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ORIGINAL ARTICLE

ELMO CPAP: an innovative type of ventilatory support for COVID-19-related acute respiratory distress syndrome

Andréa Mazza Beliero[1,2], Ana Paula Pires Lázaro[3,4], Marza de Sousa Zaranza[1,5], Giovanna Mazza Cruz Lima[4], Álvaro Rolim Guimarães[5], Nilcyeli Linhares Aragão[5], Gdayllon Cavalcante Meneses[5], Marcelo Alcantara Holanda[5,6], Polianna Lemos Moura Moreira Albuquerque[4,7], Geraldo Bezerra da Silva Júnior[3,4], Paula Frassinetti Castelo Branco Camurça Fernandes[2]

1. Instituto Dr. José Frota, Prefeitura Municipal de Fortaleza, Fortaleza (CE) Brasil.
2. Programa de Pós-Graduação em Saúde Coletiva, Centro de Ciências da Saúde, Universidade Estadual do Ceará, Fortaleza (CE) Brasil.
3. Programa de Pós-Graduação em Saúde Coletiva, Centro de Ciências da Saúde, Universidade de Fortaleza, Fortaleza (CE) Brasil.
4. Curso de Medicina, Centro de Ciências da Saúde, Universidade de Fortaleza, Fortaleza (CE) Brasil.
5. Programa de Pós-Graduação em Ciências Médicas, Departamento de Medicina Interna, Faculdade de Medicina, Universidade Federal do Ceará, Fortaleza (CE) Brasil.
6. Departamento de Medicina Clínica, Faculdade de Medicina, Universidade Federal do Ceará, Fortaleza (CE) Brasil.
7. Departamento de Análises Clínicas e Toxicológicas, Faculdade de Farmácia, Universidade Federal do Ceará, Fortaleza (CE) Brasil.

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ABSTRACT

Objective: To assess whether the use of ELMO, a helmet for noninvasive ventilation created in Brazil, had a positive impact on the prognosis of patients with hypoxemic respiratory failure caused by severe COVID-19. **Methods:** This is a retrospective study of 50 critically ill COVID-19 patients. Epidemiological, clinical, and laboratory data were collected on ICU admission, as well as before, during, and after ELMO use. Patients were divided into two groups (success and failure) according to the outcome. **Results:** ELMO use improved oxygenation parameters such as Pao_2, FIO_2, and the Pao_2/FIO_2 ratio, and this contributed to a gradual reduction in FIO_2, without an increase in CO_2, as determined by arterial blood gas analysis. Patients in the success group had significantly longer survival ($p < 0.001$), as determined by the Kaplan-Meier analysis, less need for intubation ($p < 0.001$), fewer days of hospitalization, and a lower incidence of acute kidney injury in comparison with those in the failure group. **Conclusions:** The significant improvement in oxygenation parameters, the longer survival, as reflected by the reduced need for intubation and by the mortality rate, and the absence of acute kidney injury suggest that the ELMO CPAP system is a promising tool for treating ARDS and similar clinical conditions.

Keywords: Respiratory distress syndrome; COVID-19; Noninvasive ventilation; Intensive care units.

INTRODUCTION

COVID-19 emerged as a pandemic in March of 2020. The shortage of mechanical ventilators and specialized health workforce in ICUs were the crucial points in resource allocation and planning.[1] The use of invasive mechanical ventilation (IMV) was often associated with an extremely high mortality rate during the first and second waves in Brazil, reaching up to 80% and 89.5% in two observational studies.[2,3] Therefore, noninvasive respiratory support strategies to prevent orotracheal intubation (OTI) were very much needed during the pandemic and were unfortunately not sufficiently available to the large number of severely ill patients, making the situation even more challenging to the Brazilian public health system.

