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Evaluation of Neuroinammatory and Neurocognitive Effects of Noninvasive Ventilation Modes in COVID-19 Patients

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Material and Methods: This study was conducted on 50 patients using HFNC (n:25) or NIMV (n:25), who followed up with COVID-19 pneumonia in the Neurology Intensive Care Unit (ICU) in September 2020. Demographic data, COVID-19 severity scales (Brescia-COVID Respiratory Severity Scale (BCRSS), Rapid COVID-19 Severity Index (QCSI), H-Index), serum neuro-inflammatory parameters, Coronavirus Anxiety Scale (CAS) and Montreal Cognitive Assessment Scale (MOCA) were evaluated and compared on the first and seventh days in both groups. In addition, thorax computed tomography (CT) findings and Total Lung Severity Score (TLSS) were evaluated.

Keywords: *Cognitive assessment; COVID-19 pneumonia; HFNC; NIMV.*

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Results: Both groups were homogeneous in terms of age, gender, and education level. Each participant had at least one RT-PCR test of positivity. At the end of the 7th day, QCSI and H-Index were higher in the NIMV group. Also MOCA was lower and CAS scores were higher in the NIMV group. ESR, NLO, pro-calcitonin, and troponin values from neuro-inflammatory parameters were higher in the NIMV group on the 7th day ($p<0.05$). The distributions in these groups are statistically significant ($p<0.05$).

Conclusion: In this study, it is predicted that the noninvasive oxygen module to be selected on behalf of patients to be monitored in intensive care conditions may affect COVID-19 severity, neuro-inflammatory levels and cognitive processes. In this aspect, the use of HFNC should be given priority in patients considered for noninvasive ventilation. New studies are needed in this area.

Keywords: Cognitive assessment; COVID-19 pneumonia; HFNC; NIMV.

I. Introduction

Noninvasive ventilation is an alternative approach that was developed to avoid complications in patients with acute respiratory failure (1-6). It is often used for acute exacerbations of chronic obstructive pulmonary disease, because such exacerbations may be rapidly reversed and because the hypercapnic ventilatory failure that occurs in patients with this disorder seems to respond well to noninvasive ventilation (5,7-13). The value of HFNC for acute hypoxemic respiratory failure (unrelated to COVID-19) has been extensively studied. Of eight meta-analyses published since 2017, we concluded HFNC was associated with reduced rates of MV compared with conventional oxygen therapy or NIPPV in the setting of acute hypoxemic respiratory failure (14, 15, 16, 17), Four meta-analyses evaluated the use of HFNC after liberation from MV (17–19, 20); and demonstrated a reduction in the need for re-intubation and re-initiation of MV (20). No meta-analysis of HFNC use, either before or after MV, found HFNC to be associated with worse outcomes. In this study, we investigated the central and peripheral effects of the non-invasive ventilation module to be selected in the management of COVID-19 patients. In this context, we evaluated the effect of (HFNC) and NIMV use on COVID-19 severity scales and neuro-inflammatory markers in terms of peripheral exposure, as well as the relationship between COVID-19 anxiety and changes in MOCA scales in terms of central involvement in acute and subacute stages.

II. Materials and Methods

a) Study Design and Patient Cohort

This single-center, prospective study was conducted with 50 patients older than 18 years of age who were hospitalized in the Neurology ICU in September 2020 in Ankara City Hospital because of COVID-19. The study was carried out after obtaining the written consent of each participant. Patients who were followed up with HFNC or NIMV in intensive care conditions and who were able to comply with cognitive impairment tests were included. Demographic data including age, gender, education level, history of central neurological disease, history of peripheral neurological disease, symptom onset time, number of positive RT-PCR, the time between positive RT-PCR finding and symptom onset, and neurological complaints were recorded. The relevant datas were collected using a standardized case-report form. All data were performed by the corresponding researcher (E.D.U.). All the patients included in this study were tested for influenza A virus, influenza B virus, respiratory syncytial virus, and parainfluenza virus, and these infections were excluded

