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Sedation in Critically-Ill COVID-19 Patients

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Why Do We Need Sedation in Critically-Ill COVID-19 Patients?
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How Should We Manage Sedation in Critically-Ill COVID-19 Patients?
Boris Jung *(Montpellier, France)*

The COVID-19 pandemic has wreaked havoc across the globe. Clinicians worldwide have been battling the pandemic while managing critically-ill patients infected with the coronavirus. Critical cases of COVID-19 are characterised by respiratory failure, septic shock and multiple organ dysfunction. Sedation of critically-ill patients is a complex intervention, especially keeping in mind that COVID-19 is a new disease and determining optimum levels of sedation through the course of the infection remains challenging for clinicians.

This symposium discussed sedation in critically-ill COVID-19 patients and provided an overview of the need for sedation, when to sedate and how to manage sedation in these patients. The symposium concluded with a Question and Answer session where experts answered important questions regarding sedation and management of these patients.

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Why Do We Need Sedation in Critically-Ill COVID-19 Patients?

COVID-19 patients present to the hospital with lung involvement and interstitial pneumonia eventually associated with lung collapse. The clinical picture is dominated by severe hypoxaemia without dyspnoea/tachypneoa and normal respiratory mechanics; this condition has been defined as silent hypoxia. The picture may evolve, and these patients may present with severe refractory hypoxaemia associated with dyspnoea/tachypnoea, use of accessory muscles of respiration, and respiratory mechanics impairment.

Silent hypoxia is linked to the mechanism of dyspnoea. Dyspnoea occurs due to a perceived mismatch between the outgoing efferent signals from the respiratory centre to the ventilatory muscles and incoming afferent signals from the lungs and the chest wall to the respiratory centre. These afferent signals may be triggered by hypercapnia or severe hypoxaemia, airway and interstitial inflammation and impaired lung mechanics. COVID-19 patients can have impairment of lung function, both at the alveolar level and at the intravascular level but a very low level of oxygenation (as low as 30 mmHg) needs to be reached to have dyspnoea, which is mediated by an increase in CO_2, in minute ventilation and in the effort to breathe. In the beginning, patients can be treated with simple oxygen therapy followed by mechanical respiratory support as needed (Dhont et al. 2020).

Goals of Mechanical Respiratory Support in COVID-19 Patients

The most important goals of mechanical respiratory support are:

- To improve oxygenation
- To support the respiratory muscles
- To prevent additional lung injury

Noninvasive Support and Guidelines in Hypoxaemic Acute Respiratory Failure

Besides standard oxygenation techniques, different forms of non-invasive support can be used in hypoxaemic patients. These include Nasal High Flow (NHF), continuous positive airway pressure (CPAP), and non-invasive positive pressure ventilation (NIPPV). NHF delivers high gas flow and is a technique that can increase the airway pressure and can generate a positive end-expiratory pressure (PEEP). With CPAP, a single value of airway pressure is set and this pressure is usually higher than that provided by NHF. With NIPPV two levels of pressure are set: the lowest is maintained during expiration and the highest is reached during inspiration to support the respiratory muscles.

COVID-19 is a new disease. The ERS/ATS clinical practice guidelines for use of noninvasive ventilation in hypoxaemic acute respiratory failure should be referred to when dealing with this patient population. Several studies show conflicting results, and overall there is no effect of NIV on mortality. Given the uncertainty of evidence, the guidelines state that it was not possible to offer any reccomendation about the use of NIPPV in hypoxaemic patients (Rochwerg et al. 2017).

