Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Sedation, narcotic and neuromuscular blockade in mechanically ventilated patients with COVID-19

Keywords:
COVID-19
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A B S T R A C T

Objective: To describe the sedation, narcotic and neuromuscular blockade usage in ventilated patients with COVID-19 pneumonia.

Design: Single-Center Retrospective Review.

Setting: George Washington University Hospital in Washington, D.C.

Patients: 62 patients with COVID-19 respiratory failure requiring mechanical ventilation admitted from March 2020 to June 2020.

Intervention: None.

Measurements and main results: Patients with COVID-19 respiratory failure required multiple sedative/narcotic infusions to achieve sedation requirements and at doses that were significantly more when compared to a general medical-surgical ICU population (represented by the MIND-USA cohort). The most common infusions were Dexmedetomadine and Propofol. Approximately 17% of our patients required a neuromuscular blockade infusion as well. Prior to intubation, narcotic utilization was stable and low.

Conclusion: Patients with COVID-19 respiratory failure requiring mechanical ventilation have higher sedation and narcotic requirements than general ICU patients.

1. Introduction

Discussions within the critical care community as well as anecdotal reports suggest that patients afflicted with COVID-19 respiratory disease require higher levels of sedation when compared to other critically ill patients. To evaluate this, we retrospectively evaluated the dose of sedatives, narcotics, and neuromuscular blockade (NMB) for patients admitted with respiratory failure from COVID-19.

2. Materials and methods

Patients admitted with COVID-19 and respiratory failure who required intubation at an academic tertiary care intensive care unit (ICU) from 03/2020 to 06/2020 were included. Exclusion criteria included significant baseline narcotic usage (Oral Morphine Equivalents [OME]>100) or dementia. Sedative and narcotic data was collected on hospital days 1,3,5,7,10,13,16,19,22,25, and 28. Infusion information was collected as time weighted daily averages. Narcotic dosages were reported as OME and benzodiazepines were reported as midazolam equivalents. Information on NMB infusions and incidence of flaccid neurological exam findings were recorded. Comparison of medians was made with the MIND-USA data set using the one sample sign test due to non-parametric distribution of data.

3. Results

62 patients were included for analysis. The most widely used infusions were Dexmedetomidine and Propofol followed by narcotics. When compared to the FDA recommended upper limit for these medications, the dosages were relatively modest, except for Dexmedetomidine which was 1.4 times higher (Table 1). However, when compared to the cohort of critically ill patients from the MIND-USA study [1], the dosages of our infusates were significantly higher in the patients with COVID-19 – the median doses of Propofol, Dexmedetomidine and narcotics were 2.89 times higher ($p < 0.01$), 5.51 times higher ($p < 0.01$) and 1.79 times higher ($p < 0.01$) respectively. The average number of infusions was 2.4 per patient. Narcotic use among patients with COVID-19 prior to intubation was consistent throughout their pre-intubation period, however the narcotic usage increased dramatically in the post-intubation timeframe (Fig. 1). The average number of patients requiring an NMB infusion was 17.6% vs the number of patients with quadriplegic paralysis was 46.6%.

4. Discussion and conclusions

Our analysis demonstrated large sedation and narcotic requirements in patients with hypoxemic respiratory failure from COVID-19. Compared to the MIND-USA cohort (where approximately 40% of patients were intubated for ARDS), our sedation dosing was

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2210-8440/

Table 1
Comparison of median of means for different infusions at GWU when compared to the FDA recommended upper limit or when compared to the MIND-USA cohort. Comparison between GWU cohort and FDA recommended upper limits demonstrated that Dexmedetomadine was used at doses beyond the FDA recommended upper limit. Comparison between the GWU cohort and the MIND-USA cohort demonstrated that all drugs were used at higher doses compared to the MIND-USA cohort. All comparisons results were significant between GWU cohort and FDA recommended upper limits and GWU and MIND-USA cohorts ($p < 0.01$).

