EDITORIAL

Roles of the clinical pharmacist during the COVID-19 pandemic

In December 2019, a respiratory illness due to a novel coronavirus, SARS-CoV-2, was first identified in China.[1] The respiratory illness due to SARS-CoV-2, termed COVID-19, is now a worldwide pandemic and has been identified in 183 countries and 266 073 people.[1] Common symptoms of COVID-19 include cough, shortness of breath, and fever; disease ranges in severity from asymptomatic infection, mild disease (in 81% of patients), to pneumonia, respiratory failure, and death.[2] Worldwide there have been 11 184 deaths associated with COVID-19, and the current data suggest that the elderly or those with comorbid conditions such as hypertension or diabetes are at the highest risk for mortality.[1,3] Although intensive precautions to limit spread in China appear to be decreasing the number of new cases within China, the global number of infections continues to rise rapidly.[1] Identification of COVID-19 in the United States has been challenging, given insufficient availability of testing supplies.[4] Although, supplies and testing are starting to increase significantly in the United States, among countries affected by COVID-19, the United States has among the lowest testing per capita.[5,6] The inability to test widely and quickly has hindered our ability to characterize the epidemiology of the disease, prevent further spread, and ensure the optimal use of other limited resources such as personal protective equipment (PPE) and medication therapy. Pharmacists play an essential and unique role within the healthcare team to optimize patient care during this COVID-19 pandemic.

Antiviral stewardship is vital during the pandemic. In lieu of antivirals with established efficacy for COVID-19, novel experimental agents are currently being evaluated in controlled studies globally for the prophylaxis and treatment of COVID-19.[7] One of the leading agents, remdesivir, was initially evaluated for the treatment of Ebola and is now being investigated for COVID-19 treatment, given its activity against RNA viruses.[8] There are several ongoing trials evaluating remdesivir for COVID-19. The currently enrolling adaptive randomized controlled trial is particularly noteworthy, as the study compares remdesivir to placebo first, and if remdesivir is associated with improved outcomes, a new therapeutic agent will be evaluated with remdesivir as the control.[9] A series of two-arm comparisons with new agents will occur with the aim of identifying the safest and most effective therapy for COVID-19. Naturally, pharmacists are essential in facilitating these investigational drug studies in health systems but they are also integral to helping obtain medication through compassionate use protocols. Remdesivir may also be obtained from the manufacturer (Gilead) under a compassionate use protocol.[10] We have assessed patients in our own institutions for eligibility for this agent

via compassionate use and have obtained it for one patient so far; this process requires obtaining authorization from the manufacturer and providing them with detailed clinical information about the patient, contacting the FDA to obtain emergency investigational new drug approval, gaining approval from the local IRB, coordinating with local investigational drug services, and obtaining patient consent. Gilead is now moving from compassionate use to expanded use protocols, highlighting the need to continuously monitor drug availability and approaches to obtaining medication. Identifying patients who may be appropriate for this or other investigational agents, collaborating with the physician sponsor and quickly coordinating with the other various parties, and receiving, preparing, and delivering drug to the patient's bedside are all key roles of the pharmacist during the COVID-19 pandemic. While investigational drug pharmacists play a significant role here, active involvement of those practicing in infectious diseases, information technology, critical care, distribution, and management can streamline the process and speed the time to therapy for study patients.

While no agents are currently FDA-approved for treatment of COVID-19, a number of drugs approved for other indications and available in the US market are of great interest for repurposing for COVID-19 treatment.[11,12] In vitro, these drugs may display direct antiviral effects, such as lopinavir/ritonavir, chloroquine, and hydroxychloroquine; or may be immune-modulating agents, such as tocilizumab or interferons. Data supporting the use of these agents are often limited to in vitro studies, animal models, or case series. Pharmacists play an essential role in reviewing and interpreting this information for their clinician colleagues, particularly when physician colleagues may be experiencing increased patient volume and thus may have limited time to read and evaluate new data as they are published. While enthusiasm for any drug that could aid in this disease may run high, it is important to take an appropriately critical approach in evaluating risks and harms. This is particularly important given that there are no randomized controlled trials demonstrating the efficacy of any agent for the treatment of COVID-19. For example, while lopinavir/ritonavir has been considered to have great promise, a recent randomized trial was unable to show a clinical benefit when compared to the standard of care.[13] Several randomized trials of these repurposed agents are recruiting, and encouraging enrollment in such trials is an important means of developing a scientific basis for their use. If these agents are used, it is the pharmacist's role to provide accurate data to the providers about safe drug delivery (eg, how to formulate oral drugs when patients cannot swallow), drug-drug interactions, and adverse effects. Patients also need appropriate