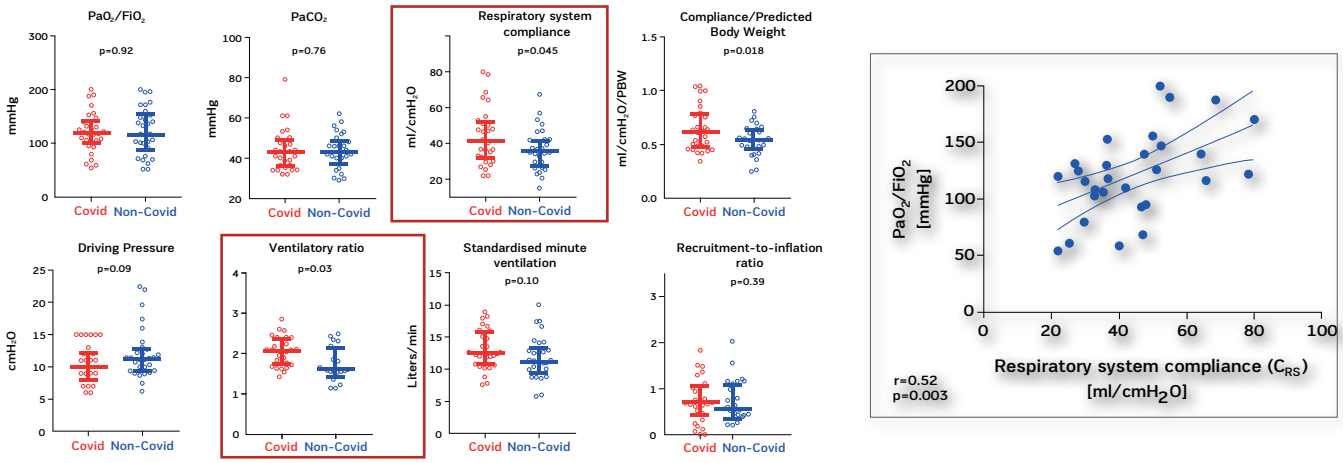

Figure 1. COVID-19 ARDS vs. ARDS from other aetiologies. Adapted from Grieco et al. 2020

Results of a recent meta-analysis may further help to guide NIPPV use in hypoxaemic patients, including those with COVID-19. Findings show that, as compared with standard oxygen, NIPPV may reduce mortality, particularly when it is delivered with helmet. As compared with both face mask NIPPV and NHF, helmet NIPPV might give better results, thus being preferable in patients with hypoxaemic respiratory failure (Ferreyro et al. 2020).

New guidelines were released regarding the use of NHF in hypoxaemic respiratory failure. Based on the results of the meta-analysis, the panel gave a strong recommendation for the use of NHF compared to standard oxygenation in these patients (Rochwerg et al. 2020).

There are risks associated with noninvasive respiratory support. These include:

- Environmental contamination
- Intubation delay
- Patient self-inflicted lung injury, due to high respiratory drive (Brochard et al. 2017).

Sedation and Analgesia During NIPPV

Sedation can manipulate respiratory drive, typically very high in COVID-19 patients, when breathing spontaneously. However, it is important to remember that the results of using analgosedation are not always positive. A study by Muriel et al. (2015) suggests that compared to no sedation, use of analgesia, sedation or both was associated with an increase in NIPPV failure and 28-day mortality. Therefore, sedation in COVID-19 patients during NIPPV is not recommended, especially because many of these patients may not have dyspnoea. If the patient's condition worsens, the only solution is to use intubation and invasive mechanical ventilation.

COVID-19 ARDS vs. ARDS From Other Aetiologies

It is being debated if COVID-19 ARDS is similar to traditional ARDS or different. At the beginning of the pandemic, these data were not available, but more data have been produced since then. In a study by Grieco et al. (2020), 30 patients with moderate to severe COVID-19 related ARDS were matched with 30 other patients with ARDS from other aetiologies. All patients were studied within 24 hours from intubation. Two PEEP levels were applied – 5 and 15 cmH_20 to assess the response of these patients to PEEP and lung recruitability.

Several parameters were compared between COVID-19 and non-COVID-19 patients **(Figure 1)**. From a clinical point of view, all measured parameters, including gas exchange, compliance, driving pressure, ventilatory ratio (a measure of deadspace), minute ventilation and the recruitment-to-inflation ratio (a measure of recruitability), were similar in COVID-19 and non-COVID-19 patients, although compliance and ventilatory ratio were statistically higher in COVID-19 patients. It is important to note that all these parameters showed a high variability both in COVID-19 and in non-COVID-19 patients. In COVID-19 patients, a direct correlation was also observed between compliance and oxygenation. Because compliance is an index of lung aeration, this correlation indicates that oxygenation improved with improving lung aeration, as it has been described in traditional ARDS (Grieco et al. 2020).