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by a serological test. Nasal and/or pharyngeal swab specimens were collected from all patients, and RT-PCR assays were performed. The patients have received the diagnosis by positive RT-PCR and chest imaging findings for COVID-19. In this study, we classified and compared the patients into two groups according to NIMV or HFNC usage. Hospitalization, treatment, management, and discharge of the patients were decided according to the guidelines of the Turkish Ministry of Health.

b) Imaging Analysis

Thorax computed tomography (CT) information was obtained from the images during the application to the emergency department. Revolution CT (GE Healthcare, Illinois, U.S.A) CT devices with 64 and 128 detectors were used. The evaluation was made by the corresponded investigator (E.D.U) on the images uploaded to the system by PACS (Picture Archiving and Communication System software) installed on the computer. Each participant's CT was evaluated for viral or bacterial pneumonia and the TLSS score was calculated.

c) Evaluation of plasma acute inflammatory reactants

Serum samples were taken from each participant on the first and seventh days. Serum acute phase reactants including erythroid sedimentation rate (ESR), neutrophil/lymphocyte ratio (NLO), C-Reactive protein, pro-calcitonin, interleukin-6 (IL-6), ferritin, fibrinogen, triglyceride, aspartate aminotransferase, D-Dimer, and troponin values were measured, and both groups compared. Related tests were carried out by Ankara City Hospital Medical Biochemistry Laboratory and evaluated by the responsible researcher (E.DU).

d) Evaluation of COVID-19 severity scales

COVID-19 severity scales were included in this study and compared between two groups, including the BCRSS, QCSI, and Hscore. The BCRSS, QCSI, and HScore were evaluated using laboratory information in the emergency department during the admission process on the first day and in the Neurology ICU at the end of the seventh day. In our study, we aimed to calculate the sensitivity and specificity values according to the cut of values in the literature, as well as find the best cut-of value of the scores. The cut of values in the literature were used for these calculations. The BCRSS and Hscore values were 3, ≥ 1, and >169 in the calculations, respectively (21–23,24, 25, 26, 27). Consistent with the existing literature, we consider using the worst parameters available in the first 24 h during admission (21–23, 24, 25, 26, 27).

BCRSS: The BCRSS was developed in Brescia, Italy, during that nation's COVID-19 crisis. This prediction rule uses patient examination features and the need for escalating respiratory support levels to suggest treatment recommendations. The scale allows clinicians to compare patients, track the trend of a patient's respiratory severity level over time, and monitor patients nearing a critical action point (28). The BRCSS uses clinical criteria to rank non-intubated patients. It assigns patients a score of 0–3 based on 4 test criteria: (1) dyspnea or staccato speech, defined as being unable to count rapidly up to 20 after a deep breath, at rest, or during minimal activity, such as sitting up in bed, standing, talking, swallowing, or coughing; (2) respiratory rate of>22 breaths/min; (3) PaO2 of<65 mmHg or SpO2 of<90% with supplemental oxygen; and (4) significant worsening of chest radiography. In intubated patients, PaO2/FiO2 below 150 mmHg determines whether the score is 5 or above, and the use of adjunctive therapies including prone positioning and neuromuscular blockade agents further increase the score (28, 29)

QCSI: The QCSI score was derived from a dataset of hospitalized COVID-19 patients in the Northwestern United States. Its primary purpose is to predict critical respiratory illness at 24 h, as defined by high oxygen requirements, non-invasive ventilation, invasive ventilation, or death (30). It is a 12-point scale that uses only three variables available at the bedside: nasal cannula flow rate, respiratory rate, and minimum documented pulse oximetry. The patients were then assigned to four risk strata (0–3) based on the following 217 scores: 0–3 low risk, 4–6 low-intermediate risk, 7–9 high-intermediate risk, and ≥ 10 high risks (30).