Infection by COVID-19 leads to systemic inflammation and hypercytokinemia, causing endothelial dysfunction and a hypercoagulable state.[4,5] The clinical spectrum ranges from mild symptoms to more severe complications with multisystemic involvement, such as vascular disorders, acute kidney injury (AKI), heart failure, and circulatory shock, as well as long-term neurological, motor, and cardiopulmonary sequelae.[6,7] The main cause of ICU admissions is acute respiratory distress syndrome (ARDS), which often requires respiratory support.[8]

The need for alternative respiratory support strategies led to the development of innovative technologies to address these problems. ELMO is a new helmet interface that offers high-flow CPAP and up to 100% FIO_2 to treat COVID-19-related acute hypoxemic respiratory failure. It was originally designed to be used without ventilators and outside the ICU.[9,10] It provides complete neck sealing and respiratory

Correspondence to:
Andréa Mazza Beliero. Rua Cícero Alves de Souza, 126, CEP 60822-810, Fortaleza, CE, Brasil.
Tel.: 55 85 99949-1004. E-mail: andreamazza2009@hotmail.com
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isolation of the patient's head, resulting in significant improvement of oxygenation parameters, no carbon dioxide rebreathing, and good patient comfort as shown in a pilot feasibility study.[11] This innovative, noninvasive equipment was designed in the state of Ceará, Brazil, in July of 2020 by a multidisciplinary taskforce from six different institutions involving the government, the industry, a public health school, and universities (Patent no. BR 20 2020 014212 2; ANVISA 82072609001).

The present investigation was designed to assess the impact of the use of the ELMO CPAP system on the prognosis of patients with hypoxemic respiratory failure caused by severe COVID-19 and to compare the major clinical and laboratory variables associated with its successful use, defined as improvement in respiratory failure without the need for IMV.

METHODS

Study design and selected COVID-19 patients

This was an observational, retrospective, single-center cohort study of critically ill COVID-19 patients admitted to the ICU of the *Instituto Dr José Frota*, a tertiary hospital located in the city of Fortaleza, Brazil, from March to May of 2021.

Data on clinical characteristics, treatment, and prognosis of these individuals were collected and correlated with mortality, survival, temporary and permanent sequelae in various organs, as well as the use of renal replacement therapy.

The sample comprised 50 adult patients (≥ 18 years of age) with a diagnosis of COVID-19 confirmed by RT-PCR who presented with hypoxemic respiratory failure secondary to COVID-19, were unresponsive to conventional oxygen therapy (non-response was defined as inability to achieve an Spo_2 ≥ 92% or with no clinical relief of tachypnea or dyspnea when using a nasal catheter with a flow ≤ 5 L/min or a reservoir mask with a flow ≤ 10 L/min), were admitted to the ICU and had an indication for ELMO use according to a pre-defined protocol. Patients admitted to the ICU were eligible for ELMO use if they were alert and cooperative.

Patients with exacerbations of lung diseases, such as asthma, COPD, and pulmonary fibrosis, were excluded. Patients with hemodynamic instability, heart disease, and/or chronic kidney disease, as well as those in use of vasoactive drugs, were excluded; these factors alone increase COVID-19 severity and the chance of needing IMV. Patients with clinically evident signs of respiratory muscle fatigue (paradoxical breathing or vigorous use of respiratory accessory muscles), nausea, vomiting, and/or ear canal disorders and those using a nasogastric or nasoenteric tube were also excluded because they had no indication for ELMO helmet use.

Data collection was performed using a cloud-based database program (Epimed Monitor ICU System; Epimed Solutions, Rio de Janeiro, Brazil). Demographic and epidemiological data, such as comorbidities (systemic arterial hypertension, diabetes mellitus, alcoholism, and lung disease), time from symptom onset to ICU admission, length of ICU stay, and outcome (discharge or death) were collected. Clinical and laboratory data were collected at ICU admission, as well as before, during, and after ELMO use.

Disease severity of patients admitted to the ICU was estimated using the Simplified Acute Physiology Score 3 (SAPS 3) collected at admission. For the diagnosis of AKI, the Kidney Disease: Improving Global Outcomes[12] criteria were used, and serum creatinine levels were measured three times within the first seven days of ICU stay.