As far as response to PEEP is concerned, the results were similar in both COVID-19 and non-COVID-19 cohorts. High-level PEEP improved oxygenation in both cohorts. There was a similar response in terms of ventilatory ratio, compliance and driving pressure in both cohorts. High PEEP resulted in a greater improvement of oxygenation in COVID-19 patients compared to traditional ARDS, but the improvement in oxygenation was not related to the index of recruitability. Recruitability was correlated to a decrease in PCO_2. Overall, findings from this study show that after the establishment of mechanical ventilation, patients with COVID-19 show a conventional ARDS phenotype (heterogeneity in respiratory mechanics, aeration loss related to the degree of hypoxaemia and inter-individually variable recruitability) and that clinicians treating COVID-19 patients should adhere to recent guidelines regarding standard ARDS management (Grieco et al. 2020).

These findings have been confirmed by another study conducted in 301 COVID-19 ARDS patients who were compared to 2634 traditional ARDS patients. In both groups, compliance was highly variable and values were very similar from a clinical perspective, although slightly higher in COVID-19 patients. Total lung weight was also similar. Authors also described lung thrombo-embolic events in COVID-19 patients, particularly when high compliance was associated with high levels of D-dimers, and these thrombo-embolic phenomena have been described also in traditional ARDS. Study authors concluded that patients with COVID-19 associated ARDS

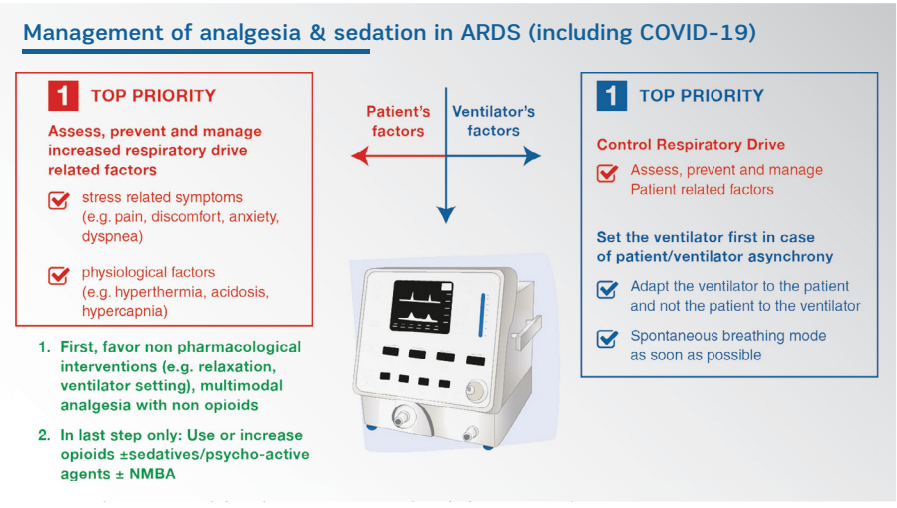

Figure 2. Management of analgesia and sedation in ARDS. Source: Chanques et al. 2020

have a form of injury that, in many aspects, is similar to that of those with ARDS unrelated to COVID-19 (Grasselli et al. 2020).

Protective Ventilation in COVID-19 ARDS

Following the previous reasoning, it is important, also in COVID-19 related ARDS, to follow the official clinical practice guidelines of the American Thoracic Society (ATS), European Society of Intensive Care Medicine (ESICM), and Society of Critical Care Medicine (SCCM) (Fan et al. 2017), for the management of mechanical ventilation in ARDS, which recommend:

- To use low tidal volume (4-8 ml/kg PBW) and low plateau pressures (<30 cmH20)
- To use prone position in severe ARDS (>12 h/day) and suggest to use higher PEEP and recruitment manoeuvres in moderate-severe ARDS.

However, it is important to individualise ventilation strategies in both traditional and COVID-19 ARDS patients. This should be done taking into consideration the risks associated with aggressive mechanical ventilation, including shear stress, overdistention, or increase in intrathoracic pressure, which can further injure the lung and have been linked to the spillover of bacteria and inflammatory mediators from the lung into systemic circulation. This can cause damage to the distal organs leading to multi-organ failure (Slutsky and Tremblay 1998).

