What is the second sedative agent to add to dexmedetomidine for sedation of COVID-19 patients?

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KEY FINDINGS

At present, there are no studies that evaluate the efficacy or safety of dexmedetomidine with another sedative agent among COVID-19 patients. Possible adverse events should be carefully considered in the choice of add-on sedative agent.

- Adequate sedation is important among ventilated COVID-19. Dexmedetomidine is an alpha2-adrenergic receptor agonist that produces sedation, analgesia and anxiolysis. It preserves respiratory function even when given in high doses.
- Due to the high cost of dexmedetomidine, a common clinical practice is to use dexmedetomidine in combination with other sedatives.
- Co-administration of dexmedetomidine with other sedatives has an additive effect. Possible adverse effects of combination treatment include hypotension, bradycardia, and delirium.
- There are no completed or ongoing clinical trials that evaluate the efficacy or safety of dexmedetomidine with another sedative agent among COVID-19 patients.
- Currently, there are no guidelines that specifically mention the recommended add-on sedative agent to dexmedetomidine for sedation of COVID-19 patients.
- The World Health Organization recommends light sedation and minimizing continuous or intermittent sedation among suspected COVID-19 patients with severe acute respiratory infection.
- Clinical practice guidelines for sedation among critically ill, mechanically ventilated adult patients recommend the use of propofol or dexmedetomidine over benzodiazepines due to decreased time to extubation, duration of stay in the intensive care unit, and incidence of delirium.

RESULTS

There are no completed or ongoing clinical trials that evaluate the efficacy or safety of dexmedetomidine with another sedative agent among COVID-19 patients.

There is a clinical trial to be conducted in China that evaluates the protective effect of dexmedetomidine among adult patients with severe COVID-19. The comparator was not stated in the registration. The outcomes include CKMB, Troponin I, neuron-specific enolase, BUN, creatinine, and lactic acid.

Recommendations from Other Guidelines

Currently, there are no guidelines that specifically mention the recommended add-on sedative agent to dexmedetomidine for sedation of COVID-19 patients.

The World Health Organization recommends provision of light sedation and minimization of continuous or intermittent sedation among patients with severe acute respiratory infection who are suspected to have COVID-19. [10]

Clinical practice guidelines for sedation among critically ill, mechanically ventilated adult patients recommend the use of propofol or dexmedetomidine over benzodiazepines due to shorter time to extubation, shorter duration of stay in the intensive care unit, and lower incidence of delirium. [11,12]

CONCLUSION

At present, there are no studies that evaluate the efficacy or safety of dexmedetomidine with another sedative agent among COVID-19 patients.

Clinical practice guidelines for management of sedation among critically ill, mechanically ventilated adult patients recommend the use of propofol or dexmedetomidine over benzodiazepines.

The use of dexmedetomidine reduces requirements for opioids and other anesthetics. Possible adverse events should be carefully considered in the choice of add-on sedative agent.

Declaration of Conflict of Interest

No conflict of interest

REFERENCES

1. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: a novel sedative-analgesic agent. 2001. *Proc (Bayl Univ Med Cent).* 14(1):13-21. doi: 10.1080/08998280.2001.11927725
2. Kaur M, Singh PM. Current role of dexmedetomidine in clinical anesthesia and intensive care. 2011. *Anesth Essays Res.* 5(2):128-133. doi: 10.4103/0259-1162.94750.
3. Weerink MAS, Struys MMRF, Hannivoort LN, Barends CRM, Absalom AR, Colin P. Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine. 2017. *Clin Pharmacokinet.* 56(8):893-913. doi: 10.1007/s40262-017-0507-7.
4. Haselman MA. Dexmedetomidine: a useful adjunct to consider in some high-risk situations. 2008. *AANA J.* 76(5):335-339.
5. Louie JM, Lonardo NW, Mone MC, Stevens VW, Deka R, Shipley W, et al. Outcomes When Using Adjunct Dexmedetomidine with Propofol Sedation in Mechanically Ventilated Surgical Intensive Care Patients. 2018. *Pharmacy (Basel)*. 6(3). pii: E93. doi: 10.3390/pharmacy6030093.

