepted 26 July 2021
Available online 28 July 2021

adjusted to maintain SpO2 at 94%. Flow and temperature were adjusted based on patient comfort and clinical response. These settings were accepted as standard settings excluding patients who had other default settings from the ICU when discharged. In that case, the settings ordered from the ICU were retained. HFNO was stopped based on clinical criteria (improvement of clinical signs of respiratory distress), PaO2/FiO2 > 300, and ability to maintain SpO2 ≥ 94% with less than 6 L/min of standard oxygen.

In this retrospective, observational cohort study, all patients with Covid-19 (defined with positive SARS-CoV2-RNA PCR test) who were admitted to the infection ward to get HFNO between April and June 2020. Duration of treatment and how it saved ICU days by prolonging the time before initiating ICU care (which is called "Step-Up'' and means primary usage of HFNO and evaluating the need of ICU), or by skipping it if the patient is stabilized with HFNO; were counted. Another possibility was to use the infection ward as a "Step-Down'', which means helping those who initially needed ICU care and then needed supportive respiratory care.

The outcomes were the duration of HFNO in the infection ward, the result of treatment (cure, death, or transfer to other hospital or care form); and complications. We compared the group as all with a subgroup of Covid-19 deaths who also had been treated with HFNO in the same ward.

The project has been approved by the Swedish Ethical Review Authority (DNR 2020–03760).

2.1. Statistical analysis

Values are means (interquartile range) unless otherwise stated. P-values for differences obtained using Fisher's exact test and Kruskal Wallis test. Statistical significance was set at $p < 0.05$.

3. Results

Out of 41 patients treated with HFNO, 80% were men and 61% had at least one chronic disease. Patient demographics are described in Table 1. Each patient received HFNO treatment for 5.6 days on average. It resulted, cumulatively, in a total saving of 229 ICU-days, 55% were discharged home after the treatment (n = 17) or to geriatric rehabilitation (n = 6).

A significant difference was noticed in age between Covid-19 non-survivors and survivors (Mean 78 vs 64 years old, p = 0.001). Comorbidities, mainly obesity and hypertension (p = 0.03 vs p = 0.05), were more frequent in patients who did not survive. No significant differences were noticed in other characteristics (sex, diabetes, heart failure, renal- and liver failure, COPD or smoking). No significant differences were noticed either in CRP, D-dimer or SOFA score (Sepsis-related organ failure assessment). Patients who survived Covid-19 needed HFNO longer time (6 days vs 4, p = 0.03). No differences were noticed in the frequency of pulmonary embolism or in the time having symptoms before visiting the hospital (See Table 1).

HFNO was also used as a step-down from ICU in 21 cases (51%) saving 126 ICU days, and in this group better tolerance of HFNO was noticed (already used in ICU). Mortality was considerably lower: 2 (9.5%) vs 10 (29%) in the group as all. It helped 4 other patients (10%) to avoid ICU completely. Patients in this group were younger and had lower SOFA score. (See Table 2).

4. Discussion

SARS-COV-2 is an emerging contagious virus causing pneumonia, which sometimes needs hospitalization in the ICU. New studies began to show the importance and effectiveness of the use of HFNO not in ICU [7,8]. Our study showed a significant valuable timesaving as we needed places in ICU for more critical cases. HFNO could successfully be used in patients with profound hypoxemia and resulted in offloading the ICU.

Table 1
Characteristics of patients with Covid-19 with HFNO treatment in the infection ward.

	All patients (n = 41)	Non-survivors (n = 12)	Survivors (n = 29)	p-value
Male sex, No, (%)	33 (80)	10 (85)	23 (80)	0.7
Age, years	68 ± 12 (48–88)	78 ± 5 (72–88)	64 ± 12 (48–88)	0.001
BMI≥30 kg/m^2, No. (%)	4 (10)	3	1	0.03
Tobacco use, No. (%)	6 (12)	3	3	0.2
Hypertension, No. (%)	18 (44)	8	10	0.05
Diabetes, No. (%)	9 (22)	3	6	0.7
Renal or/and liver failure, No. (%)	6 (15)	2	4	0.8
Heart failure, No. (%)	7 (17)	4	3	0.08
COPD, No. (%)	5 (12)	3	2	0.1
CRP[a] mg/l	150 (6–500)	112	165	0.15
Fibrin-D-dimer[a] mg/l FEU	3.7 (0,25–35,1)	1.8	4.4	0.3
Duration of symptoms prior to admission	9.6 (1–20)	9	9.8	0.49
PF ratio	84 (45–174)	84	84	0.9
SOFA Score	2.9	3.1	2.9	0.8
Pulmonary embolism, No. (%)	8 (20)	1	7	0.2
Intolerance for HFNC, No. (%)	2 (5)	1	1	0.5
Days using HFNO	5.6 (1–14)	3.9	6.3	0.03