In fact, it is known that aggressive mechanical ventilation can have harmful effects on the patient. For example, a Brazilian study compared the use of an aggressive ventilator strategy, with lung recruitment manoeuvres and a high PEEP level, in patients with ARDS to a low/moderate PEEP level strategy. Findings from this study show that aggressive mechanical ventilation was associated with increased mortality and an increase in complications like pneumothorax, barotrauma and shock, suggesting that an aggressive mechanical ventilation strategy may have deleterious effects also at the cardiovascular level (Cavalcanti et al. 2017).

Sedation may be useful to limit another risk of mechanical ventilation, that is patient ventilator dyssynchrony. If there is a mismatch between the patient's breath and ventilator-assisted breaths, and the ventilator's flow delivery does not match the patient's flow demand, it can generate a dyssynchrony, i.e. double cycling, which can have a negative impact on the patient. This can be managed by sedation while ensuring no oversedation or undersedation.

There is a relationship between ventilatory management and sedation management. A recent review of analgesia and sedation management in ARDS, including patients with COVID-19, highlights the importance of optimising sedation. As per this review, the most important priorities are to manage increased respiratory drive, and to optimise ventilation to avoid ventilator dyssynchrony (Chanques et al. 2020).

In conclusion, the primary reasons for sedation in COVID-19 patients include improving patient comfort (pain, anxiety and dyspnoea), enhancing patient safety (during special manoeuvres such as proning), facilitating lung-protective mechanical ventilation, and treating ventilator dyssynchrony by controlling the respiratory drive. Also, aims of sedation in all ARDS patients, including those with COVID-19, are to maintain patient interaction with staff and family and to promote early physical and cognitive recovery. ■

Key Points

- NIPPV should be applied on an individual basis when managing COVID-19 patients, paying attention not to delay intubation if required.
- Sedation during NIPPV is generally not needed in COVID-19 patients.
- Patients with COVID-19 show a conventional ARDS phenotype and should be treated using guidelines regarding standard ARDS management.
- There is a relationship between ventilatory management and sedation management and the priorities should be to manage increased respiratory drive, to optimise ventilation and to avoid ventilator dyssynchrony.

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How Should We Manage Sedation in Critically-Ill COVID-19 Patients?

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Clinical Practice Guidelines

The Choosing Wisely top five guidelines published a few years ago by the Chest Association of Physicians, the American Thoracic Society, the Society of Critical Care Medicine, and the American Association of Critical Care Nurses state that mechanically ventilated patients should not be deeply sedated without a specific indication and without daily attempts to lighten sedation (Halpern et al. 2014). This is a very important recommendation, especially when discussing sedation in critically-ill COVID-19 patients.

Findings from a landmark study published by the Chicago Study Group 20 years ago showed that if daily sedation is interrupted in mechanically ventilated patients, the duration of mechanical ventilation can be shortened (Kress et al. 2000).

Pain

The most recently published guidelines from 2018 recommend a checklist. The first step is to make sure that mechanically ventilated patients are not in pain. Pain should be measured using appropriate scales, and pain management should be initiated with intravenous opioid drugs but also non-opioid analgesics to spare the excessive use of opiates. The most commonly used scale is the Behavioral Pain Scale (BPS) that ranges from 3 to 12, 3 representing a patient with no pain at all and 12 being a patient experiencing very intense pain.

Sedation

The next step, once the pain is treated, is sedation. The 2018 guidelines suggest that light sedation and not deep sedation should be used in critically-ill mechanically ventilated adults. Light sedation is associated with a shorter duration of invasive mechanical ventilation and reduced tracheotomy rates (Devlin et al. 2018).

In a multi-centre study, authors showed that most of the patients were deeply sedated in their first 48 hours of the ICU stay. However, this proportion decreased with time. In this study, deep sedation was associated with a longer time to extubation and a lower survival rate. Deep sedation was also associated with a higher mortality rate three months after the ICU stay (Shehabi et al. 2012).

