Clinical Pharmacists: An Invaluable Part of the Coronavirus Disease 2019 Frontline Response

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Abstract: Although coronavirus disease 2019 was first identified in December 2019, it rapidly spread and became a global pandemic. The number of patients infected with the novel coronavirus (severe acute respiratory syndrome coronavirus 2) rose rapidly in New York State, placing great stress on healthcare systems. The traditional roles and practices of healthcare providers were dramatically redefined to meet the demand to care for the large number of ill patients. While literature reports on the experiences of many frontline staff, there is a scarcity of reports on the role of clinical pharmacists during this crisis. We report the role of critical care clinical pharmacists at a large academic medical center in New York City during this pandemic. Effective crisis management required clinical pharmacists to employ a wide array of skills and knowledge. Areas included clinical expertise, education, data analysis, health informatics infrastructure, and inventory management in times of surging medication use and manufacturer shortages. Clinical pharmacists fulfilled an essential service during the coronavirus pandemic by working to ensure the best possible outcomes for the patients they served on the frontline. Key Words: coronavirus disease; crisis response; pharmacists; pharmacy; severe acute respiratory syndrome coronavirus 2

The 2020 pandemic currently plaguing the world, was first identified in Wuhan, China, in December 2019 (1). In early 2020, the World Health Organization named the virus severe acute respiratory syndrome coronavirus 2 based on its identification and genetic composition (2). The coronavirus disease was later named coronavirus disease 2019 (COVID-19) and has spread globally within 4 months of its identification (3, 4). Public containment and medical management from every healthcare worker, including physicians, nurses, respiratory therapists, pharmacists, ancillary services, and even administrators and government, has been necessary to decelerate the disease’s impact. Scientific literature and media outlets constantly highlight the work of nurses and doctors on the frontline, but this article will specifically focus on the role of the clinical pharmacist during the coronavirus pandemic emphasizing the extraordinary work done to ensure safe effective therapy was provided to optimize health outcomes in hospitalized patients (5–8). With post-graduate education and training in direct patient care areas and specialty certification, clinical pharmacists are equipped to work alongside physicians and other healthcare professionals to coordinate care (9). In recognition of this, the Society of Critical Care Medicine (SCCM) strongly recommends that an entire team, including pharmacists, should be available for all critically ill patients to provide direct care (10).

As of March, the United States became the epicenter of COVID-19. New York State became the epicenter of the epicenter according to government officials, with the first case on March 1, 2020 (11–13). By the end of the week, 636 cases were identified per day, rising to 5,987 cases per day by March 30, 2020. This was an exponential increase to the peak of 6,160 by April 6, 2020, causing peak new hospitalizations of 1,724 reported to the state, requiring Governor Cuomo to ask New York hospitals on March 16, 2020, to increase capacity 50% with a goal increase of 100% to accommodate new hospitalizations (12, 13). Operating rooms and post-anesthesia care units and all areas with telemonitoring were converted to ICUs, requiring critical care pharmacists to create standardized list of medications, rapid response kits, and advanced cardiovascular life support medication trays for emergencies (Fig. 1). Since the Bronx, in particular, had the highest per capita rate of any borough with 2,513 cases per 100,000 people totaling 36,969 cases by April 30, 2020,
Figure 1. Hospital surge plan: Critical care bed surge plan for four discrete facilities. *Medicine floor. All protocols/procedures were communicated to pharmacy operations and either general Medicine or Critical Care Medicine (CCM) directors as necessary. ACTT 2 = Adaptive COVID-19 Treatment Trial 2; COVID-19 = coronavirus disease 2019; CPOE = computerized physician order entry.

Figure 2. Medication surge report: A visual representation of coronavirus disease 2019 (COVID-19) diagnosed ICU patient census, ventilator use, and administrations of selected medications. Census and ventilator use numbers provided by the Network Performance Group of the Montefiore Health System. Medication administrations for norepinephrine, vasopressin, fentanyl, and propofol were obtained from medication administration record data for the IV infusion dosage forms of these agents. Potassium and phosphate binder numbers were obtained from medication administration record data for sevelamer, calcium acetate, patiromer, sodium zirconium cyclosilicate, and sodium polystyrene sulfonate.
there was a remarkable surge in resource utilization at our urban multicenter academic medical facility located in the Bronx and lower Westchester (Fig. 2).