Characteristics of 41 patients with Covid-19 and HFNO treatment admitted to the infection ward at Södersjukhuset, Stockholm, between April and June 2020. Values are means (interquartile range) unless otherwise stated. P-values for differences across exposure categories were obtained using Fisher's exact test for categorical and Kruskal Wallis for continuous data; COPD, Chronic obstructive pulmonary disease; CRP, *C*-reactive protein; PF ratio, PaO2/FiO2 ratio; SOFA score sepsis-related organ failure assessment.

[a] When the treatment was initiated.

Keeping frequent controls to determine the need of ICU is of great importance.

One study in Cape Town explored usage of HFNO as a Step-Up in two resource-limited hospitals where it was primary used in severe ARDS due to Covid-19 both in ICU and medical wards [7]. About half of patients who got HFNO did not need ICU and it was successfully weaned, but nearly half of the patients died.

Our study did not compare patients receiving HFNO with those having COT (Conventional oxygen therapy). However, based on other studies, there were no differences in mortality in ARDS [9]. HFNO resulted meanwhile in decreased requirement for tracheal intubation and had lower risk for escalation of oxygen therapy when compared with COT [9].

Our study was single-centered and observational with no control group and followed retrospectively 41 patients. Death occurred in 12 patients where deterioration was noticed but there was no intention to transfer to ICU. It was considered as a preferable treatment for hypoxia rather than traditional oxygen masks. Two patients could not tolerate HFNO technique and therefor used COT instead.

It is important to note that the medical treatment was different during the study time. Steroids were not included in the treatment protocol during the study period (April-Juni). All the patients received anticoagulation either in full dose or for prophylaxis. No other medications were used in Sodersjukhuset (such as IL-6 inhibitors or Remdasivir). Intermittent proning was used in most cases.

5. Conclusion

This study shows that HFNO treatment in non-critical care

Table 2
Characteristics of patients with Covid-19 with HFNO treatment in the infection ward.

	All patients (n = 41)	Step-Up (n = 20)	Step-Down (n = 21)	p-value
Male sex, No, (%)	33 (80)	18 (90)	15 (71)	0.14
Age, years	68 ± 12 (48–88)	76 ± 9 (52–88)	62 ± 11 (48–86)	0.001
BMI≥30 kg/m^2, No. (%)	4 (10)	3	1	0.28
Tobacco use, No. (%)	6 (12)	5	1	0.07
Hypertension, No. (%)	18 (44)	9	9	0.9
Diabetes, No. (%)	9 (22)	3	6	0.3
Renal or/and liver failure, No. (%)	6 (15)	2	4	0.4
Heart failure, No. (%)	7 (17)	4	3	0.6
COPD, No. (%)	5 (12)	5	0	0.01
CRP[a] mg/l	150 (6–500)	147	153	0.9
Fibrin-D-dimer[a] mg/l FEU	3.7(0,25–35,1)	3.7	3.7	0.9
Duration of symptoms prior to admission	9.6 (1–20)	8	11	0.04
PF ratio	84 (45–174)	83	85	0.9
SOFA Score	2.9	3.3	2.5	0.005
Pulmonary embolism, No. (%)	8 (20)	2	6	0.14
Intolerance for HFNC, No. (%)	2 (5)	2	0	0.14
Days using HFNO	5.6 (1–14)	5.2	6	0.5
Mortality (%)	12	10(29)	2(9.5)	0.003

Characteristics of 41 patients with Covid-19 and HFNO treatment admitted to the infection ward at Södersjukhuset, Stockholm, between April and June 2020. Values are means (interquartile range) unless otherwise stated. P-values for differences across exposure categories were obtained using Fisher's exact test for categorical and Kruskal Wallis for continuous data; COPD, Chronic obstructive pulmonary disease; CRP, *C*-reactive protein; PF ratio, PaO2/FiO2 ratio; SOFA score sepsis-related organ failure assessment.

[a] When the treatment was initiated.

environment can offload the ICU units when the need for ICU and ventilators is maximized. HFNO is useful outside the ICU especially as a step-down as the patients are stabilized. The usage of HFNO as primary treatment can also be considered but requires frequent controls as the risk for deterioration is high.

CRediT authorship contribution statement

Issa Issa: Writing – review & editing. **Mårten Söderberg:** Supervision, All authors reviewed the results and approved the final version of the manuscript.

Declaration of competing interest

Issa Issa and Mårten Söderberg declares that they have no conflict of interest.

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