Light sedation can be defined using scales. One of the most used scales is the Richmond Agitation and Sedation Scale, known as the RASS scale. Light sedation is between -2 to +1. Light sedation and sometimes even no sedation can be performed in many mechanically ventilated patients. In a randomised trial published in 2020 in the New England Journal of Medicine, the authors showed that no sedation or light sedation could be performed in many patients admitted to the ICU, those who are mechanically ventilated and even with pneumonia or ARDS (Olsen et al. 2020). As shown in **Figure 1,** results from the study show that in the light sedation group, the mean RASS score was between -2 and -3 in most patients. An important thing to note is that in these ICUs in Scandinavia mostly, the patient to nurse ratio was 1:1, meaning that the nurses were readily available to make sure that the patient wouldn't self-extubate or be at risk of severe agitation.

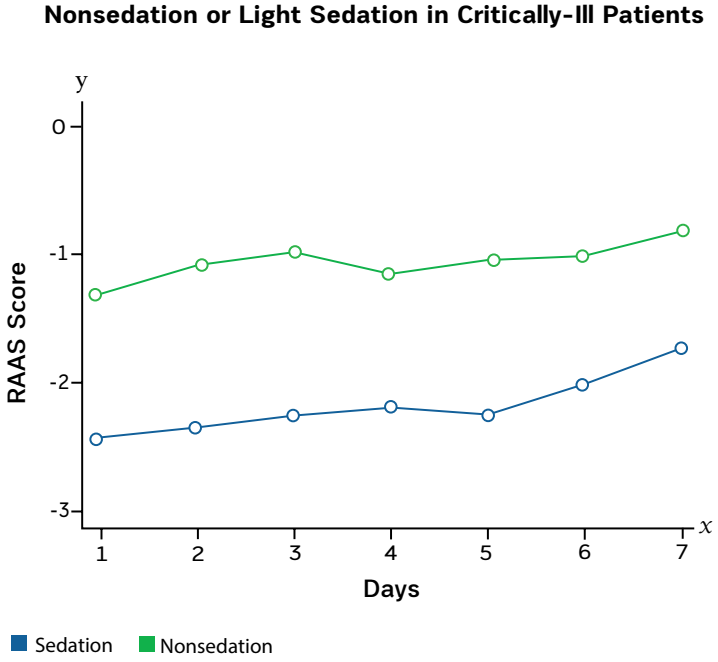

Figure 1. Nonsedation or Light sedation in critically-ill, mechanically ventilated patients. Adapted from Olsen et al. 2020

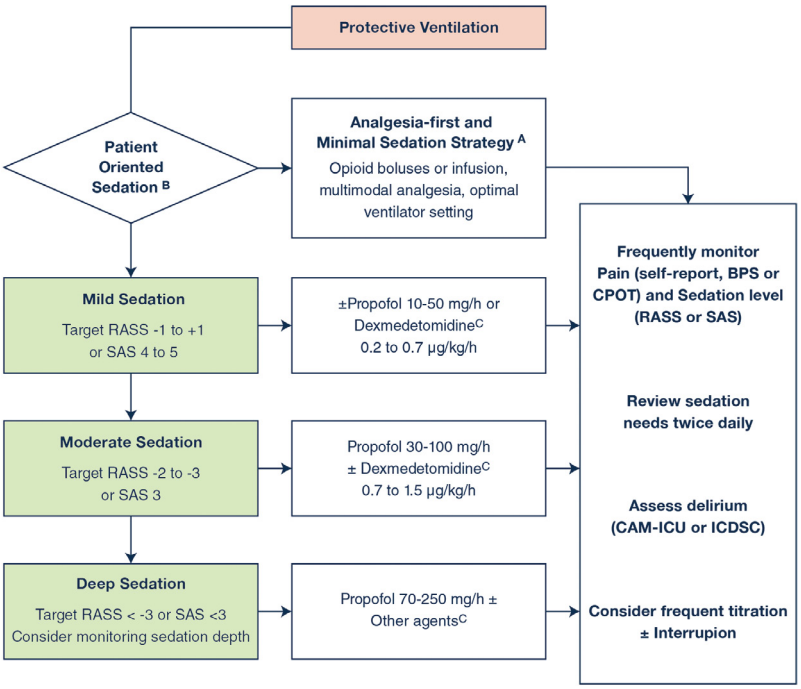

Figure 2. Analgesia and sedation without NMBA for protective lung ventilation strategy. Source: Chanques et al. 2020

Which Drugs Should Be Used?

