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Utility of High Flow Nasal Cannula during Pulmonary Rehabilitation in COVID-19 Patients in Acute Respiratory Failure

Teresa Paolucci [1,*], Giorgia Patrizio [2], Domenico Pietrantonio [3], Giorgia Rapacchiale [3], Antonella Spacone [4], Giustino Parruti [3], Giancarlo Graziani [5], Marzia Damiani [2], Vitalma Liotti [2] and Carlo D'Aurizio [2]

1 Physical Medicine and Rehabilitation, Department of Oral, Medical and Biotechnological Sciences (DSMOB), University G. D'Annunzio of Chieti, 66100 Chieti, Italy
2 Physical Medicine and Rehabilitation Unit, Pescara General Hospital, 66020 Pescara, Italy; giorgia.patrizio@asl.pe.it (G.P.); marzia.damiani@libero.it (M.D.); vitalma.liotti@ausl.pe.it (V.L.); carlo.daurizio@asl.pe.it (C.D.)
3 Infectious Disease Unit, Pescara General Hospital, 66020 Pescara, Italy; domenico.pietrantonio@asl.pe.it (D.P.); giorgia.rapacchiale@asl.pe.it (G.R.); giustino.parruti@ausl.pe.it (G.P.)
4 Pulmonary Medicine Unit, Pescara General Hospital, 66020 Pescara, Italy; spaconeantonella@gmail.com
5 Physical Medicine and Rehabilitation, Santo Spirito Hospital, 00193 Rome, Italy; giancarlo.graziani@aslroma1.it
* Correspondence: teresa.paolucci@unich.it

Abstract: High-flow nasal cannula (HFNC) has often been used in the treatment of acute respiratory failure during pulmonary rehabilitation setting. The aim of this retrospective study was to investigate the utility of HCFN during the early rehabilitation in COVID-19 pneumonia. Twenty-two patients (10 males and 12 females, mean age 64.5 ± 5.9 years) with COVID-19 pneumonia were considered. Medical data and rehabilitative scales were used to evaluate acute hypoxemic respiratory failure ($PaO2/FiO2 < 300$), treated with HFNC three times during evaluation. Overall clinical outcomes from the evaluation of the synergy between HFNC strategy and rehabilitation were evaluated. A statistically significant improvement was observed at T2 (and of treatment) in 1 minute sit to stand test (1STST) (4 ± 3 vs. 17 ± 5, $p < 0.05$), short physical performance battery (SPPB) (4.3 ± 2.81 vs. 9.15 ± 2.39, $p < 0.05$), SpO2% post effort (93 ± 1.26 vs. 98 ± 1.01, $p < 0.05$), respiratory rate post effort (RR) (24 ± 3.91 vs. 20 ± 3.13, $p < 0.05$), heart rate (HR) (97 ± 11.9 vs. 87 ± 9.17, $p < 0.05$), P/F rate (235 ± 7.35 vs. 331 ± 10.91, $p < 0.05$), SpO2 (86 ± 4.54 vs. 97 ± 1.01 $p < 0.05$), RR (20 ± 4 vs. 12 ± 1.39, $p < 0.05$). Then, treated HFNC patients showed a good improvement in physical performance at T2 and a good compliance with treatments proved to be extremely useful in the control and reduction of dyspnea and fatigue symptoms.

Keywords: COVID-19; rehabilitation; pulmonary; exercise

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1. Introduction

The coronavirus disease 2019 (COVID-19) appeared for the first time in December 2019, in Wuhan, Hubei Province, China. Within 3 months, COVID-19 had quickly spread worldwide, with incidence of COVID-19 cases increased to be declared a pandemic by the WHO on 11 March 2020 [1]. COVID-19 is quite heterogeneous in its clinical manifestations, ranging from no symptoms to critical illness. Older age, male sex, race, and comorbidities as diabetes, hypertensive cardiopathy, chronic pulmonary disease, chronic kidney disease, cancer, and liver disease have been tightly associated with worse outcomes [2–4].

Asymptomatic infection or mild respiratory disease is by far the most frequent outcome. About one-third of patients, however, hospitalized progress to interstitial pneumonia, causing acute hypoxemic respiratory failure in a proportion of cases, up to 1 in 10, quite challenging for health care system capacities worldwide [5].