counseling about their use and potential harms, especially if use in the community becomes widespread.

One of the fundamental roles of pharmacists is to ensure the availability and timely provision of the safest and most effective therapy. In this role, pharmacists must plan for, identify, and mitigate drug shortages during the COVID-19 pandemic. This is crucial given that drug shortages can lead to prescribing of suboptimal therapy and have been associated with patient harm.[14] When there are limited suppliers of raw materials or active pharmaceutical ingredients (API), drug shortages easily occur. This is concerning given the US pharmaceutical supply chain is dependent on producers outside the United States; many raw materials and as many as 80% of APIs are sourced from China or India.[15] There has already been at least one drug shortage as a direct result of the pandemic and more are anticipated.[16] Therefore, pharmacists must work proactively, identify effective therapeutic alternatives, enforce the implementation of drug shortage mitigation strategies, and if needed, prioritize drug supply to the patients who are most likely to benefit. Given that there are many agents and APIs produced by only a single or handful of companies, many different therapeutic classes may be affected by the pandemic. And although many shortages are due to manufacturing issues, shortages may also occur due to increased demand, as is the case with some repurposed COVID-19 therapies. At our institutions, we developed formulary restriction criteria for COVID-19 therapies that are in limited supply (ie, hydroxychloroquine), have educated providers about the restrictions, and have implemented electronic alerts to prescribers upon ordering. We monitor compliance to the restrictions to prolong our supply in order to ensure future patients in need will be able to receive the drug. We have previously outlined more detailed prospective approaches to managing anti-infective shortages.[17] In addition, broader shortage guidelines and ongoing national drug shortage monitoring are available from the American Society of Health-System Pharmacists.[18,19]

Pharmacists must also support the healthcare team and infection preventionists to stop the spread of disease. We can take steps to minimize unnecessary PPE use by helping limit unnecessary entry into the patient room. This can be done by aligning medication administration times, IV to PO conversion when possible to decrease nurses needing to respond to pump alerts, and ensuring lab draws, including therapeutic drug monitoring are necessary and if possible are timed with other patient interactions. We can also limit staff to aerosolized exposure of the virus by developing treatment protocols that limit unnecessary nebulizer use and instead favor use of metered dose inhalers for inpatients. Furthermore, medication teaching of patients who are COVID-19-positive or persons under investigation for COVID-19 can be facilitated by telehealth approaches to minimize exposure to pharmacists.

Lastly, pharmacists are a trusted and accessible resource for the public during this public health emergency, especially community pharmacists. Pharmacists must educate their patients and the public on effective strategies to prevent acquisition and further spread of infection (eg, optimal hand hygiene, social distancing, staying home if having respiratory symptoms), symptomatic relief, and the best resources for current COVID-19 information (ie, CDC, local public health departments). In addition, prescriber inattention to refill requests may occur due to their own illness or increased need to focus on inpatient care; some states have invoked emergency pharmacist authorities to allow for pharmacist refilling.[20] To increase testing access, some community pharmacies are also setting up COVID-19 testing sites.

In conclusion, the genesis of the COVID-19 pandemic occurred less than 4 months ago, our knowledge about the disease is changing daily, and it is uncertain how long the pandemic will last. Pharmacists play a key role as the drug information expert in evaluating literature related to new or repurposed therapies and can help make system-level and patient-specific treatment decisions, as well as ensure access to these therapies and other drugs on shortage due the pandemic. By serving as a resource to physicians and other medical providers, patients, and the public, pharmacists are essential in mitigating adverse consequences due to the COVID-19 pandemic.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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