Guidelines recommend that benzodiazepines should not be used because the use of other drugs is associated with a shorter duration of mechanical ventilation, shorter duration of ICU stay, and less delirium. Benzodiazepines also have one major side effect - more self-extubation.

ARDS is one of the few indications of deep sedation. Deep sedation can be defined by a RASS score between -4 to -5 (Devlin et al. 2018). Some of these patients may need neuromuscular blocking agents (NMBA) to treat ARDS. Findings from a landmark study published in France ten years ago in the New England Journal of Medicine show that Cisatracurium, which is one of the most commonly used NMBA, is associated with better survival compared to placebo (Papazien et al. 2010). More recently, the ROSE trial published by the PETAL Clinical Trials Network in the U.S. did not produce the same results. Findings from this RCT, which enrolled 1000 patients showed that light sedation could be performed by day one in almost 30% of ARDS patients. However, none of them were COVID-19 patients (Moss et al. 2019).

With respect to the use of NMBAs in ARDS, the guidelines and recent reviews based on the RCTs suggest that NMBAs should be avoided in ARDS unless there is:

- Moderate to severe ARDS with a P/F ratio < 150 AND
- Severe dyssynchronies despite deep sedation OR
- High level of inspiratory efforts or respiratory drive
- NMBAs should be reassessed within 24 hours

Another important review published and coordinated by Chanques et al. (2020) summarises how sedation and NMBAs should be used in ARDS patients. According to this review, protective ventilation is the key in ARDS, but if protective ventilation is obtained, it is important to first target mild sedation with almost awake patients using small doses of propofol with or without dexmedetomidine. Moderate sedation should be used if mild sedation is not tolerated by increasing the dose of propofol and dexmedetomidine. Deep sedation should remain at the end of the checklist if the patient is not fully synchronised to the ventilator. Propofol should be used as the first-line drug and then other agents. It is important to keep in mind that some of these patients may need NMBAs even if they are deeply sedated.

Is There a Difference Between COVID-19 Patients and Routine ARDS Patients?

The answer to this question is both yes and no. Yes, because there have been many patients admitted to the ICU for respiratory failure related to COVID-19 disease, generating a very high health care workers workload. Because ARDS is a very classic indication of deep sedation, and in some of these patients, light sedation is not associated with protective ventilation, many of these patients would require deep sedation. That is why during the pandemic, there have been many deeply sedated patients in ICUs. Also, COVID-19 is a droplet and airborne transmitted disease. Since there have been many patients admitted to the ICU for respiratory failure, generating a very high workload for healthcare workers, and requiring them to wear personal protective equipment, there is a temptation for deeply sedating patients to decrease the risk of incidents such as self-extubation. Because of this high use of sedation during these times and the high flow of patients in severely affected regions, there is a risk of a shortage of deep sedation drugs.

Over the last few months, there have been many reviews and expert opinions, but no comparative studies have been conducted that show that one of these drugs (benzodiazepines, dexmedetomidine, ketamine, volatile sedation, non-opioid analgesics, morphine and other opioids) would be better than the other in COVID-19 patients. Hence, for most clinicians, the strategy has been to follow local policy as well as make decisions based on the availability of drugs. Some of these drugs, such as volatile sedation, are under investigation in ARDS. There is an ongoing RCT in France where intravenous sedation drugs are compared to volatile sedation to see whether volatile sedation would be associated with better outcomes (Ammar et al. 2021; Adams et al. 2020).

COVID-19 and the Brain

One particularity of the COVID-19 disease is that the hippocampus is one of the targets of the virus generating a local inflammatory brain response. There is also a possible brain invasion of the virus through olfactory nerves

and systemic acute brain injury related to hypoxia, inflammation, and endothelialitis. All these pathophysiological pathways lead to cognitive impairment and a high risk of ICU-associated delirium. Recovery times are not yet known, but may be prolonged. No study so far has reported the need for higher doses of sedative drugs in ARDS patients with or without COVID-19 disease.

