DR. GUSTAVO NAVARRO BETONICO (Orcid ID : 0000-0002-6110-0932)

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Corresponding author email id: nefroprudente@yahoo.com.br

The spread of novel coronavirus disease (COVID-19) urged a never-seen coordinated global response to prepare the health system, including primary care, hospital facilities and intensive care units (ICUs). Lessons have been learned from countries who suffered the pandemic at the beginning, helping the ones which are on different phases of the spreading curve. Currently, optimizing intensive care resources is mandatory as admittance to the ICUs remains rising exponentially. While public and private health system struggle for changing the slope of the curve, intensivists prepare the facilities for a tsunami of respiratory failure patients with COVID-19.[1]

Unfortunately, most of ICUs worldwide do not have single rooms, which could facilitate the isolation efforts. The complexity of critical care patients, who will often undergo mechanical ventilation, dialysis and a prolonged in-hospital period, challenge and urges for unprecedent strategies.

Preparing ICUs for patients with COVID-19 have changed staff dynamics regarding the personal protective equipment (PPE) requirements, team interaction and prompt re-training. Strategies to mitigate the SARS-CoV-2 spread between ICU personnel included specific staff designation for each COVID-19 patient and swapped at the next shift, aiming to minimize workload. As the possibility of insufficient PPE became close, the strategy of minimizing personnel entries on patient's room should be adopted and staff members should be trained to perform all the procedures: administer medication, adjust pumps and ventilator, check vital signs. Despite the efforts, a staff-shortening period is expected and strategies to boost morale and engage personnel includes catering special meals, bring family messages and release daily bulletins about the regional and local epidemiological status of COVID-19.[2]

From March 19th to April 13th, 53 patients were admitted with possible or confirmed COVID-19 to the Emergency Medicine Discipline ICU at the University of Sao Paulo. Overall,

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the clinical picture of these patients is very similar to the previous reported literature, with mean age at fifty's, 58% male, a high prevalence of hypertension (58%) and significant disease severity (64% on invasive mechanical ventilation and 51% on vasoactive drugs). Unfortunately, few data are available regarding overall Brazilian ICU scenario, because the country has distinct public and private healthcare systems and information is not available for ICU patients from both of them. Brazilian private system is responsible for the care of 25% of Brazilian population that has access to private insurance. For these patients, the rate of 25/100,000 ICU beds per inhabitants is a better number than several high-income countries. These units were the first to receive COVID-19 cases in Brazil, following the wealthiest people that had travelled to Europe and other countries. On the other hand, for the remaining 75% of the population, the number of ICU beds in the public system is 7.6/100,000 inhabitants, a rate that per se is not inadequate. However, the distribution of these beds is very unequal, with large poorest regions of the country lacking ICU beds. These beds are progressively being filled by COVID-19 cases, and provisory hospitals and ICU beds are being built in order receive these patients. In this difficult epidemiological scenario, there is a clear expectation of witnessing a measles, dengue, and COVID-19 syndemic, among other conditions that afflict the Brazilian people. In this context, the healthcare system, especially in the northeast ant northern Brazil, is not prepared to face this pandemic that is growing at alarming rates across the world.[3] As an example, when the pandemic hit Maranhão, a northern very low income state located in Amazonia, with 6.8 million population, it had only 232 intensive care beds, concentrated in just three cities. After hustling to build out capacity, it has 761 ICU beds and offers some level of intensive care in 11 cities, according to state authorities. Two field hospitals are being built in order to bring the number of ICU beds to 910. However, untrained staff and lack of expertise on critical care will challenge the public and private health system located on Brazilian Northeast and North regions. Table 1 shows the marked death rates variability within Brazilian regions, highlighting the less income North region presenting the highest mortality rate.[4]

	Cases	Deaths	Incidence	Mortality
Brazil	291,579	18,859	138.7	9.0
Central-west	8,886	204	54.5	1.3
Northeast	100,416	5,537	175.9	9.7
North	55,580	3,608	301.6	19.6
South	13,088	392	43.7	1.3

Southeast	113,609	9,118	128.6	10.3

Table 1: Brazilian COVID-19 statistics on May, 20th. Incidence/100,000 population. Mortality rate/100,000 population.

