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Critical medication shortages further dwindling hospital resources during COVID-19



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The coronavirus disease 2019 (COVID-19) pandemic has impacted millions of people worldwide and created a shortage of healthcare resources [1,2]. The need for personal protective equipment (PPE), ventilators, hospital beds, and frontline medical professionals to care for patients with COVID-19 and protect medical professionals is well publicized [1]. In response, field hospitals were established to supplement hospitals already operating above surge capacity and various manufacturers started making PPE and ventilators. As the capacity to care for patients increases, we need to call attention to the many medication shortages which hospitals are struggling with, and how these have the potential to adversely affect patient outcomes and staff safety.

Drug shortages are not unique to COVID-19. Normally, utilization of an alternative first-line agent or changing to a different product packaging is enough to successfully navigate the shortage. The sharp increase in number of critically ill patients during COVID-19, many of whom require similar essential medications, greatly contributed to the ongoing shortages of multiple first-line critical care medications and their alternatives.

The most prominent of the shortages are the post-intubation intravenous (IV) opioid analgesics and sedatives, which include fentanyl, sufentanil, hydromorphone, morphine, propofol, dexmedetomidine, midazolam, and lorazepam [2]. The limited availability of these agents has resulted in deviations from the national guidelines [3]. The preferred sedatives after intubation are propofol and dexmedetomidine, which reduce intensive care unit length of stay (LOS) and duration of mechanical ventilation when compared to benzodiazepines [3]. Due to shortages and the higher sedation requirements to maintain ventilator synchrony in COVID-19 patients [2], benzodiazepines like midazolam and lorazepam are utilized more frequently as either continuous infusions or intermittent bolus therapy depending on their availability at institutions. Reliance on IV boluses without continuous infusions increases the amount of time that nurses spend in a patient's room and the amount of PPE utilized. Supplemental enteral opioids and benzodiazepines are an option; however, there are not established protocols to allow successful incorporation of them into the patient's sedation and analgesia regimen without much trial and error. Benzodiazepines are an established risk factor for delirium, which further prolongs LOS and mortality [3]. Longer durations of ventilation are a risk factor for ventilator-associated pneumonia [3]. Ketamine is primarily studied for its opioid-sparing effects [3]; however, the concurrent

shortages caused it to be utilized more frequently as a sedative. Recently, non-sedation strategies that utilize only as needed morphine IV bolus doses did not demonstrate a difference in clinical outcomes, but an increase in self-extubations and self-removals of lines or other equipment was observed [4]. The sedative and opioid analgesic shortages have the potential to affect patient outcomes, including extended hospitalization and increased utilization of resources like PPE and ventilators that are already being rationed.

Neuromuscular blocking agents used during rapid sequence intubation, to promote ventilation synchrony and treat acute respiratory distress syndrome (ARDS) are also on shortage [2]. ARDS is now treated with IV bolus doses of paralytics (e.g. rocuronium or vecuronium) instead of the continuous infusions (e.g. cisatracurium) and it is unknown how that shift in practice will impact clinical outcomes. Lack of, or under dosing of, paralytics can create a more challenging intubation environment, which may further increase the risk to staff present in the room during this aerosol-generating procedure.

Antibiotic utilization decisions are also challenging. Vancomycin, ceftazidime, meropenem, and piperacillin-tazobactam are all on shortage [2], which may cause institutions to rely on suboptimal antibiotics based on their antibiograms or alternative medications with additional adverse effects like QTc prolongation. The small volume fluids used to prepare these antibiotics are also on shortage [2], which forces institutions to move away from extended infusions of antipseudomonal β -lactam that are known to lower mortality compared to intermittent administrations [5]. Additionally, IV antibiotics with less frequent administration times may become difficult for institutions to obtain in order to meet the increased demand even if the medication does not appear on the American Society of Health-System Pharmacists' drug shortage list [2]. This is due to allocation of product based on purchase history prior to COVID-19. Shortages and allocations further restrict our ability to optimize antimicrobial regimens according to institutional antibiograms, safety profile, and administration strategies that optimize bactericidal effects or promote staff safety.

The critical shortage of medications has shifted practice towards agents known to have greater adverse effect profiles, utilization of hospital resources, and mortality. Without our preferred medications, we are further depleting our limited hospital resources, PPE, and putting staff at greater risk due to increased time in patient rooms. Previous calls to action from medical professions [1] resulted in increased supplies and resources from the government and independent companies. The same urgent response is needed to increase production and access to these critical medications to enable providers to optimally care for patients during COVID-19 epidemic. Without action, hospitals will be forced to ration or be without these life-saving medications during the peak and plateau phases of COVID-19 hospital visits.

Prior presentations

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- [1] Phua J, Weng L, Ling L, et al. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. *Lancet Respir Med*. 2020;8:506–5017. In press.
- [2] American Society of Health-System Pharmacists (ASHP). Current drug shortages [Internet]. ASHP Drug Shortage List. [cited 2020 Apr 25]. Available from: . <https://www.ashp.org/Drug-Shortages/Current-Shortages>.
- [3] Devlin JW, Skrobik Y, Gélinas C, 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. *Crit Care Med*. 2018;46:e825–73.
- [4] Olsen HT, Nedergaard HK, Strøm T, et al. Nonsedation or light sedation in critically ill, mechanically ventilated patients. *N Engl J Med*. 2020;382:1103–11.
- [5] Vardaka KZ, Voulgaris GL, Maliaros A, Samonis G, Falagas ME. Prolonged versus short-term intravenous infusion of antipseudomonal β -lactams for patients with sepsis: a systematic review and meta-analysis of randomised trials. *Lancet Infect Dis*. 2018; 18:108–20.