Hscore: The Hscore is composed of nine variable components as follows: three clinical variables (high fever, organomegaly, underlying immunosuppression), five biochemical variables (triglycerides, ferritin, serum transaminases, fibrinogen, presence of cytopenia), and one cytological variable (findings of hemophagocytosis in the bone marrow) (31). Although there are different cut-off values, the most reliable one in hemophagocytic syndrome (HPS) was 169, and it accurately classified 90% of patients with 93% sensitivity and 86% specificity (31).

e) Evaluation of cognitive function rating scale and COVID-19 anxiety scale

All 50 patients were subjected to the neurocognitive assessment scale on the first and seventh days. Compliance with the test was confirmed by performing a full physical and neurological examination of each patient before the test application. Patients who could not comply with the test were excluded from the study. For the neurocognitive evaluation, MoCA test (8), which has proven effective in COVID-19 patients, and CAS scales (32), which are significant in eld studies in terms of COVID-19 anxiety were used.

MoCA: The MoCA is a widely used screening assessment for detecting cognitive impairment (33). It is a one-page 30-point test administered in approximately 10 minutes that assesses: Short-term memory,

visuospatial abilities, executive functions, attention, concentration, working memory, and language (34). Scores on the MoCA range from 0 to 30 and ranges indicate ≥26 = normal, 18–25 = mild impairment, 11–17 = moderate impairment and ≤10 = severe impairment. According to the validation study, the sensitivity and specificity compared with 18% and 100% respectively for the MMSE. Subsequent studies in other settings were less promising, though superior to the MMSE (35,36)

CAS: The CAS is a 5-item scale with robust reliability and validity based on a study conducted with 775 adults (37). It includes the cognitive (i.e., repetitive thinking; worry; processing biases; dreaming; planning), behavioral (i.e., dysfunctional activities; avoidance; compulsive behaviors), emotional (i.e., fear; anxiety; anger), and physiological (i.e., sleep disturbances; somatic distress; tonic immobility;) dimensions of coronavirus anxiety. Each item was rated on a 5-point scale to react to the frequency of the symptom, ranging from 0 (not at all) to 4 (nearly every day).

f) Statistical Analysis

SPPS 25 (IBM Corp. Released 2017) statistical package program was used to evaluate the data. In the study, descriptive statistics (mean, standard deviation, median, minimum-maximum values, number, and percentile) were given for categorical and continuous variables. The homogeneity of the variances was checked with the Levene test. Normality assumption was checked with the Shapiro-Wilk test. The differences between the two groups, 'Student's-T Test' if the parametric test prerequisites are met; If not, the 'Mann Whitney-U' test was used. Relationships between categorical variables were analyzed with Fisher's Exact Test and Pearson Chi-Square test. The relationship between two continuous variables was evaluated with the Pearson Correlation Coefficient and Spearman Correlation Coefficient. A $p<0.05$ level was considered statistically significant.

III. Results

The study was conducted with patients receiving oxygen supplementation with 25 HFNC and 25 NIMV. Patients who were intubated during their follow-up or who had to take HFNC or NIMV support together were excluded. The mean age was 52.5±2 years. Both groups were homogeneous in terms of age, gender, and education level. Among the demographic data, 3 patients had epilepsy and 9 patients had diabetic polyneuropathy. Each participant had at least one RT-PCR test of positivity. PCR negative time was measured in 26 patients. The mean value was 12±2. The most common complaints among the participants were sleep disturbance (46%), headache (45%), and lightheadedness (45%). Two patients presented with epileptic seizures. During the treatment period, all patients were treated with favipiravir, while 10 patients were treated with anakinra, 3 patients with tocilizumab, and 3 patients with pulse prednol (1000 mg IV). At presentation, 30% of the patients' thoracic CT scans were typical for viral pandemic pneumonia, and 6% were typical for bacterial pneumonia. 14% had viral-bacterial pneumonia superimposition. The TLSS scale for assessing the severity of COVID-19 pneumonia was 2.36±2 in the HFNC group and 2.6±2 in the NIMV group. BCRSS, QCSI, and HScore were evaluated in the evaluation of COVID-19 severity scales between groups. BCRSS 1st and 7th-day measurement and QCSI 1st day measurement did not differ statistically between groups ($p<0.05$). In Hscore 1st-day measurement, the HFNC group mean was 89,8±2 and the NIMV group mean was 98±2. HScore 7th-day measurement was lower in the HFNC group than the NIMV group mean In QCSI and HScore 7th-day measurement, the HFNC group mean was 7.44±2 and the NIMV group mean was 10.52±2. In QCSI and HScore 7th-day measurement, the HFNC group mean was lower than the NIMV group mean ($p<0.05$) (Table 1).