In conclusion, severe COVID-19 patients may need deep sedation and NMBAs but the goal should always be to target light sedation once we make sure that mechanical ventilation is lung and muscle protective. ■

Key Points

- Mechanically ventilated patients should not be deeply sedated without a specific indication and without daily attempts to lighten sedation.
- Light sedation is associated with a shorter duration of invasive mechanical ventilation and reduced tracheotomy rates.
- ARDS is one of the few indications of deep sedation and some patients may require NMBAs to treat ARDS.
- Protective ventilation is the key in ARDS; if not obtained, the first target should be mild sedation.
- Moderate sedation should be used only if mild sedation is not tolerated. Deep sedation should remain at the end of the checklist.

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Important Questions Answered

During the question/answer session, Prof Vito Marco Ranieri discussed some important questions with Prof Salvatore Maurizio Maggiore and Prof Boris Jung regarding sedation regimen, respiratory muscle paralysis, sedation in COVID-19 patients specifically and how it is different from other regular ICU patients.

Ranieri: What is your opinion on deep sedation using remifentanil and propofol targeting RASS -4?

Maggiore: Before this pandemic, this analgosedation regimen was our standard, and that was usually the way we sedated patients. We do know that COVID-19 patients require prolonged sedation, and we also know, that, in general, the longer the sedation, the longer the patient stays in the ICU. Therefore, deep sedation increases the risk of prolonged sedation.

Jung: I would say that we do use remifentanil for other types of patients that are not COVID-19. We haven't used remifentanil either, exactly for the reason that Prof Maggiore mentioned because most of them would need prolonged sedation. That is why we use sufentanil in our unit.

Ranieri: How often is respiratory muscle paralysis needed in the presence of deep sedation?

Jung: I don't have any exact numbers, but we've seen around 200 COVID-19 patients in my unit. I would say that, in deeply sedated patients, at least 30 to 40% need continuous NMBAs, and around 20 to 25% would need prolonged NMBAs infusion for more than 48 hours.

Maggiore: I agree. We have a similar experience. The rate of patients receiving NMBAs was even higher. But this is dependent on the criteria for admission to the ICU and the severity of patients at ICU admission. All patients in our ICU were severely ill, especially in the beginning. I would say that the percentage of patients receiving NMBAs, in our case, was between 50% and 60% and the use of NMBAs was often prolonged for more than 48 hours.

Ranieri: So in a way, both of you challenge the knowledge that you can replace the use of respiratory muscle paralysis with deep sedation, a concept that some years ago was proposed by several groups?

Maggiore: The problem is not just severity but also the procedures that are undertaken in these patients. For example, for us, it is usual that during pronation, the patients are paralysed. I know that proning is performed without sedation in other instances, but considering the number of patients who were pronated during COVID-19, around 80% in our case, and the high workload for the personnel, I feel it was safer to perform this procedure when patients were paralysed.

Jung: We have the same experience. In our unit, 70% of patients underwent prone positioning with high use of NMBAs at the very early stage of their stay because of the high workload.

Ranieri: Are COVID-19 patients difficult to sedate, and what is your opinion on the use of dexmedetomidine for sedation as an alternative to propofol and morphine-like agents?

Maggiore: We did not find that COVID-19 patients are more difficult to sedate compared to classical ARDS. Also, we did not use dexmedetomidine in the very early phase. We usually use this drug when shifting to a light sedation strategy.

Jung: I agree. There are a lot of studies out there that have shown that dexmedetomidine may not be the best agent to provide deep sedation but can be an alternative for light sedation. I wouldn't say that it's propofol versus dexmedetomidine at the very early stage.

Ranieri: Any experience with dexmedetomidine with NIV?

Maggiore: Not for us because we applied non-invasive mechanical respiratory support almost exclusively outside the ICU and management of sedation in this scenario would be even more complicated.

Ranieri: What is your experience in the use of EEG monitoring to optimise sedation and patient comfort?