Drug	GWU – Median (25th –75th Percentile)	FDA Upper Limit	Ratio	Drug	GWU – Median (25th – 75th Percentile)	MIND-USA Median	Ratio
Propofol (mcg/kg/min)	31.2 (29.1–35.2)	80	0.39	**Propofol (mg/day)**	4031 (3815–4757)	1391	2.89
Dexmedetomadine (mg/kg/hr)	1.5 (1.2–1.7)	1.1	1.4	**Dexmedetomadine (mcg/day)**	3400 (2891–3625)	617	5.51
Narcotics – OME (mg/hr)	15.1 (9.0–19.1)	60	0.25	**Narcotics (mg/day)**	363 (216–458)	203	1.79
Midazolam Equivalents (mg/kg/hr)	0.02 (0.01–0.02)	0.1	0.15	**Midazolam Equivalents (mg/day)**	35 (24–48)	4	8.87
Ketamine (mg/kg/hr)	0.21 (0.19–0.22)	2	0.10	–	–	–	–

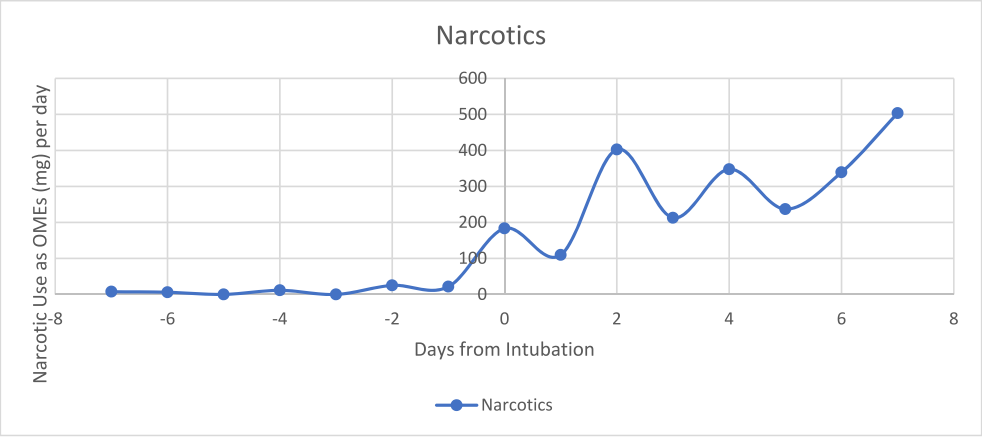

Fig. 1. Narcotic utilization in intubated patients in the days preceding intubation and the days following intubation. Narcotic rates remained stable in the pre-intubation period and use increased dramatically following intubation.

significantly higher for all sedative infusions; most notably for Dexmedetomadine and Propofol. Furthermore, we noted multiple sedative infusions per patient per day, which is atypical of our routine ICU practice. The incidence of quadriplegic paralysis was also higher compared to the number of patients requiring NMB infusions. Additive or synergistic effects of COVID-19 with sedatives/NMB is one plausible explanation for these findings. Previous editorials have postulated that SARS-CoV-2, like other members of the Coronaviridae, may be neurotropic [2]. Furthermore, initial studies out of Wuhan China have shown evidence of SARS-CoV-2 in CSF samples, as well as cases of encephalitis and Guillain-Barre Syndrome [3]. The need for different sedative requirements and increased incidence of quadriplegic paralysis, as demonstrated by our findings, lends further credence to the notion that the virus impacts the neurological system in measurable ways. Given the retrospective nature of this study, comparison to the MIND-USA should be analyzed with caution, as the two cohorts differ in incidence of ARDS and AKI. Our cohort included two patients on VA-ECMO which can skew results given the alterations in pharmacokinetics/pharmacodynamics that occur with ECMO [4]. Despite these limitations this study highlights the significant sedative/narcotics requirements of ventilated patients with COVID-19 respiratory failure. Future studies that examine the multitude of neurologic effects that SARS-CoV-2 causes and the potential for interaction with sedatives, narcotics and NMB are warranted.

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