Table-1: Comparison of COVID-19 Severity Scales (Day 1-7) in NIMV and HFNC group

	HFNC(mean±2)	NIMV(mean±2)	P
BRESCIA SCORE 1.Day Measurement	2,64	2,84	0,658€
BRESCIA SCORE 7. Day Measurement	2,40	2,84	0,447€
QUİCK COVID-19 SEVERİTY INDEX (QCSI) 1. Day Measurement	8,44	8,66	0,933€
QUİCK COVID-19 SEVERİTY INDEX (QCSI) 7. Day Measurement	7,44	10,52	**0,04*€**
H SCORE 1.Day Measurement	89,8	98	**0,042*¥**
H SCORE 7.Day Measurement	77,12	112	**0,001**¥**

**p<0,01 *p<0,05

n: Number*; %:* %*:* Percentage; € Mann Whitney-U test ¥ Student's t test

MOCA and CAS scores were calculated in the evaluation of cognitive and anxiety status between groups. CAS score and MOCA 1st-day measurement did not differ statistically in HFNC and NIMV groups ($p<0.05$). MOCA 7th-day measurement values were 19.48±2 in the HFNC group and 15.84±2 in the NIMV group. At the MOCA 7th-day measurement values, the mean of the HFNC group was higher than the mean of the NIMV group ($p<0.05$) (Table 2).

Table-2: Comparison of MoCA (Day 1-7) in NIMV and HFNC group

	HFNC(mean±2)	NIMV(mean±2)	P
MONTREAL COGNİTİVE ASSESSMENT (MOCA) (1. Day Measurement)	19,2	18,84	0,117€
MONTREAL COGNİTİVE ASSESSMENT (MOCA) (7. Day Measurement)	19,48	15,84	**0,044*¥**

**p<0,01 *p<0,05
n: Number*; %: Percentage;*
€ Mann Whitney-U test ¥ Student's t test

Of those with positive CAS 7th-day measurement, 33.3% were in the HFNC group (n: 12) and 66.7% were in the NIMV group (n: 24) (Table 3). The distributions in these groups are statistically significant ($p<0.05$).

Table-3: Comparison of CAS (Day 1-7) in NIMV and HFNC group

				Groups		Critical Value	P
				HFNC	NIMV		
Coronavirus Anxiety Scale (CAS)	1.Day Measurement	Negative	n	3	1	1,087	0,297
			%	75,0%	25,0%		
		Positive	n	22	24		
			%	47,8%	52,2%		
	7. Day Measurement	Negative	n	13	1	**14,286**	**0,001****
			%	92,9%	7,1%		
		Positive	n	12	24		
			%	33,3%	66,7%		

**p<0,01 *p<0,05
n: Number*; %:* Percentage;
1 Chi-Square Test

Serum acute inflammatory parameters were measured on the first and seventh days of the groups. In the first day measurements; 34.3% of those with a high IL-6 value were in the HFNC group (n:12) and 65.7% in the NIMV group (n:23); 60.6% of those with a high AST value are in the HFNC group (n:20) and 39.4% in the NIMV (n:13) group; those with high troponin values were 44.2% in the HFNC group (n:15) and 55.8% in the NIMV group (n:22). On the seventh day measurements of serum acute phase reactants; 38.7% of patients with high ESR values were in the HFNC group (n:13) and 61.3% in the NIMV group (n:6); 44.4% of those with high NLO values were in the HFNC group (n:20) and 55.6% in the NIMV group (n:25); 44.2% of those with high pro-calcitonin levels were in the HFNC group (n:19) and 55.8% in the NIMV group (n:24); 40.5% of those with high troponin levels were in the HFNC group (n:15) and 59.5% in the NIMV group (n:22) (Table 4). Distributions in these groups are statistically significant ($p<0,05$).