The immediate effect of this unprecedented surge was a looming shortage of first-line medications for the treatment of COVID-19–related complications. The crisis placed an enormous amount of stress on the entire medication supply chain: health system pharmacies, distributors, and manufacturers could not keep up with this rapid increase in demand for medications such as sedatives, analgesics, vasopressors, and electrolyte modifiers for patients with acute kidney injury (Fig. 2). In response, clinical pharmacists established daily teleconferences to keep abreast of the data on medication utilization and shortages, as well as to address the clinical implications of depleting first-line treatments for COVID-19 patients. They tailored existing business intelligence data reporting tools (SAP Business Objects) linked to medication order and administration data in a replicate electronic medical record database (EPIC Caboodle) to analyze medication surge trends daily to provide crucial dialogue between clinicians and buyers. Clinical pharmacists met with operational directors daily to review these data and project the inventory requirements for the upcoming weeks. Likewise, the prompt shortage detection helped pharmacy leadership communicate directly with manufacturers, requesting direct supply rather than waiting for wholesaler delivery (14). In cases where adequate supply could not be obtained in a timely manner, clinical pharmacists used the established communication channels with their clinical teams to implement preemptive shortage management strategies that avoided therapeutic interruptions, optimized patient care, and mitigated stress for other frontline staff. Examples of these strategies included the use of hydromorphone as first-line analgosedation in select patient populations to avoid depletion of fentanyl supply or using succinylcholine as our preferred paralytic for rapid sequence intubation (in the absence of contraindications) to avoid running out of vecuronium or rocuronium stock. To ensure rapid system-wide implementation of strategies such as the use of alternative analgosedation for an entire unit, clinical pharmacists established direct email communication chains with the Chair of the Medicine and Critical Care departments, who included these recommendations in their daily briefings to hospitalists and advanced practice practitioners in those areas.

In addition to the shortages, the lack of proven treatments for COVID-19 resulted in a wide array of experimental therapies being tested in COVID-19 patients. Unfortunately, no medication was Food and Drug Administration (FDA) approved or clinically safe and effective against COVID-19 in the early period of the pandemic. Drugs that potentially decrease viral uptake and replication like lopinavir/ritonavir, chloroquine, and hydroxychloroquine were readily available, but supply was depleted within 2 weeks, so clinical pharmacists restricted these medications by adding them to the antimicrobial stewardship designation, which mandated infectious disease specialist consult and approval. Additionally, immunomodulators like tocilizumab, anakinra, and baricitinib were extremely difficult to acquire, so clinical pharmacists reviewed baseline laboratories like C-reactive protein and ferritin in patients with persistent fevers to determine patients who would benefit, then directed the primary team to critical care, immunology, or rheumatology services for final approval. Investigational drug therapies with preliminary data, such as remdesivir, sarilumab, and lenzilumab, were only available to patients through clinical trials, compassionate use, and expanded access programs (15, 16). Multidisciplinary efforts involved clinical pharmacists screening and educating providers regarding the feasibility and accessibility to assure safe and effective use of investigational drugs. These pharmacists met with investigational drug services, monitored adverse events, and served as coinvestigators on clinical trials such as NCT04343651, NCT04347239, NCT04280705, and NCT04315298 (17–20). This influx of new therapies required clinical pharmacists to work with the information technology department to rapidly create and link appropriate records in the computerized physician order entry system (EPIC), admixture preparations system (DoseEdge), automated dispensing cabinets (Pyxis), and the smart infusion pumps (Alaris). Pharmacists also identified patients who were not candidates for clinical trials. If the patients were eligible to receive study drugs through compassionate use and expanded access programs, they completed Emergency Investigational New Drug Applications from the FDA, obtained the drug from the pharmaceutical company, and gained approval from the local investigational review board (21).