Maggiore: We have no experience of this. These patients received deep sedation during the very early phase,but we have not used this technique. When a patient is improving, I believe that the best strategy is to try to stop sedation as soon as possible and continue to monitor clinically the neurological status regularly.

Jung: In our unit, we use the BISPECTRAL index in patients who were paralysed within a target of 40 to 60. It's not a magical tool, but it can be useful.

Ranieri: What is your opinion on the use of volatile sedation?

Jung: Our team decided not to use volatile sedation during the first wave mainly because of the risk of airborne and droplet transmission to the healthcare workers. But in our usual practice otherwise, we use it quite a few times a year. We have also used it during the second wave for a patient who was really difficult to sedate and who needed a very high dose of propofol. So, we switched to volatile sedation, which worked. But overall, we chose not to use a lot of volatile sedation during COVID-19 because of the risk of infection transmission.

Maggiore: We are introducing this technique. Therefore, we do not have sufficient experience with this.

Ranieri: Are there any differences between the first and second waves in terms of the need for sedation? What has been your experience?

Maggiore: We have not observed any difference. In our experience, patients we have seen during the second wave are similar to the first wave, therefore there has not been much difference in terms of sedation.

Jung: I agree. We have also not observed any difference.

Ranieri: Do you think that the sedation policy is strongly influenced by the level of organisation or support that we are able to provide in terms of human resources? If you have a full set of ICU with the required staff in terms of nurses and physicians, you may use a more sophisticated sedation policy. But if you are running 150 ICU beds with nurses coming from the operating theatre, or there is an intensivist recruited from the urologist floor, you may use a more basic approach for sedation. What do you think?

Maggiore: I completely agree. This is also true during the management of classic ICU patients, not just COVID-19, for example, during procedures like weaning, and also for ARDS management. This is not something new, and yes, I agree.

Jung: We usually use a nurse driven protocol to lighten sedation as much and as early as possible. With such a high workload and the hygiene precautions it is however difficult to enter so many times in ICU rooms to adjust sedation. There is therefore a temptation of using like you said a much easier and more basic sedation protocol. However I'd really recommend to reassess the need of deep sedation at least every 4h both for the patients outcome and to optimise ICU length of stay.

Ranieri: You discussed the ROSE Trial regarding the use of NMBAs in patients with ARDS and also compared it to the ACURASYS Study. Would you like to highlight the difference between the two trials and summarise apparently contradictory results?

Jung: There are many differences between the two trials. In the ROSE trial, the PEEP level was very high compared to the ACURASYS trial. Patients could be enrolled earlier in the ROSE trial, and ventilation strategy was also different between the two trials. What I would suggest, as the authors of these studies did, is that if you start using NMBAs in ARDS patients, you may want to reassess its indication at least every day or every 24 hours to make sure that the patient really needs an NMBA because the two trials were very different from one another.

Maggiore: The two studies actually compared totally different things because the level of sedation was different, and the level of PEEP was higher in the ROSE trial. We have data showing that maintaining some form of spontaneous breathing with a high PEEP level may be protective for the lung. This may be one of the reasons the results of the ROSE trial are quite different as compared to the ACURASYS trial.

Ranieri: There is a perception that COVID-19 patients are more complex than others, that the level of stress these patients are experiencing is different than the usual level of stress in regular patients admitted to the ICU. There has also been an exponential increase in workload. The patient's stress and the patient's need for sedation are probably tied to the healthcare system that has also reached the limits. Is that why these patients appear to be different? Or are these patients similar to other ICU patients with the same need in terms of sedation, mechanical ventilation, and it is the healthcare workers who are different. What do you think?

Maggiore: I completely agree. We have always been aware of the limits of the system in terms of beds and equipment. However, the real issue is the personnel in terms of numbers, competencies, and workload. We have data showing that healthcare workers during the first wave of the pandemic had, in fact, a very high level of burnout. This is a fact.

Jung: I would not say that these patients are more difficult to care about than the usual virus associated ARDS with extra precautions taken regarding venous thrombosis. I would however say that the massive volume of patients, the risk of contamination and the high workload have made things very tough and demanding worldwide. ■

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