Arterial hypoxemia is the leading feature of severe cases of COVID-19. Consequently, its management should rely on prompt and steady oxygen supplementation, aiming to improve oxygenation and to assist respiratory efforts throughout different support modalities, until intubation with invasive ventilation.

High-flow nasal cannula (HFNC) is often used to treat respiratory failure during COVID-19 pneumonia [6–9]. HFNC combines the possibility of delivering high flows of gases, actively humified and heated, with the use of a comfortable nasal interface, well tolerated by patients.

HFNC decreased the need for intubation or treatment escalation compared with standard oxygen delivery systems in critically ill patients without COVID-19 and with acute hypoxemic respiratory failure, and recent clinical practice guidelines strongly recommended its use; similarly, HFNC performed better than standard oxygen delivery supplies in COVID-19 settings [10]. This beneficial effect is probably due to its ability to match patients' respiratory flow demands more adequately, to reduce inspiratory effort, and decrease the risk of patients' self-inflicted lung injury, which may have important implications for the management of the heterogeneous pulmonary manifestations of patients with COVID-19. Furthermore, heating and humidification by HFNC help to maintain hydration and mobilize secretions, which positively affects secretory imbalances in patients with COVID-19.

Use of HFNC in the intensive care gained great attention as a bridge therapy after early extubating, too [11,12]. Recent studies have shown that HFNC improves respiratory drive and lung mechanics and enhances CO2 removal [13,14].

Patients with acute hypoxemic respiratory failure, such as in COVID-19 severe pneumonia, are prone to hypokinetic (immobilization) syndrome, defined as the risk of deterioration of the body's systems as a result of prescribed or unavoidable musculoskeletal inactivity.

Pulmonary rehabilitation is another setting whereby HFNC may be used in patients with chronic obstructive pulmonary disease and bronchiectasis, as HFNC could immediately increase patients' exercising endurance and decrease dyspnea caused by exercising [15].

Recent studies revealed that a large proportion of patients with severe COVID-19 suffer significant physical deconditioning and impairment of activities of daily living (ADLs) [16]; furthermore, in patients with prolonged hospitalization, bed rest-related damage can cause slow and often incomplete functional recovery, with persistently reduced exercise capacity and impaired cognitive-emotional functioning.

The main objectives of early rehabilitation are to counteract the onset of respiratory complications in critically ill patients with COVID-19, restore respiratory and physical independence, prevent subsequent dependence on mechanical ventilation, help recover exercise capacity, and to preserve or recover autonomy in ADLs. This can be achieved counteracting atelectasis and reducing secretion retention, where present, by promoting recruitment of lung volumes, improving regional and global compliance, improving the ventilation/perfusion ratio, reducing airway resistance and work of breathing, optimizing oxygenation, and finally preserving respiratory and peripheral muscle strength.

Rehabilitation targets are pursued through position management, early mobilization, respiratory management, reconditioning of muscle strength, re-education of static and dynamic balance, and resumption of walking. During the COVID-19 pandemics, respiratory rehabilitation proved to be a fundamental element in the management of severe patients, restoring their autonomy and quality of life [17]. With all such premises, we hypothesized that use of HFNC might play a major role during the rehabilitation of COVID-19 patients, improving their comfort and adherence to each rehabilitation step.

2. Materials and Methods

2.1. Subjects and Study Design

This is a retrospective observational study of 22 adult patients older than 45 and less than 80 years old, with COVID-19 in spontaneous breathing, hospitalized during pandemic at the Infectious and Pulmonary Diseases Unit, Pescara General Hospital, Italy, during year 2021, treated with HFNC and pulmonary rehabilitation, and pharmacological treatments: all enrolled patients were treated with steroid therapy, prophylactic dose low molecular weight heparin, and (azithromycin antibiotic therapy), those with bacterial over infection received broad-spectrum piperacillin tazobactam antibiotic therapy or targeted antibiotic therapy if isolates were present.

