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Dexmedetomidine in COVID-19: probing promises with prudence!



Dear Editor,

I read with interest the recent article featured in the journal by Stockton and Kyle-Sidell, wherein they report an improved oxygenation and avoidance of intubation with the use of dexmedetomidine (DEX) in a COVID-19 patient with worsening hypoxemia [1]. As outlined in the index case, DEX infusion can augment compliance to non-invasive ventilation in COVID-19 patients given its analgesic-sedative profile with minimal respiratory depression and, anti-delirium and opioid-benzodiazepine-sparing potential. In this context, Zhao et al. also propose an anti-inflammatory and a cytoprotective role of DEX in ameliorating the COVID-19 cytokine storm related organ dysfunction premised on putative mechanisms emanating from preclinical research [2]. While the aforementioned propositions offer newer avenues for optimal safe sedation in this peculiarly predisposed cohort (particularly with the snowballing need to conserve the shortened conventional analgesic supply), few important points mandate elucidation with regards to the upcoming role of DEX in COVID-19:

- (i) A range of studies have highlighted the temporal association between DEX-infusion and hyperthermia [3]. At the same time, the recent description of DEX-associated hyperpyrexia in three critically ill COVID-19 patients by Czepiel et al., adds to the contextual significance amid the pandemic [4]. Moreover, the resultant hyperpyrexia in critically ill patients can lead to cellular damage, capillary dilatation, interstitial extravasations and vascular stasis that can have a deleterious impact on the subsequent morbidity and mortality in this vulnerable subset [4]. In addition, common risk-factors such as obesity for DEX-associated hyperthermia and COVID-related mortality, compound the situation furthermore [4].
- (ii) Long-term infusions of DEX raises a concern for the withdrawal phenomenon. This can be all the more troublesome in COVID-19 cohort with descriptions accumulating on the prolonged sedation requirement in this setting [5,6]. While the peak DEX-doses >0.8 µg/kg/h and daily cumulative DEX-doses >12.9 µg/kg/day have been described to be associated with an elevated withdrawal incidence [7], lack of presentation of the contextual DEX-dose administered in the COVID-19 patient featured in the Stockton and Kyle-Sidell case-report, captivates attention [1]. However, withdrawal can be prevented with the meticulous use of drug or mitigated with clonidine [5].
- (iii) In addition, once on invasive mechanical ventilation, a precision approach to sedation in COVID-19 patients, as epitomized by Payen et al., appears to be prudent centralising the focus on inter-individual variability and synchronizing the level of ventilator support to the subsequent target of sedation, thereby directing the subsequent choice of sedative agents, including DEX [8,9].

The discussion highlights that proposition of novel therapies should be associated with a beckon to err on the side of caution so as to assist physicians make informed decisions and exercise appropriate vigil, very much the case in the aforementioned context as we still ardently await the results of ongoing studies such as: 'Use of Dexmedetomidine in Light to Moderate Sedation in the Patient in the Palliative Situation of a Sars-cov-2 / COVID-19 Infection' (PRODEX, NCT04350086) and 'Immunomodulatory Profile of Dexmedetomidine Sedation in Patients Recovering After ARDS Covid-19' (DEXDO-COVID, NCT04413864).

Nevertheless, delving into the current scenario of the riddling uncertainties in staging an ideal management plan against the novel intriguing viral enemy [10,11], I get reminded of the Bertrand Russell quote: *When one admits that nothing is certain one must, I think, also add that some things are more nearly certain than others...*

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Author roles

RM conceptualized and wrote the entire comment.

References

- [1] Stockton J, Kyle-Sidell C. Dexmedetomidine and worsening hypoxemia in the setting of COVID-19: A case report [ahead of print, 2020 May 27]. *Am J Emerg Med*. 2020. <https://doi.org/10.1016/j.ajem.2020.05.066>.
- [2] Zhao H, Davies R, Ma D. Potential therapeutic value of dexmedetomidine in COVID-19 patients admitted to ICU. [ahead of print, 2020 October 2]. *Br J Anaesth*. 2020. <https://doi.org/10.1016/j.bja.2020.09.031>.
- [3] Krüger BD, Kurmann J, Corti N, Spahn DR, Bettex D, Rudiger A. Dexmedetomidine-associated hyperthermia: a series of 9 cases and a review of the literature. *Anesth Analg*. 2017;125:1898–906.
- [4] Czepiel KS, Lucas AT, Whalen MJ, Mojica JE. Dexmedetomidine-Associated Hyperpyrexia in Three Critically Ill Patients With Coronavirus Disease 2019. *Crit Care Explor*. 2020;2:e0213.
- [5] Ammar MA, Sacha GL, Welch SC, Bass SN, Kane-Gill SL, Duggal A, et al. Sedation, Analgesia, and Paralysis in COVID-19 Patients in the Setting of Drug Shortages. [ahead of print, 2020 Aug 26]. *J Intensive Care Med*. 2020. <https://doi.org/10.1177/0885066620951426>.
- [6] Kotfis K, Williams Roberson S, Wilson JE, Dabrowski W, Pun BT, Ely EW. COVID-19: ICU delirium management during SARS-CoV-2 pandemic. *Crit Care*. 2020;24:176.
- [7] Bouajram RH, Bhatt K, Croci R, Baumgartner L, Puntillo K, Ramsay J, et al. Incidence of dexmedetomidine withdrawal in adult critically ill patients: a pilot study. *Crit Care Explor*. 2019;1:e0035.
- [8] Payen JF, Chanques G, Futier E, Velly L, Jaber S, Constantin JM. Sedation for critically ill patients with COVID-19: which specificities? One size does not fit all. *Anaesth Crit Care Pain Med*. 2020;39:341–3.
- [9] Magoon R. Implications of Practice Variability: Comment. *Anesthesiology*. 2020 Oct 1;133:943–4.
- [10] Magoon R. Pulmonary vasculature in COVID-19: mechanism to monitoring [ahead of print, 2020 October 5]. *Korean J Anesthesiol*. 2020. <https://doi.org/10.4097/kja.20536>.
- [11] Magoon R, Ohri R. Compounded research challenges amid the COVID-19 pandemic [ahead of print]. *Anaesth Crit Care Pain Med*. 2020. <https://doi.org/10.1016/j.accpm.2020.09.002>.

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