Patients in whom ELMO use was considered successful were those who accepted and adapted well to wearing the helmet for at least eight continuous hours for at least three days, as well as showing improvement in vital signs, such as reduced respiratory effort, lower respiratory rate, and lower heart rate, resulting in an increase in Spo_2, in addition to improvement in arterial blood gases.

Clinical results were described: first, ELMO use failure and final outcome (discharge or death) were considered and, second, the time from hospital admission to discharge or death and reasons for ELMO use failure.

To verify the effects of ELMO use on pulmonary gas exchange, two arterial blood gas samples were collected: one at 30 min before ELMO use and one after 1 h of ELMO use. During the use of ELMO, the Pao_2/Fio_2 ratio (in mmHg/%) was measured, and improvement in this ratio was considered indicative of a good response to therapy. Vital signs were continuously monitored and recorded before and during ELMO use, as well as 1 h after ELMO removal. PEEP levels varied between 5 and 12 cmH_2O, and Fio_2 resulting from the gas mixture reached a flow of 60 L/min, being progressively reduced according to the patient's needs.

More details on the protocol for ELMO use are shown in the supplementary file.

Statistical analysis

Categorical data were evaluated as absolute and relative frequencies. For comparison of relative frequencies between groups, the chi-square test or the Fisher's exact test was used according to expected frequencies in 2 × 2 tables. Variables with continuous data were first explored for normality using the Shapiro-Wilk test, and, for the analysis of data asymmetry, histograms and Q-Q plots were used. Normal data were expressed as means ± standard deviations, whereas non-normal data were expressed as medians and interquartile ranges. For comparisons of continuous data between independent groups, the Student's t-test or the Mann-Whitney test was used according to normality. For dependent groups, paired t-test or Wilcoxon test (in non-normal data) was used.

Moreover, the prognostic value of ELMO use from ICU admission for chance of two-month survival was evaluated using Kaplan-Meier analysis treating intubation and death as dependent events. To test the differences between the groups regarding ELMO use, the log-rank Mantel-Cox test was applied. Data were analyzed using the IBM SPSS Statistics software package, version 23.0 (IBM Corporation, Armonk, NY, USA). Values of $p < 0.05$ were considered statistically significant.

Ethical aspects

This study was approved by the institutional Research Ethics Committee (CAAE Protocol no. 67933523.1.0000.5047) and registered on the Brazilian National Research Ethics Committee platform (Protocol no. 4.026.888). All procedures are in accordance with Resolution no. 466/2012, which regulates research involving human participants in Brazil. The patients were informed about the study purpose, and upon acceptance to participate, they signed the free and informed consent form before the beginning of the evaluation. As some admitted patients required immediate ICU care and were unable to sign the term, a family member signed it.

RESULTS

During the study period, of the 296 patients admitted to the ICU, 53 (17.9%) met the criteria for ELMO use; however, 1 patient was excluded from the study due to incomplete data, and 2 were excluded because they died within the first 48 h of the study. Of the 50 patients who were included in the study, the majority were male (n = 31; 62%), and the mean age was 53.2 ± 13.6 years. A success rate of 56% (28/50 patients) was observed (Figure 1). Demographic characteristics, ventilatory parameters, and acid-base parameters on patient admission are described in Table 1.

All patients in the study had at least one comorbidity, often systemic arterial hypertension (in 44%) and diabetes mellitus (in 20%); however, there were no statistically significant differences between the failure and success groups regarding comorbidities (Table 1). Patients in the failure group had a higher mean SAPS 3 when compared with those in the success group (Table 1). All patients reported dyspnea at admission despite being on oxygen therapy. More than half of the patients (56%) had hypoxemia despite oxygen therapy use. No hypercapnia was observed in either group upon admission.

Improvement in oxygenation parameters was observed in both groups during ELMO use, but it was higher in the success group, mainly in Pao_2 and the Pao_2/Fio_2 ratio. $Paco_2$ did not significantly change in either group (Figure 2 and Table 2).

