

The following manuscript was accepted for publication in Pharmaceutical Sciences. It is assigned to an issue after technical editing, formatting for publication and author proofing
Citation:

Mahmoodpoor A, Ekrami E, Soleimanpour H. Dexmedetomidine: An All sedation-In–one drug in critically ill patients with COVID-19, Pharm. Sci. 2020, doi: 10.34172/PS.2020.53

Commentary

Dexmedetomidine: An All sedation-In–one drug in critically ill patients with COVID-19

Ata Mahmoodpoor¹, Elyad Ekrami², Hassan Soleimanpour^{1,2*}

¹Department of Anesthesiology and Critical Care, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

²Student research committee, Tabriz University of Medical Sciences, Tabriz, Iran. 3-Emergency Medicine Research Team, Tabriz University of Medical Sciences, Tabriz, Iran.

*Corresponding author: Hassan Soleimanpour Emergency Medicine Research Team, Tabriz University of Medical Sciences, Tabriz, Iran. Tel: +989141164134, Fax: +98-4133352078, E-mail: soleimanpourh@tbzmed.ac.ir or h.soleimanpour@gmail.com

The coronavirus disease 19 (COVID-19) caused by SARS-CoV-2 emerged as a public health threat in December 2019 and spread as a pandemic in March 2020. The virus can invade both respiratory and central nervous systems and can result in significant organ dysfunction¹. COVID-19 associated respiratory distress syndrome is an acute hypoxemic event which requires respiratory assistant. Hypoxemia itself and ventilation support (invasive or non-invasive) can induce agitation and require appropriate management. Direct invasion of virus to CNS can induce inflammation and delirium in these patients which requires accordance treatment². There are currently no sedation guidelines specific for this patient population requiring high doses and prolonged drug administrations. But we actually know that sedation of mechanically ventilated patients with COVID-19 poses unique challenges and has multiple important implications. Younger age, high respiratory drive and hyperinflammation translates

to need an appropriate drug or a combination therapy. Application of the ABCDEF bundle can provide a framework to help physicians accomplish patient care that will help the acute management as well as improvement of long-term outcome³. A subgroup of COVID-19 patients with ARDS likely require prolonged period of sedation to facilitate lung protective ventilation or extracorporeal therapies till weaning^{4,5}. Choosing appropriate drug for sedation during this period is very important as antiviral drugs have many complications which can be more augmented with sedative drugs. Opioids are ideal analgesic drugs but have some complications like nausea, vomiting, ileus, intolerance to feeding, abdominal distension during prolonged ICU stay which cause the ventilation more difficult. All drugs used to treat mentioned complications increase the adverse effects of antivirals especially QT interval. All benzodiazepines and opioids increase the incidence of delirium in critically ill patients which leads to worse outcome in these patients. Barbiturates may increase metabolism of hydroxychloroquine and consequently decrease its effect. The use of inhalational anesthetics like isoflurane and sevoflurane may be a rational alternative that is also supported by anti-inflammatory and lung-protective effects of inhalational anesthetics but should be performed in locations with appropriately designed scavenging systems which is not available in many situations especially in resource-limited countries. Based on the mentioned sentences dexmedetomidine can be considered as drug of choice for management of pain, agitation and delirium in COVID-19 patients. Regarding organ dysfunction which is very common in COVID-19 critically ill patients, previous studies showed a positive effect of dexmedetomidine. Wu et al showed that dexmedetomidine decreased ventilation induced inflammation and injury responses by inhibiting alveolar neutrophil recruitment, inhibited lipid peroxidation and relieved pulmonary edema⁶. These effects were seen in both interstitial lung disease, COPD and morbid obese patients. Previous studies also showed that dexmedetomidine improved renal function in critically ill septic patients⁷. Results of two previously performed

systematic reviews showed that clinical application of dexmedetomidine in cardiac surgery patients could reduce risk of abnormal hemodynamics with good safety and had a cardioprotective effect in adults and children^{8,9}. They recommended a reduction in dexmedetomidine dose only in critically ill patients with diastolic dysfunction. Dexmedetomidine also is an ideal drug for sedation during intubation of critically ill patients especially for controlling the hemodynamic responses after intubation. The various complications of sedative and analgesics, alone and in combination makes dexmedetomidine a good choice for these purpose. This drug is particularly important for patients with respiratory failure, for whom the preservation of spontaneous ventilation and airway tone is crucial which is so important in critically ill COVID-19 patients¹⁰. Dexmedetomidine appears to have promising results in the field of neuroprotection, cardioprotection, and renoprotection, which are the most commonly involved organ in COVID-19 patients¹¹. A recently published report described dexmedetomidine use in a critically ill COVID 19 patient with worsening hypoxemia. They showed that use of dexmedetomidine resulted in improved oxygenation and avoiding intubation by improving compliance with non-invasive ventilation¹². Prolonged periods of sedation in critically ill COVID-19 patients can result in delirium (benzodiazepines), hypertriglyceridemia (propofol), opioid dependency/withdrawal (fentanyl), psychomimetic complications (ketamine), life threatening arrhythmis (haloperidol) and drug accumulation (benzodiazepines /fentanyl) which all can be minimized by dexmedetomidine usage¹³.