We included patients who met the diagnostic criteria of bilateral pneumonia with secondary state of AHRF, PaO2/FiO2 < 300 in room air, and need for HFNC with enrichment of oxygen, considering: only patients in the fifth day of admission (at T1) were able to independently maintain a sitting position for at least 30 min and to achieve orthostatic position independently also for a short time while maintaining parametric stability were recruited. The exclusion criteria were diseases that prevented physical loading; previous stroke, surgery of the spine; vertebral fractures. Patients were excluded if they had previous myocardial infarction, lower extremity arterial disease, major neurological problems, and severe poor vision. The study was approved by the local institutional review board, and all patients provided written informed consent.

2.2. Study Variables

The data collected by the specialist in pulmonology were age, gender, smoking history, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease—COPD, obstructive sleep apnea syndrome—OSAS), computed tomography (CT) scan of the chest and lung at hospital admission and clinical signs during hospitalization, peripheral oxygen saturation (SpO2), heart rate (HR), respiratory rate (RR), arterial blood gas test data, ratio of arterial oxygen partial pressure (PaO2 in mmHg) to fractional inspired oxygen (FiO2 expressed as a fraction, not a percentage) (P/F r.). Data collected from the rehabilitation team were the FiO2 (fraction of inspired oxygen) administered to the patients, the respiratory rates (RR), heart rates (HR), peripheral saturations (SpO2), and the evaluation scales for disability, performance, and dyspnea.

2.3. Evaluation Times

Three evaluation times were taken into consideration: T0 (at admission in the Covid-19 Emergency Division); T1 (at five days from the admission in the hospital); T2 after 20 days of hospitalization. From T0 to T1, whole observed patients had been experienced in physical and respiratory rehabilitation.

2.4. Rehabilitative Program

The patients were subjected to systematic changes of posture to optimally redistribute ventilation and optimize gas exchange by promoting alveolar interdependence. In agreement with the in-patient ward staff, care was taken whenever possible to alternate lateral decubitus and the assumption of a semi-prone or prone position and to avoid the "*slumped*" posture, which further reduces lung volume, by favoring correct positioning in a semi-sitting and, as soon as possible, sitting position. The application of the individual rehabilitation plan also included the execution of dyspnea control techniques, the execution of physiotherapy maneuvers aimed at the treatment of the deep lung with the aim of reducing the respiratory rate and therefore ventilatory asynchronism, the application of the slow inhalation-breath hold technique, and the application of the slow exhalation technique in circumstances where it has proved possible and appropriate to apply them [18]. The individual rehabilitative plan, also, included musculoskeletal exercises involving limbs mobilization and, at the same time, breathing coordination exercises performed in bed under the supervision and monitoring of the respiratory physiotherapist. The rehabilitative exercise intensity administered corresponded to a dyspnea score on the Modified Borg Dyspnea Scale ≤ 3.

At fifteen days of rehabilitation (from T1 to T2), the patients underwent respiratory physiotherapy and physical reconditioning sessions, whose overall duration varied from 30 to 60 min, modulated on therapeutic needs and the patients' subjective tolerance to fatigue, with respect to a Borg Dyspnea level of less than or equal to 3 and providing appropriate moments of recovery within each session.

Moreover, the patients continued with the systematic posture changes in bed and with the progressive recovery and increase in the time taken to maintain the sitting position, first on the bed, legs out, with back support and then in the chair. The rehabilitation plan included the implementation and consolidation of energy-saving techniques, breath control, and dyspnea symptoms during postural transitions and bed-chair transfers as well as during the progressive recovery of ambulation. During exercise sessions, musculoskeletal exercises were carried out with both upper and lower limbs to maintain and recover muscle strength in a posture of maximum postural stabilization and progressively in a sitting and orthostatic position. Each phase of the implementation of the rehabilitative plan was carried out under medical control (saturation, heart rate, and respiratory rate) and with a gradual evolution of the level of independence during the exercise.