The average number of days from symptom onset to ICU admission was similar between the groups (Table 3). Regarding the causes of ELMO therapy failure, it was observed that 10 individuals (45.4%) showed signs of delirium, characterized by agitation, and altered level of consciousness, and therefore were unable to use ELMO. In addition. 11 patients (50%) developed worsening of symptoms, requiring subsequent intubation. Of the 22 patients in the failure group, only 1 rejected

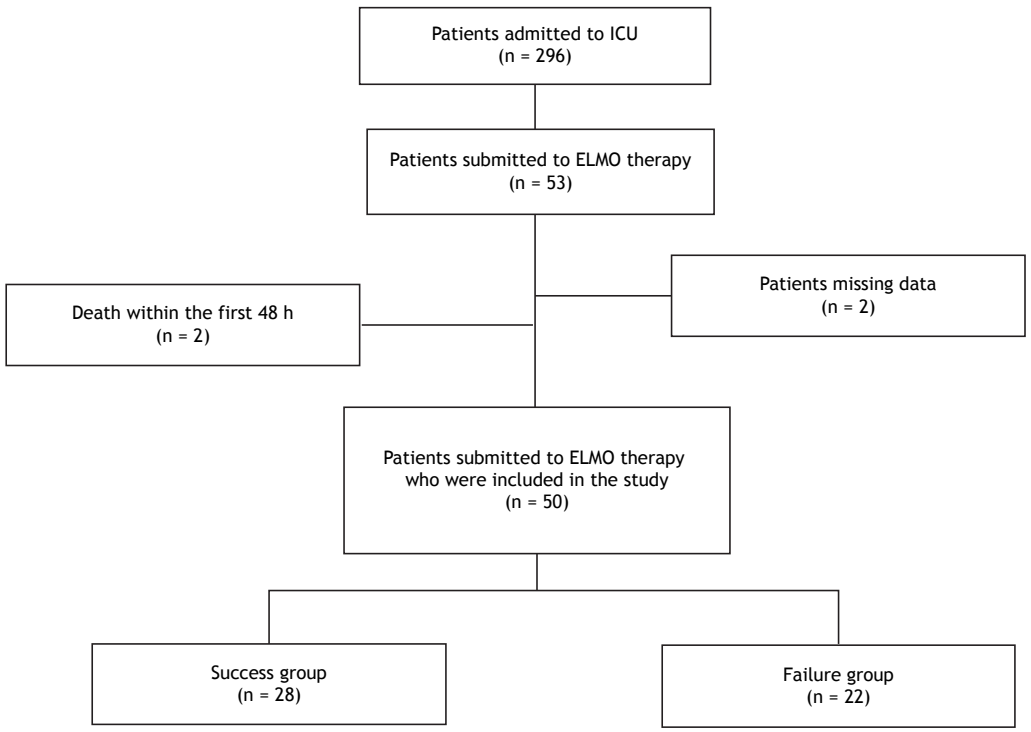

Figure 1. Flow chart of the patient selection process.

Table 1. Clinical and epidemiological characteristics, and ventilatory and biochemical parameters at ICU admission of patients with severe COVID-19 who used the ELMO system, by treatment outcome.[a]

Characteristic	Total	Group		p
		Failure	Success	
	(n = 50)	(n = 22)	(n = 28)	
Sex, male	31 (62.0)	11 (50.0)	20 (71.4)	0.121
Age, years	53.2 ± 13.6	53.8 ± 12.9	52.7 ± 14.3	0.940
SAPS 3	57.21 ± 9.67	60.45 ± 9.44	53.80 ± 8.90	0.030
Previous lung disease	7 (14.0)	4 (18.2)	3 (10.7)	0.684
Diabetes mellitus	10 (20.0)	5 (22.7)	5 (17.9)	0.732
Alcoholism	3 (6.0)	1 (4.5)	2 (7.1)	1.000
Systemic arterial hypertension	22 (44.0)	11 (50.0)	11 (39.3)	0.449
Hypoxemia (Spo_2 < 92%)	28 (56.0)	15 (68.2)	13 (46.4)	0.124
Dyspnea	50 (100)	22 (100)	28 (100)	-
Ventilatory and biochemical parameters				
Spo_2, mmHg	89.47 ± 14.59	84.86 ± 21.21	92.93 ± 4.05	0.147
pH	7.44 ± 0.06	7.45 ± 0.04	7.43 ± 0.07	0.102
Pao_2, mmHg	83.8 ± 30.8	81.6 ± 31.4	85.5 ± 30.8	0.538
$Paco_2$, mmHg	37.1 ± 9.6	35.8 ± 7.2	38.2 ± 11.2	0.443
HCO_3, mmol/L	24.7 ± 2.2	24.3 ± 2.2	25.0 ± 2.1	0.339
BE, mmol/L	1.2 [−0.2 to 2.3]	0.2 [−1.1 to 2.5]	1.25 [0.05-2.13]	0.292
Lactate, mmol/L	1.73 [1.13-2.17]	1.85 [1.13-2.52]	1.48 [1.09-2.13]	0.97
Sao_2, %	93.2 ± 4.3	92.5 ± 4.9	93.7 ± 3.8	0.049
Pao_2/Fio_2	126.3 ± 42.5	126.7 ± 49.1	125.9 ± 37.4	0.435