Based on the safety profile, anti-inflammatory effects, and positive effects on important organ functions, it seems that dexmedetomidine can be used as an ideal drug for management of pain, delirium, sedation and intubation in critically ill COVID-19 patients in ICU and for remote location sedation/anesthesia for these patients out of ICU settings. Management of pain, agitation and delirium in critically ill patients with COVID-19 requires information about individual characteristics and comorbidities, safety profiles of drugs and health care system

limitations. Potential for interactions with investigational drugs used in clinical trials (some blinded to ICU staff) needs to be considered. Till now, the clinical experience with dexmedetomidine use in COVID-19 patients is low and we need more trials with high level of evidence to show its clinical effectiveness in critically ill COVID-19 patients. Although we believe that one size does not fit all in medicine, dexmedetomidine may be a free size drug which is shaping up for different indications.

References

1. Kotfis K, Williams Roberson S, Wilson J.E, Darowski W, Pun B.T, Ely E.W. COVID-19: ICU delirium management during SARS-CoV-2 pandemics. *Critical care* 2020; 24: 176.
2. Mahmoodpoor A, Shadvar K, Ghamari AK, Mohammadzadeh Lameh M, Asghari Ardebili R, Hamidi M, et al. Management of critically ill patients with COVID-19: what we learned and what we do. *Anesth Pain Med.* 2020 June; 10(3):e104900.
3. Pun BT, Balas MC, Barnes-Daly MA, Thompson JL, Aldrich JM, Barr J, et al. Caring for critically ill patients with the ABCDEF bundle: results of the ICU liberation collaborative in over 15,000 adults. *Crit Care Med.* 2019; 47(1):3–14
4. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. COVID-19 in critically ill patients in the Seattle region - case series. *N Engl J Med.* 2020 March 30
5. Golestani-Eraghi M, Mahmoodpoor A. Early application of prone position for management of Covid-19 patients. *J Clin Anesth.* 2020 May 26; 66:109917. doi: 10.1016/j. jclinane. 2020. 109917
6. Wu Ch-Yu, Lu Y, Wang M.L, Chen J.Sh, Hsu Y.Ch, Yang F.S, et al. Effects of Dexmedetomidine Infusion on Inflammatory Responses and Injury of Lung Tidal Volume Changes during One-Lung Ventilation in Thoracoscopic Surgery: A Randomized Controlled Trial. *Mediators of Inflammation* Volume 2018, Article ID 2575910

7. Nakashima T, Miyamoto K, Shima N, Kato S, Kawazoe Y, Ohta Y, et al. Dexmedetomidine improved renal function in patients with severe sepsis: an exploratory analysis of a randomized controlled trial. *J Intensive Care* 2020; 8, 1. <https://doi.org/10.1186/s40560-019-0415-z>
8. Ging Z, Ma L, Zhong Y, Li J, Lv J, Xie Y. Myocardial protective effects of dexmedetomidine in patients undergoing cardiac surgery: A meta-analysis and systematic review. *Experimental and Therapeutic Medicine*. 2017; 13(5): 2355-61.
9. Wang G, Niu J, Li Z, Lv H, Cai H. The efficacy and safety of dexmedetomidine in cardiac surgery patients: A systematic review and meta-analysis. *PLOS ONE* 2018; 13(9): e0202620. <https://doi.org/10.1371/journal.pone.0202620>
10. Mahmoud M, Mason K.P. Dexmedetomidine: review, update, and future considerations of paediatric perioperative and periprocedural applications and limitations. *British Journal of Anaesthesia* 2015; 115(2): 171–82.
11. Grewal A. Dexmedetomidine: New avenues. *J Anaesthesiol Clin Pharmacol*. 2011; 27(3): 297–302.
12. Stockton J, Kyle-Sidell C. Dexmedetomidine and worsening hypoxemia in the setting of COVID-19: A case report. *Am J Emerg Med*. 2020 May 27. pii: S0735-6757(20)30425-3. doi: 10.1016/j.ajem.2020.05.066.
13. Hanidziar D, Bittner EA. Sedation of Mechanically Ventilated COVID-19 Patients: Challenges and Special Considerations. *Anesth Analg*. 2020 Apr 22: 10.1213. Published online 2020 Apr 15. doi: 10.1213/ANE.0000000000004887.