6. Buckley MS, Agarwal SK, MacLaren R, Kane-Gill SL. Adverse Hemodynamic Events Associated With Concomitant Dexmedetomidine and Propofol for Sedation in Mechanically Ventilated ICU Patients. 2019. J Intensive Care Med. 2019:885066619884548. doi: 10.1177/0885066619884548.
7. Garisto C, Riicci Z, Tofani L, Benegni S, Pezzella C, Cogo P. Use of low-dose dexmedetomidine in combination with opioids and midazolam in pediatric cardiac surgical patients: randomized controlled trial. 2018. Minerva Anestesiol. 84(9):1053-1062. doi: 10.23736/S0375-9393.18.12213-9.
8. Kim JG, Lee HB, Jeon SB. Combination of Dexmedetomidine and Ketamine for Magnetic Resonance Imaging Sedation. 2019. *Front Neurol*. 10:416. doi: 10.3389/fneur.2019.00416.
9. Mogahd MM, Mahran MS, Elbaradi GF. Safety and efficacy of ketamine-dexmedetomidine versus ketamine-propofol combinations for sedation in patients after coronary artery bypass graft surgery. 2017. *Ann Card Anaesth*. 20(2):182-187. doi: 10.4103/aca.ACA_254_16.
10. World Health Organization. Clinical management of severe acute respiratory infection when COVID-19 is suspected. 2020. Accessed April 13, 2020 from https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected.
11. Devlin JW, Skrobik Y, Gelinas C, Needham DM, Slooter AJC, Pandharipande PP, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. 2018. Crit Care Med. 46(9):e825-e873. doi: 10.1097/CCM.0000000000003299.
12. Celis-Rodríguez E, Birchenall C, de la Cal MÁ, Castorena Arellano G, Hernández A, Ceraso D, et al. Clinical practice guidelines for evidence-based management of sedoanalgesia in critically ill adult patients. 2013. *Med Intensiva*. 37(8):519-574. doi: 10.1016/j.medin.2013.04.001.

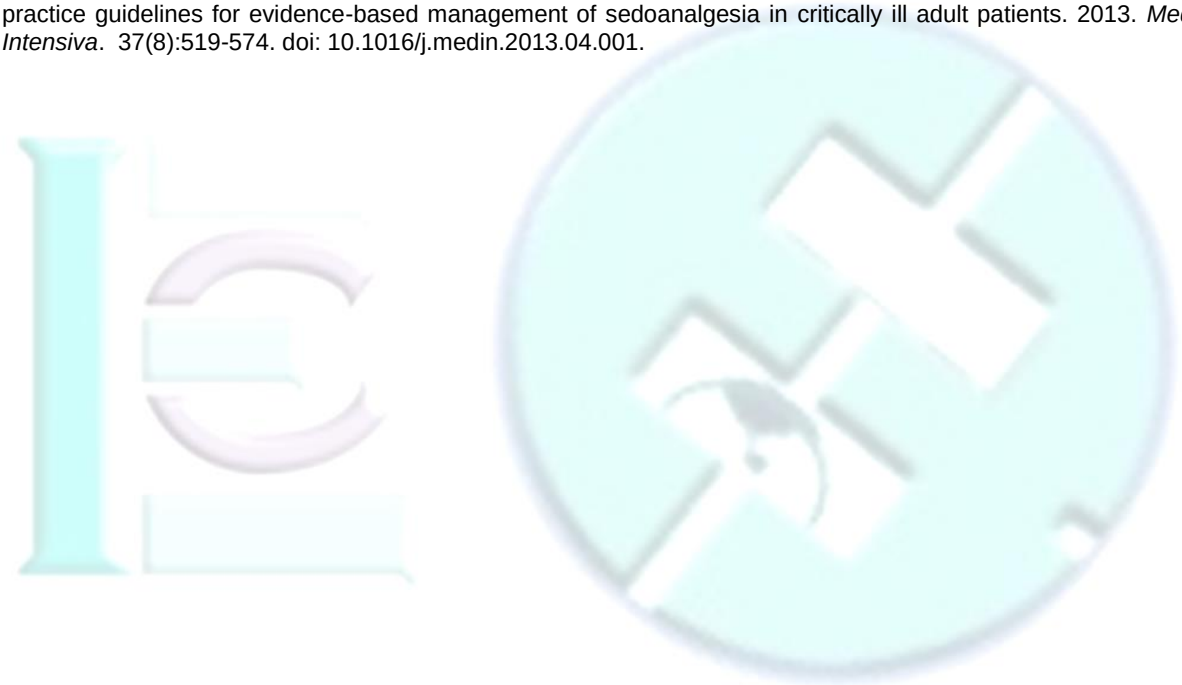

Table 1. Characteristics of clinical trials

No.	Clinical Trial ID / Title	Status	Start and estimated primary completion date	Study design	Country	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
1	Evaluation of the protective effect of dexmedetomidine on patients with severe novel coronavirus pneumonia (COVID-19) ChiCTR2000030853	Not yet recruiting	Not stated	Interventional study	China	Adults with symptomatic COVID-19 infection	Dexmedetomidine	Not stated	CKMB, Troponin I, neuron-specific enolase, BUN, creatinine, lactic acid