2.5. HFNC Treatment Strategy

HFNC, high-flow devices (AIRVO™ 2; Fisher & Paykel Healthcare, Auckland, New Zealand) were utilized for respiratory support. The sizes of the nasal cannulas (Fisher & Paykel) were chosen based on patients' nostrils. The humidifier temperature was set to 31 °C, 34 °C, or 37 °C according to the comfort degree of the patients, and the fraction of inspired oxygen (FiO2) was adjusted to maintain oxygen saturation by pulse oximetry (SpO2) at 93% to 96%. The maximum flow rate also had to be adjusted according to the patients' maximum tolerance (40–60 L/min).

2.6. Physiotherapy Scales

The short physical performance battery (SPPB) examines three important and separate aspects of lower limb function, with subscale scores providing information on gait speed, lower limb strength and power, and balance.

The test is simple to administer in terms of space requirements and materials to be used, which has made it particularly advantageous in the context of COVID-19 wards and takes only a few minutes to administer so it can be integrated into patient management without substantial delay [19]. The score varies from a minimum of 0 to a maximum of 12 resulted by the sum of 3 sub-score: *balance assessment, gait assessment and the ability to perform the sit-to-stand* [20].

The 1-minute sit to-stand test (1-STST) is a reliable test for the determination of exercise desaturation; peak desaturation during the test is correlated with ventilatory deficit. Impairment of respiratory exchange is associated with exertional dyspnea, limitation of physical activity and quality of life [21]. The modified Borg Scale for Dyspnea (mBDS) peculiarity of these rating scales is that they consist of a verbal anchorage, in particular, certain numerical values are matched with a specific adjective. The aim is to assign to a perception a well-defined quantitative/numerical measure, and only that. This combination of numerical values and verbal anchors, developed from psychophysical methods and precise studies of quantitative semantics, is not used randomly, therefore it should never be modified; specifically, in the administration, adjectives are not modified, nor are they moved, nor are the instructions changed.

The mBDS is the most used to assess symptoms of shortness of breath, specifically the subjective experience of respiratory discomfort characterized by qualitatively distinct sensations that vary in intensity; it provides valuable information when used correctly [22].

Dyspnea assessment is certainly capable of distinguishing patients with different severity of dyspnea, but it is not very sensitive in capturing changes in the symptom in the same subject over a short to medium period. It is therefore important for dyspnea to be characterized more precisely with other systems that allow changes in dyspnea to be assessed over a short period of time. The most widely used method is the Borg Dyspnea

Scale, applied immediately before and at the end of a standardized exercise tolerance test [23].

2.7. Statistical Analysis

Statistical analysis was conducted using STATA statistical software. We used Shapiro–Wilk for testing normality of data. A descriptive analysis was expressed as mean ± standard deviation (SD) and t-Student test was used for significance testing, as appropriate for paired samples. Significance was indicated by a p value < 0.05.

3. Results

Thirty patients were observed, but eight were excluded from the analysis because their clinical course worsened resulting in pneumonia and therefore they underwent NIV treatment, along with other complications which made them unsuitable for physiotherapy tests. Then, twenty-two patients (10 males, 12 females) were eligible for the study and treated with HFNC, mean age 64.5 ± 5.9 years (Table 1).

Table 1. Patient characteristics (comorbidities).

Age (Years) (Mean ± SD)	64.5 ± 5.9
Hypertension	9 (47%)
COPD	2 (10%)
OSAS	2 (10%)
Diabetes	6 (31%)
Smokers/Ex Smokers	3 (15%)

COPD = chronic obstructive pulmonary disease; OSAS = obstructive sleep apnea syndrome.

Only one patient presented with no comorbidities. At baseline, patients showed acute hypoxemic respiratory failure (AHRF) and mean P/F of 235 ± 7.35. At T1, the mean of FiO2 during treatment with HFNC was 34.46 ± 7.22 to obtain a SpO2 mean of 95% ± 0.59%. At T2, P/F ratio with HFNC was 331 ± 10.91; only one patient used HFNC with enrichment of oxygen (FiO2 28%) (Table 2).

Table 2. Respiratory function profile.