[a]Values expressed as n (%), mean ± SD, or median [IQR]. SAPS 3: Simplified Acute Physiology Score 3; HCO_3: bicarbonate; and BE: base excess.

ELMO use due to claustrophobia, anxiety symptoms, and increased respiratory rate (> 40 breaths/min).

The median length of ICU stay for patients in the failure and success groups was 19 and 15 days, respectively ($p < 0.05$). Overall, only 40.9% of the patients in the failure group were discharged from the ICU, while all the patients in the success group were discharged. The average daily duration of ELMO use was approximately 8 h.

It was observed that all patients who were successfully treated with ELMO CPAP therapy survived over the days until discharge without the need for OTI. However, 59.1% of the patients in the failure group died during the hospitalization period (Table 3 and Figure 3). The level of CPAP used ranged from 5 to 12 cmH_2O in both groups.

DISCUSSION

Many patients with COVID-19 experience mild to moderate symptoms (81%); however, if ARDS is present, oxygen therapy and some type of ventilatory support are essential.[10] This study showed satisfactory results with the use of the ELMO CPAP system in patients with mild to moderate hypoxemic respiratory failure due to complications from COVID-19.

Analysis of the acute effects on gas exchange before and during ELMO use disclosed a significant improvement in Sao_2, Pao_2 and the Pao_2/Fio_2 ratio. Its use is based on the rationale that PEEP and Fio_2 are the mainstays of respiratory support when the use of a nasal catheter and/or a reservoir mask fails. The improvement in oxygen levels related to the use of the ELMO helmet may have contributed to the survival of more than half of the patients who used it in this study. Patients with COVID-19 have diffuse alveolar damage, reduced respiratory system compliance, and impaired gas exchange.[13] Thus, adequate management of the pressures offered during assisted ventilation and of oxygenation parameters is essential for survival of these patients.

In the present study, we found that the use of the ELMO system was able to offer CPAP through a continuous oxygen flow and compressed air to patients who needed oxygen therapy for severe hypoxemia, resulting in improved oxygenation and gas exchange, allowing the gradual reduction of Fio_2, and avoiding the deleterious effects of oxygen without causing carbon dioxide rebreathing or hypercapnia. The device was used successfully in 28 patients. Moreover, our study showed a significant increase in the median Pao_2/Fio_2 ratio within the first hour of ELMO use.

One study demonstrated that when the Pao_2/Fio_2 ratio doubled from a median of 100 mmHg to 200 mmHg and remained above 150 mmHg during the first week, there was an association with a 91% probability of patient recovery without the need for OTI. This effect can be explained by the effect of CPAP on the recruitment of edematous and/or collapsed alveoli, with immediate improvement in the ventilation/perfusion ratio.[14]

Some studies support the hypothesis that positive pressure may favor a more uniform distribution of

perfusion, diverting blood flow from pulmonary areas with shunt and edema to those with a high ventilation/perfusion ratio.[15]