Table-4: Comparison of Serum Acute Phase Reactants (Day 1-7) in NIMV and HFNC group

				Groups		Critical Value	p
				HFNC	NIMV		
Erythrocyte Sedimentation Rate (ESR)	1.Day Measurement	Normal	n	6	7	0,104	0,747
			%	46,2%	53,8%		
		High	n	19	18		
			%	51,4%	48,6%		
	7.Day Measurement	Normal	n	13	6	**4,160**	**0,041***
			%	68,4%	31,6%		
		High	n	12	19		
			%	38,7%	61,3%		
Neutrophil / Lymphocyte Ratio (NLO)	1.Day Measurement	Normal	n	0	1	1,020	0,312
			%	0,0%	100,0%		
		High	n	25	24		
			%	51,0%	49,0%		
	7.Day Measurement	Normal	n	5	0	**5,556**	**0,018***
			%	100,0%	0,0%		
		High	n	20	25		
			%	44,4%	55,6%		
Procalcitonin µg/L	1.Day Measurement	Normal	n	3	2	0,222	0,637
			%	60,0%	40,0%		
		High	n	22	23		
			%	48,9%	51,1%		
	7.Day Measurement	Normal	n	6	1	**4,153**	**0,042***
			%	85,7%	14,3%		
		High	n	19	24		
			%	44,2%	55,8%		

IL-6 pg/Ml	1.Day Measurement	Normal	n	13	2	**11,524**	**0,001****
			%	86,7%	13,3%		
		High	n	12	23		
			%	34,3%	65,7%		
	7.Day Measurement	Normal	n	7	4	1,049	0,306
			%	63,6%	36,4%		
		High	n	18	21		
			%	46,2%	53,8%		
AST U/L	1.Day Measurement	Normal	n	5	12	**4,367**	**0,037***
			%	29,4%	70,6%		
		High	n	20	13		
			%	60,6%	39,4%		
	7.Day Measurement	Normal	n	13	7	3,000	0,083
			%	65,0%	35,0%		
		High	n	12	18		
			%	40,0%	60,0%		
Troponın ng/L	1.Day Measurement	Normal	n	6	1	**4,153**	**0,042***
			%	85,7%	14,3%		
		High	n	19	24		
			%	44,2%	55,8%		
	7.Day Measurement	Normal	n	10	3	**5,094**	**0,024***
			%	76,9%	23,1%		
		High	n	15	22		
			%	40,5%	59,5%		

$^{**}p<0,01$ $^{*}p<0,05$

n: Number*; %:* Percentage;

1 Chi-Square Test

IV. Discussion

In this study, we aim to evaluate to what extent the ventilation module to be selected affects the severity of the disease, the change of neuroinflammatory markers, and cognitive impairment in the acute and subacute periods in COVID-19 patients who have not yet been intubated. In this respect, our study is the first as far as we know.

The etiology of the SARS-CoV-2 is certainly multifactorial, but the exact pathophysiological mechanisms leading to the neurological and psychiatric consequences of COVID-19 are still not clear. Reports about anosmia (loss of the sense of smell) (38) and ageusia (loss of taste) in patients with COVID-19 infection turned attention toward possible affection of the central nervous system (CNS) (39–42). Other early complications include impaired consciousness, agitation, dizziness, and headache (40). Rogers and colleagues (43) conducted a systematic review and found a few studies that did systematic assessments of cognition in patients following SARS-CoV and MERS-CoV infection. During the acute phase, around a third of the patients experienced impaired memory, concentration, or attention (44). After the illness, around one-fifth of all patients had one or more of the aforementioned cognitive impairments. A letter dating from June 2020 (44) reported that a third of their discharged COVID-19 patients showed a dysexecutive syndrome consisting of "inattention, disorientation, or poorly organized movements in response to the command". As more unusual symptoms emerged, it became gradually clear that COVID-19 could affect a wide variety of organs and tissue (45-47). In our study, both central and peripheral nervous system effects of COVID-19 were investigated, and sleep disturbance (46%), headache (45%), and lightheadedness (45%) were found to be the most common symptom of patients upon admission. Two patients were found to have epileptic seizures.