	T0	T1	T2	*p* Value
P/F r.	235 ± 7.35	237 ± 8.15	331 ± 10.91	<0.05
FiO2%	21 ± 9.34	34.46 ± 7.22	22.95 ± 3.45	<0.05
SpO2%	86 ± 4,54	95 ± 0.59	97 ± 1.01	<0.05
HR b/min	88 ± 7.68	76 ± 8.78	68 ± 5.32	<0.05
RR r/min	20 ± 4	16 ± 2.05	12 ± 1.39	<0.05

T0 (at admission in the COVID-19 Emergency Division); T1 (at five days from the admission in the hospital); T2 after 20 days of hospitalization; P/F r = PaO2/FiO2; FiO2% = fraction of inspired O2; SpO2% = oxygen saturation; HR b/min = heart rate; RR r/min = respiratory rate per minute.

Statistically significant results were observed in the evaluation of the functional profile with respect to the evaluation scales used as reported in Table 3 for $p < 0.05$. At the end of rehabilitation, after 20 days of hospitalization 21/22 patients no longer needed oxygen therapy support.

Table 3. Functional and rehabilitative profile during hospitalization.

Functional Profile	T1 Effort	T2 Effort	*p* Value
1STST	4 ± 3	17 ± 5	<0.05
SPPB	4.3 ± 2.81	9.15 ± 2.39	<0.05

SPPB = short physical performance battery; 1STST = 1 minute sit to stand test.

4. Discussion

Resuming our study hypothesis, that is, that the use of HFNC might play a major role during the rehabilitation of COVID-19 patients, we observed good results and adequate patient compliance with the rehabilitation treatment considering the data that were recorded. Furthermore, we have not observed relapses or exacerbations that have forced the suspension of the rehabilitation process. There were previous systematic reviews with the use of HFNC in respiratory diseases related to pulmonary rehabilitation [24] and the most available evidence was about pulmonary exercise programs or muscle exercise. HFNC, as a new therapeutic manner in COPD patients with high efficiency compared to conventional oxygen therapy and high adherence rate and comfortable experience compared to non-invasive ventilation, emerged as a new method for pulmonary rehabilitation in AHRF due to COVID-19 [25,26]. In our study we used this treatment, not only to correct the hypoxemia but also during the rehabilitation program to obtain better tolerance to the rehabilitative exercise. In fact, the rehabilitation in COVID-19 patients must be patient-centered and tailored to individual patient needs; any pulmonary rehabilitation programmed should take into account comorbidities that may affect a patient's progress [27,28].

Most importantly, HFNC therapy could be used if CPAP is not tolerated, as Bonnesen et al. reported in a recent review that investigated the current treatment of patients with COVID-19 and acute respiratory failure and the best ventilation strategies [29].

The rehabilitation outcomes expressed by the results of physiotherapy tests, such as the number of rises from the chair and the SPPB test scores measured at T2, were very satisfactory and showed a clear improvement in physical performance between T1 and T2 evaluation times. In support of the improving trend, it should be noted that in the face of better performance, there is a reduction in the subjective perception of respiratory fatigue linked to physical exercise, lower heart rate values, and higher O2 saturation values at the end of the effort, indicating greater tolerance to the same. The support of the HFNC during rehabilitation proved to be extremely useful in the control and reduction of dyspnea symptoms, positively influencing the tolerance of patients toward physical exercise with a consequent improvement in their adherence to rehabilitation allowing a more rapid recovery of walking and an increase in the intensity of the better tolerated rehabilitation exercise.

In particular, exercise has been demonstrated to confer protection against functional deterioration in institutionalized older adults during COVID-19 lockdown/confinement situations [30,31].

It should be noted that the limitation of this study is the small number of patients considered and the absence of a control group (CG). At the same time, it should be noted that it is of interest in the field of outcomes and compliance with the rehabilitation pathway, in order to consider it as a starting point for further randomized control study.

5. Conclusions

The use of HFNC during the rehabilitation process in COVID-19 pneumonia mild cases (PaO2/FiO2 between 200–300) seems to guarantee a better compliance of the patient to the rehabilitation exercise and a more rapid functional recovery by reducing hospitalization times. Considering the intrinsic limitations in retrospective observational studies and the lack of CG, the data reported in our study are encouraging but further randomized controlled trials are necessary to better define the use of HFNC during rehabilitation path and to define a clinical and functional profile of the patients best responsive to this type of treatment.

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