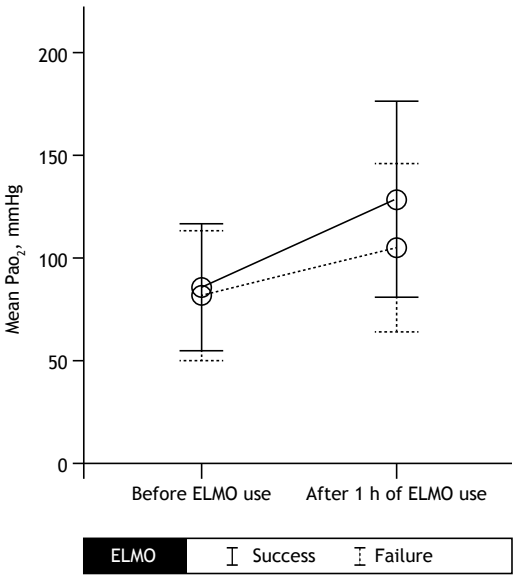

Figure 2. Box plot of Pao_2 before and after 1 h of ELMO use by outcome group (failure and success).

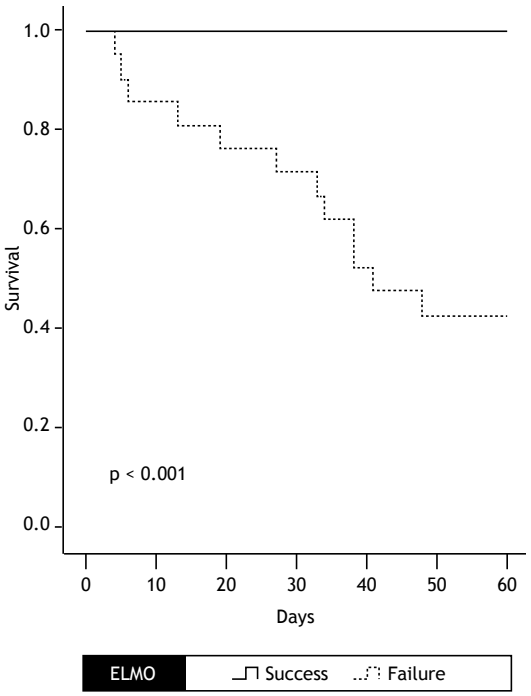

Figure 3. Chance of two-month survival—dependent events: death and intubation—by outcome group (failure and success). *Log-rank Mantel-Cox test.

Table 2. Ventilatory and biochemical parameters of patients with COVID-19 before and during ELMO use, by treatment outcome.[a]

Parameter	Failure group (n = 22)		p	Success group (n = 28)		p
	Before ELMO use	During ELMO use		Before ELMO use	During ELMO use	
Sao_2, %	92.5 ± 4.9	95.9 ± 2.5	0.001	93.7 ± 3.8	96.2 ± 2.4	0.010
pH	7.45 ± 0.04	7.44 ± 0.04	0.567	7.43 ± 0.07	7.43 ± 0.04	0.908
Pao_2,mmHg	81.6 ± 31.4	104.8 ± 41.1	0.067	85.5 ± 30.8	128.1 ± 47.8	< 0.001
$Paco_2$, mmHg	35.8 ± 7.2	35.5 ± 3.1	0.694	38.2 ± 11.2	37.6 ± 5.6	0.797
HCO_3, mmol/L	24.3 ± 2.2	24.3 ± 2.5	0.651	25.2 ± 2.1	25.2 ± 2.2	0.48
BE, mmol/L	0.2 [−1.1 to 2.5]	0.6 [−0.5 to 3.6]	0.173	1.25 [0.05-2.13]	0.9 [0.0-2.7]	0.948
Lactate, mmol/L	1.85 [1.13-2.52]	1.6 [1.0-2.12]	0.511	1.48 [1.09-2.13]	1.66 [1.23-2.00]	0.518
Pao_2/Fio_2	126.7 ± 49.1	177.08 ± 83.27	0.024	125.9 ± 37.4	217.56 ± 113.13	< 0.001

[a]Values expressed as mean ± SD or median [IQR]. HCO_3: bicarbonate; and BE: base excess.