Current observational reports view that a significant proportion of patients with COVID-19 pneumonia can be treated non-invasive (i.e., high flow nasal cannula (HFNC) or non-invasive ventilation (NIV)) instead of invasive mechanical ventilation (IMV). HFNC and NIMV are the leading noninvasive ventilation methods used in COVID-19 patients (48). In our study, HFNC and NIMV were used as non-invasive mechanical ventilation methods in ICU, depending on necessity.

HFNC oxygen therapy refers to the delivery of humidified and heated oxygen at high flows, typically 20-60 L/min, which is titrated to a precise fraction of inspired oxygen (Fi O2). The advantages of delivering oxygen in this manner include improved comfort by satisfying patients on demand, creating an oxygen reservoir in the upper airway, and reducing physiological dead space (reduced CO2 rebreathing) (49). Recent meta-analyses suggest that the application of HFNC in the setting of acute hypoxemic respiratory failure can reduce the risk of intubation and invasive mechanical ventilation by 15% compared with conventional oxygen therapy without affecting mortality. (50). A recent computer simulation study concluded that strategies incorporating HFNC for patients not urgently needing intubation could result in greater mechanical ventilator availability and fewer deaths. Propensity score-matched analyses comparing HFNC and other means of respiratory assistance suggest a lesser likelihood of intubation (51), a higher number of ventilator-free days, and a reduction in ICU length of stay (52) with the former. In previous studies on the use of oxygen support with HFNC in hypoxic respiratory failure, better patient comfort, decreased respiratory distress, regressed tachypnea, better oxygenation and decreased intubation requirement have been found (53).

Non-invasive ventilation (NIV) is delivered through a face mask or a helmet that is placed over the patient's head. The helmet interface potentially presents a safer alternative (from an infection control perspective) because it eliminates leaks. In the settings of acute congestive heart failure and acute hypercapnic respiratory failure due to COPD, NIV has been extremely effective in preventing intubation and reducing mortality (54, 55). NIV was associated with higher intensive care unit mortality among ARDS patients with PaO2 / Fi O2 9.5 mL/ kg predicted body weight) and poor oxygenation at baseline (PaO2 /Fi O2 9 mL/kg of predicted body weight and PaO2 /FiO2 ≤200 mmHg independently predicted NIV failure (54). A post hoc analysis reported a higher risk of intubation and mortality for patients treated with NIV versus HFNC in a group of immunocompromised patients with acute respiratory failure (55). In our study, the central and peripheral system effects of NMIV and HFNC use in COVID-19 patients were evaluated and the effects on COVID-19 severity scales, serum neuro-inflammatory markers levels, and cognitive impairment were compared between two groups. Consistent with the literature so far, it has been statistically proven that the use of HFNC at the end of the 7th day has a positive effect on both the COVID-19 severity scores. We evaluated BCRSS, QCSI, and HScore on the 1st and 7th-day. There is no difference between BCRSS and QCSI scores on the 1st-day. HScore 1st-day measurement was higher in the NIMV group. HScore 7th-day measurement was lower in the HFNC group. In QCSI and HScore 7th-day measurement, the HFNC group mean was lower than the NIMV group ($p<0.05$).