As long as routine ICU resources are available, patients should be admitted and treated in accordance with institutional well-established criteria. Specific ICU interventions should only be undertaken in cases in which the benefits are clearly demonstrated. For example, in resource-shortage scenario there are some ethical considerations that Extracorporeal Membrane Oxygenation (ECMO) should not be routinely used in patients with COVID-19. However, ECMO can still be used in justified cases and after careful assessment of the personnel and resources required. Patients capable of making their own decision should be encouraged to emphasize their wishes on different possible complications (resuscitation status and extent of intensive care). When the usual intensive-care interventions are withheld, comprehensive and adequate palliative care must be provided.[5]

Regarding the intensive care in COVID-19 patients, primary target organs are usually the lungs. Previous studies report an incidence of 10 to 15% of COVID-19 patients requiring ventilatory support due to respiratory failure. At the first beginning of the pandemic, the protocols guided that patients developing O_2 need through nasal catheter greater than 5 liters/minute to maintain SpO2 > 93% and/or have respiratory rate > 28 respiratory incursions per minute or CO_2 retention ($PaCO_2$ >50 mmHg and/or pH < 7.25) should be promptly intubated and ventilated mechanically. However, this strategy has been questioned and postponing intubation trough high-flow nasal catheters and helmet-mask noninvasive ventilation could be a strategy in a well-trained ICU team.[6,7] Strategies such as prone positioning in awake patients associated with high flow nasal catheters have been used and are associated with improvements in hypoxemia in these patients.[6]

Whenever invasive mechanical ventilation needs to be stablished, rapid-sequence intubation must be performed and safety procedures for airborne transmission followed, like complete PPE, occlusion of the endotracheal tube and the use of capnography devices to check for the correct tube position.

Before starting ventilation on COVID-19 patients with severe lung disease, one must try to identify two different phenotypes. The one "type L", is characterized by high pulmonary compliance associated with low response to positive end expiratory pressure PEEP. The other phenotype, “type H”, seems to be more like typical acute respiratory distress (ARDS) and is associated with high elastance and better response to higher PEEP.[8] Protective invasive mechanical ventilation may be initiated in volume or controlled pressure mode (VCV or PCV) with 6 ml/kg of predicted weight tidal volume and plateau pressure less than 30 cmH_2O, with driving pressure less than 15 cmH_2O. The optimal PEEP on COVID-19 patients remains to be established. Intensive care staff should adjust the lowest PEEP to maintain SpO_2 between 90-95%, with $FiO_2 < 60\%$ (in cases of $FIO_2 > 60\%$, ARDSNET PEEP/FIO_2 table for lower PEEP/higher FiO_2 table may be used – figure 1). Brazilian experience advise against the use of ARDSNET higher PEEP table for severe ARDS in COVID-19 patients. These patients when ventilated with this strategy have been shown pulmonary hyperinflation and worse prognosis.[7]

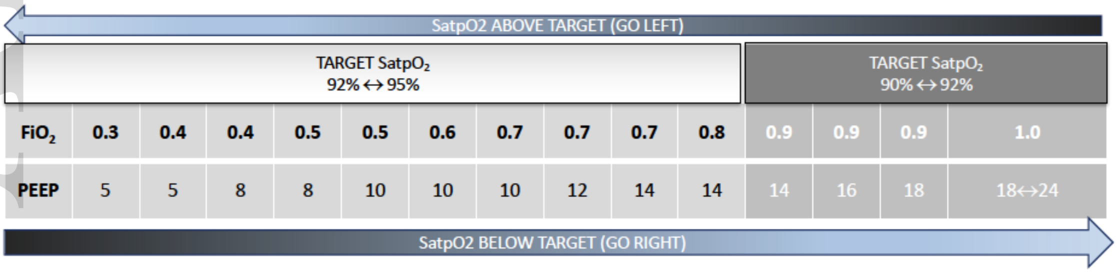

Figure 1: Adapted by Brazilian Intensive Medicine Association - AMIB from: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med. 2000. 342 (18). 1301-8. $SatpO_2$: oxyhemoglobin saturation measured by pulse oxymeter. FiO_2: fraction of inspired oxygen. PEEP: positive expiratory end pressure.[9]