In addition to investigational agents for COVID-19, many protocols for critically ill patients were rapidly implemented in the face of uncertain evidence, with minimal opportunity for lengthy contemplation or risk-benefit deliberation. Thromboprophylaxis was one such topic of uncertainty, especially in the critically ill, where the risk of bleeding and clotting was the highest throughout the health system. Literature out of China regarding abnormal laboratory variables in COVID-19 patients left clinicians perplexed (22). Clinical pharmacists’ review of the protocols prompted multidisciplinary discussions on the risks versus benefits of employing various agents and regimens for thromboprophylaxis, or therapeutic anticoagulation strategies with little supportive evidence. In such cases where medications were used off-label without quality evidence supporting or refuting their use, pharmacists’ extensive training in clinical pharmacology proved invaluable in guiding rational decision making. Pharmacists used their clinical expertise to review retrospective data, case reports, expert opinions, drug interactions, adverse reactions, and contraindications to formulate potential dosing of these investigational drugs or approved drugs prescribed off-label. As a result, a pharmacist-led multidisciplinary team created an anticoagulation protocol for COVID-19 patients, which maximized evidence-based use of pharmacotherapy, and at the same time, provided guidance for safe use of anticoagulants for clinicians wishing to take on a more aggressive anticoagulation approach for their patients.

Finally, with the inflow of patients exceeding traditional ICU bed capacity, many intubated patients needed to be cared for outside of a traditional ICU setting by clinicians without primary critical care specialization. A critical step to ensure patient safety was implementing sedation guidelines to aid clinicians with treating ventilated patients in these nontraditional areas (23). This task proved extremely challenging due to looming medication shortages.

**Commentary**

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Opioid analgesics and benzodiazepines were chosen as the backbone of analgesia and sedation ensuring physician familiarity and relative low risk of hemodynamic compromise. The first line of those were fentanyl and midazolam, considering safety and ease of use, however, overuse would invariably lead to severe shortage (23). Pharmacists led education regarding bolus use and the addition of enteral agents to preserve IV agents for more acute situations. They also emphasized boluses prior to increasing continuous sedation to avoid unnecessary over-sedation and waste, drug accumulation, and future tolerance and withdrawal in addition to other relevant side effects (24, 25). For chronic cases where patients were unable to wean off opioid or benzodiazepine infusions, the addition of enteral or even transdermal agents were considered to safely transfer patients to lower acuity units or floors (26). Without the luxury of time, adequate medication supplies, or storage space, aggressive efforts emphasized using oral therapy. Methadone, chlordiazepoxide, lorazepam, and quetiapine were chosen to reduce opioid and sedative requirements while simultaneously keeping patients sedated at their target Richmond Agitation-Sedation Scale score, and potentially decreasing the occurrence of delirium (27, 28). The most important aspects of this protocol were to make it adaptable, understandable, and efficient. A simplified flow chart was distributed to hospitalists (Fig. 3). Additionally, clinical pharmacists created protocols with two to three alternative pathways to account for the inevitable shortages of preferred medications. Information was then disseminated throughout the medical center with the assistance of pulmonary specialists, who recorded a detailed lecture and were often consulted for ventilator management, hospitalist-led daily briefings with their peers, and daily emails with a Department of Medicine intranet link to the resources.

In conclusion, clinical pharmacists played an invaluable and often unrecognized role in managing the health system’s response to the COVID-19 pandemic. The work of clinical pharmacists to manage and mitigate drug shortages allowed clinicians to continue to provide the highest level of care throughout the health system. The education and acquisition assistance in off-label, investigational, and compassionate use medications expedited therapy in the most critical cases. The skills and knowledge of clinical pharmacists allowed for rapid development and dissemination of critical drug information. Importantly, algorithm development prevented medication therapy errors by clinicians practicing in unfamiliar settings. The pandemic response was a multidisciplinary effort in which clinical pharmacists not only worked tirelessly behind the scene but alongside their colleagues on the front line at the epicenter of the COVID-19 pandemic. Incorporating a clinical pharmacist in the preparations and management of any crisis is a crucial step in preparing for future disasters, epidemics, or pandemics such as COVID-19. Importantly, SCCM likewise recommends clinical pharmacists’ placement into the staffing models for expansion of ICU services (10).

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