There is evidence that severe COVID-19 patients show hyper-inflammation, hyperferritinemia, and hypercytokinemia. Siddiqi and Mehra stated that in the hyperinflammation phase of COVID-19, there is a significant increase in biomarkers and inflammatory cytokines such as interleukin (IL)-2, IL-6, IL-7, ESR, NLO,

troponin, CRP, ferritin, PCT, and D-dimer. It has been reported that uncontrolled hyperinflammation can lead to cardiopulmonary collapse and multiple organ failure (56). To determine the effect of COVID-19 on the neuroinflammatory process and to compare the prognostic change of this process, we measured laboratory values on the first and seventh days in both groups. In the first day measurements of serum acute phase reactants; IL-6 values were higher in the NIMV group, and AST and troponin values were higher in the HFNC group. On the seventh day measurements of serum acute phase reactants; ESR, NLR, pro-calcitonin and troponin levels increased in the NIMV group and had a high that reached statistical significance.

Considering current data, patients in various degrees suffer from short-term cognitive impairment following COVID-19 infection. Compared to healthy controls, all the included studies reported that a higher percentage of patients had a global cognitive impairment. Regarding specific cognitive domains, principally attentional and executive functions seem to be prone to impairments (57). Dysfunctions of the higher mentation go unnoticed, especially if they are mild and occur in otherwise asymptomatic persons (58). Such unrecognized deficits have been brought out in asymptomatic subjects in many other diseases by targeted cognitive tests like MoCA (59, 60). The ICU patient follow-up process creates cognitive impairment in patients because it affects the patient's psychological and physical comfort and because COVID-19 inflammation adversely affects the central nervous system. In this process, we believe that the noninvasive ventilation method to be chosen in non-intubated patients can change the cognitive impact of the patients. MoCA scores were compared to cognitive evaluation scales in both groups. The MoCA day 1 measurement was similar in both groups, while the average for day 7 was higher in the HFNC group. There is not enough data to support this statistically significant data in our study, and there is not enough data yet on which noninvasive method affects cognitive influence for the better.

During an infectious disease outbreak, a significant proportion of people tend to experience clinically significant levels of fear and anxiety (61). Consistent with this, acute infection and mortality rates related to COVID-19 caused widespread fear and anxiety (62, 63). Studies conducted in China demonstrate this, reporting that between 50% (64) and 70% (65) of the participants showed moderate to high psychological symptoms (64, 65). Consistent with this, Wang et al. (64) found that approximately one-third of the participants reported moderate-to-severe anxiety, while for Tian et al. (65) the participants reported high scores for obsessive compulsion, interpersonal sensitivity, phobic anxiety, and psychoticism. Many studies have shown that HFNC is tolerated as well and reduces anxiety better than other means of oxygen supply (66) respected by comfort scores (67), generated noise scores, dryness of the nose scores, and subjective appearance of patient's comfort and complaint (68). The study by Sztrymf et al. (69) included patients who tolerated HFNC for up to 7 days without major side effects. In our study, we compared first and seventh-day CAS scores to measure coronavirus anxiety in the HFNC and NIMV groups. While no statistically significant difference was observed in the first-day scores, we showed that 66.7% of those with high 7th day measurements were in the NIMV group. The present results are in line with data showing that HFNC has a better effect on anxiety.

Limitations of the Study

The present study was based on a detailed interview with the patient (and/or a carer) that was carried out within 7 days of hospital admission for COVID-19 pneumonia. The parameters examined within the study do not include the significance level of the parameters that have reached statistical significance in chronic return of COVID-19 pneumonia. In addition, the limited patient population included in the study brings to mind the idea that different results can be obtained when similar studies are conducted with larger patient groups of different ethnic origins.

V. Conclusion

In this study, patients ventilated with NIMV or HFNC were evaluated with demographic data, COVID-19 severity scales, serum acute phase reactant parameters, and cognitive scales. We concluded that COVID-19 severity scales and serum acute inflammatory parameters, which may be important in the follow-up and treatment of COVID-19, increase in patients using NIMV, and that the use of NIMV is related to poor cognitive impairment, which may adversely affect the prognosis in patients and increase the need for treatment. There is not enough data to compare the data on the two noninvasive ventilator modules that we compared in the study. In this respect, our study will contribute to the literature.

Conflict of Interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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