Table 3. Clinical complications and outcomes of patients with severe COVID-19 who used the ELMO system in the ICU at a tertiary care hospital in the city of Fortaleza, Brazil.[a]

Variable	Group		p
	Failure (n = 22)	Success (n = 28)	
From symptom onset to ICU admission, days	10.5 [8-13]	10 [8.5-12.0]	0.655
Final outcome			
Hospital discharge	9 (40.9)	28 (100)	< 0.001
Death	13 (59.1)	0 (0.0)	
Time from admission to death, days	30 [9.5-38.0]	0	< 0.001
Time from admission to discharge, days	19 [15-30]	15 [11-16]	< 0.001
Acute renal injury			
Yes	12 (54.5)	0 (0.0)	< 0.001
No	10 (45.5)	28 (100)	

[a]Values expressed as n (%) or median [IQR].

In our study, patients in the failure group were more severely ill according to the SAPS 3 already on admission. Although SAPS 3 is not part of the ELMO protocol, there are similar parameters among the forms of assessment, such as vital signs and use of IVM. In a study of 1.464 patients, SAPS 3 was found to perform satisfactorily in the prognosis of in-hospital mortality in patients with COVID-19 admitted to the ICU.[16]

The patients in our study wore the ELMO helmet for at least eight continuous hours a day, with an initial PEEP of 5 cmH_2O, increased according to Spo_2 levels. After ELMO helmet removal, the patients were placed on oxygen therapy using a nasal catheter with a flow at 3-5 L/min, according to Spo_2 levels. A study carried out with the same helmet showed no adverse effects in such patients.[11]

During the period when the intervention took place, there was a reduction in the number of patients who required IMV. Of the 50 patients that comprised the study sample, 28 (56%) did not require IMV and were discharged from the hospital, corroborating the recommendations of previous studies, which hypothesized a reduction of approximately 60% of cases that later required IMV.

In the present study, it was possible to observe that none of the patients in whom ELMO was used successfully developed AKI. However, half of the patients in the failure group developed AKI, and some died, in line with studies that correlated the occurrence of AKI, COVID-19, and increased mortality.[17] Although IMV is sometimes necessary as a lifesaving intervention in critically ill patients, its implementation affects the renal system, reaching a three-fold increased risk of AKI,[18,19] especially when associated with IMV and elevated PEEP.[20,21]

The main findings of the present study, such as improvement in oxygenation parameters and possibly better prognosis of patients with COVID-19-related ARDS, suggest that the new ELMO helmet is a promising technological innovation with a positive impact on these individuals.

The limitations of this study are primarily related to the lack of a control group, making it impossible to compare the intervention with other types of non-invasive ventilatory support. Second, this study was carried out in a single center and had a retrospective design. Third, insufficient recording of data in some medical records limited the access to information for a more in-depth evaluation. On the other hand, the study adds some little explored information related to the use of NIV, the use of a new type of helmet, and its direct and indirect effects on renal function in severely hypoxemic patients, stimulating the construction of alternative strategies that can minimize the undesirable effects of IMV with positive pressure. Another advantage is that ELMO can be used outside the ICU.

Future research will be necessary to evaluate different groups, with similar clinical pictures prospectively and over a longer period of time, comparing the use of the ELMO CPAP with other types of respiratory support in order to verify their clinical effects in critically ill patients with hypoxemic respiratory failure of other etiologies.

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AUTHOR CONTRIBUTIONS

AMB: study conception and planning, data selection and interpretation, and project administration. APPL, MSZ, ARG, ARG MMPD, GMCL, NLA, and LCBCF: study design, and literature research and selection. GBSJ, MAH, and PFCBCF: critical revision of the manuscript. GCM: study design, data interpretation, and formal analysis. PLMMA: funding acquisitions. All authors read and approved the final version of the manuscript.

CONFLICTS OF INTEREST

MAH participated as the final reviewer of this manuscript. However, this author was one of the technical developers of the ELMO helmet and holds the patent registration. The other authors have no conflict of interest to disclose.

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