The progressive increase of inflammation and an unusual trend of hypercoagulation could be responsible for prolonged mechanical ventilation in COVID patients, but there is still controversial data on this issue.[10]

Weaning process follows the same steps and criteria of patients with ARDS or severe respiratory failure. It is necessary to ensure a clinical improvement that allows adequate levels of sedoanalgesia in order to perform a Spontaneous Breathing Trial (EBT). The use of T-piece is not recommended due to the aerosolization risk. Following success in EBT, patient should be extubated (or disconnected from the ventilator if tracheostomized) and placed on O2 supplementation. Similarly as in pre-intubation step it is recommended a nasal catheter with maximum O2 of 5l/min to avoid airborne particles. Regarding tracheostomized patients, appropriate Heat and Moisture Exchange (HME) filter with lateral input should be placed for supplementary oxygen flow, avoiding the tracheostomy mask. In very specific cases one can choose noninvasive ventilation or high-flow nasal catheter after extubating, but aerosolization risk must be weighted.[7]

The hemodynamic profile is also affected by COVID-19 disease. Specifically for the mechanically ventilated patients, vasoactive drugs such as norepinephrine is often necessary. Whether this reflects sepsis-induced hypotension or is secondary to the high requirement of sedative to maintain adequate ventilation is unknown. On the other hand, the fluid management of these patients is usually very conservative, similar to protocols used in ARDS in general and in COVID-19-associated ARDS in particular.[11]

A subgroup of COVID-19 patients with critical illness has a significant release of inflammatory mediators, mimicking a cytokine storm.[12] Evidences suggesting this picture includes increased concentrations of interleukin (IL)-2, IL-7, granulocyte colony stimulating factor, interferon-γ inducible protein 10, monocyte chemoattractant protein 1, macrophage inflammatory protein 1-α, and tumor necrosis factor-α.[13] Also, these patients commonly have increased ferritin and IL-6 concentrations, and elevations of both markers are independent factors associated with poor outcomes in this scenario.[14] Possible interventions to ameliorate cytokine storm in this subgroup are corticosteroids, IL-1 blockade with anakinra and IL-6 blockade with tocilizumabe, but all these interventions lack adequate evidences produced by randomized clinical trials.

Another concern addresses the clinical findings of thrombotic events and coagulation activation during COVID-19. At the very beginning of the pandemic, studies demonstrated an association between increased D-dimer concentrations and worse prognosis in these patients.[15] Later studies suggested significant activation of the coagulation pathways highlighting a subgroup of COVID-19 patients with high risk of arterial and venous thrombotic events.[16,17] The use of prophylactic heparin was associated with better prognosis in small retrospective studies.[18] Taken together, these results suggest that coagulation disturbances are part of the pathogenesis of COVID-19-induced multiple organ failure. Whether this is an epiphenomenon or is an important pathway amenable to therapeutic intervention with anticoagulants remains to be fully discovered.

During COVID-19 pandemic, best practices compliance sometimes are not undertaken in an attempt to find the optimal solution for each patient. On the other hand, lessons learned from bedside experience managing COVID-19 patients can help to anticipate critical issues and prepare the ICU team to maximize safety and incorporate clinical expertise. Intensive care practitioners should review critical care treatment regularly and when the patient's clinical condition changes. This review includes an assessment of whether the treatment goals are clinically realistic or not. One should interrupt critical care treatment when it is no longer considered possible to achieve the desired outcomes, but the decision will never rely on economic, social or religious issues, but on frailty scores, for example Clinical Frailty Score (CFS) or another medical reason. Recording the palliative care decision shared with the family is essential to leave any doubt and to reduce conflicts. Because cardiopulmonary resuscitation brings great hazard to health care involved, this situation must be weighted in patients with CFS more than 5.[19]

Sharing experiences and devoting time searching for answers to the above issues should be a coordinate and scientific-based effort. In addition, each health facility should stimulate the development of local protocols adapted to its resources, staff training and cultural peculiarities, keeping in mind that COVID-19 pandemic will soon refrain but a second peak will occur, as the slope of the curve become flattened and the end of lockdown become closer

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