



## Global drug shortages due to COVID-19: Impact on patient care and mitigation strategies



Hisham A. Badreldin<sup>a,b,c,\*</sup>, Bassam Atallah<sup>d,e</sup>

<sup>a</sup> Department of Pharmacy Practice, College of Pharmacy, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

<sup>b</sup> King Abdullah International Medical Research Center, Riyadh, Saudi Arabia

<sup>c</sup> Department of Pharmaceutical Care Services, King Abdulaziz Medical City, Riyadh, Saudi Arabia

<sup>d</sup> Department of Pharmacy Services, Cleveland Clinic Abu Dhabi, Al Maryah Island, Abu Dhabi, United Arab Emirates

<sup>e</sup> Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH, USA

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### ABSTRACT

Coronavirus disease 2019 (COVID-19) arising from Wuhan, China, is currently outbreaking worldwide. The World Health Organization (WHO) has declared COVID-19 to be a global pandemic. COVID-19 could cause a wide range of symptoms ranging from self-limiting fever, sore throat, and cough to more severe symptoms that could lead to acute respiratory distress syndrome. As a result of the lockdown and increased demand, drug shortages could become a growing global issue. This article aims to shed light on the potential impact of drug shortages as a result of this pandemic on patient outcomes and the role of pharmacists and pharmacy policy-makers in alleviating this emerging problem.

### Introduction

A new strain of coronaviruses (CoV-2) causing severe acute respiratory syndrome coronavirus (SARS-CoV-2), now termed the coronavirus disease (COVID-19), was discovered in late December 2019.<sup>1</sup> A few months later, the World Health Organization announced the COVID-19 pandemic.<sup>2</sup> All countries that have been affected by this pandemic took several measures to reduce the influx of patients to their medical wards and intensive care units thus allowing their healthcare system to cope with the surge. Restricting the international commercial and trading channels as a mean for containment was one of the said measures implemented by several countries.<sup>3</sup>

As a result, a potential problem could be emerging on the horizon as a result of these measures, namely global drug shortages. The United States Food and Drug Administration (FDA) defines drug shortages as ‘The period of time when the demand exceeds the supply of the drug’. Drug shortages may be triggered by many reasons, such as inadequate quantities of raw materials, legislative, manufacturing, or procurement issues, and drug discontinuation from the market.<sup>4,5</sup> Historically, most countries that have been struck by this problem have been able to overcome it within an acceptable time frame in a way that didn't have a significant impact on patient care. Previous evidence has shown that drug shortage is associated with significant difficulty in obtaining

bioequivalent drugs, high additional costs in obtaining bioequivalent drugs, and increased risk of adverse patient outcomes.<sup>5</sup>

During these unprecedented times, the global drug supply could severely get impacted by this pandemic, and the results of this shortage could be catastrophic and may last for an extended period, primarily due to the global economic disruption at unprecedented speed and scale. This article examines the potential impact of this problem on patient outcomes and the role of pharmacists and pharmacy policy-makers in mitigating this problem.

#### *Impact of drug shortage on patient outcomes*

It is still unknown when the global trading channels will reopen. This may jeopardize the decision-making process regarding any anticipated drug shortage. During these times, the drug shortage could lead to serious consequences when it comes to patient outcomes. Certain patients might get transferred to other medical centers in order to access the required drugs affected by the local shortages.<sup>6</sup> The risk of medication errors may be heightened, including that of drug omission, dispensing, or administration. For instance, replacing an institutional formulary medication that is experiencing shortage with another non-formulary medication involves creating a new computerized physician order entry build, familiarizing physicians with the new order entry, as

\* Corresponding author. Pharmacy Practice Department, College of Pharmacy, King Saud bin Abdulaziz University for Health Sciences, P.O. Box 3660, Riyadh, 11481, Saudi Arabia.

E-mail address: [Aldeenh@ksau-hs.edu.sa](mailto:Aldeenh@ksau-hs.edu.sa) (H.A. Badreldin).

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well as pharmacists and nurses with preparation and administration. All of these additional steps carry a higher risk of error particularly in a pandemic situation where it is common to see healthcare providers deployed from their routine practice area or even patient population to serve in a new setting. It may also increase the frequency of patient monitoring, which increases the projected healthcare costs.<sup>6</sup> The conduction of clinical trials will also be affected by drug shortages thus delaying the delivery of essential, lifesaving, and breakthrough drugs.<sup>7</sup>

Moreover, the prescribed alternative drug may be less effective or may place the patient at a higher risk of developing unwarranted adverse effects.<sup>8,9</sup> A drug shortage could also result in an increased risk of a drug overdose as a result of changing drug concentrations and strengths.<sup>8,9</sup> Certain healthcare institutions may rely on their inpatient pharmacy to compound certain drugs that are in shortage. Compounding high-risk medications and mistakenly exceeding the usual amount of the active ingredient could place patients at risk of developing serious adverse effects as a result of overdosing.<sup>10</sup> The extended timeframe of drug shortage could cause an abrupt emergence of another public health crisis, such as influenza as a result of scarcity in influenza vaccines.<sup>11</sup>

Patients might find themselves having overwhelming out-of-pocket expenses in order to acquire the drug in shortage.<sup>12</sup> The extended timeframe of drug shortage may increase the risk of patient deterioration, worsen the acuity of patient illness, postpone or cancel crucial surgical procedures, prolong the hospital stay, and increase the rate of mortality.<sup>13,14</sup> Also, it might increase the patient's levels of distress, frustration, and confusion.<sup>15</sup> The magnitude of drug shortage is difficult to quantify or predict, and countries with low-to-middle income could drastically suffer from the prolonged consequences of drug shortages during this pandemic.<sup>16</sup>

#### Role of the pharmacist in COVID-19 related drug shortages

Pharmacists play an important role in mitigation of emerging drug shortages related to the pandemic. First and foremost, pharmacists aim to secure the most evidence-based medications for COVID-19 patients to improve outcomes. For example, recently, this has involved the compassionate use basis for drugs such as remdesivir. This medication has resulted in a numerical reduction in time to clinical improvement in patients with severe symptoms.<sup>17</sup> Pharmacists are involved in corresponding with health authorities, granting institutional review board approvals, and submitting the necessary related paperwork. However, the role of the pharmacists does not stop here. It extends to preparing the required computerized order entry build, communicating with supply chain, and up till the process of actually preparing the medication for administration. This is in addition to the role of the clinical pharmacist in collaborating with physicians to select candidates for the medication and optimizing overall medical therapy.

Another contemporary issue that pharmacists are an integral part of is that of emerging drug shortages of recently repurposed medications such as hydroxychloroquine, azithromycin, and lopinavir/ritonavir but also of some over the counter cough and cold medications. The media and high-level political attention given to such therapies have resulted in a dramatic increase in demand. The pharmacist is entrusted with advocating for appropriate prescribing and also continuing to secure such medications for patients who depend on them for their main indications. The pharmacist is not only involved in provider and patient education but also helping in setting institutional and community pharmacy policies on appropriate prescribing and dispensing of these medications. As has been previously suggested in a report from China, systematic pharmacist approach begins with drug demand analysis to identify drugs of interest, formulate special approval procedures and design best practice alerts to avoid inappropriate prescribing and drug hoarding.<sup>18</sup>

Intensive care medications have been particularly affected given the significant surge in use and demand for narcotics, sedatives and

neuromuscular blockers. Pharmacists are expected to be involved in strategies to deal with these shortages which involve evaluating and switching to alternative generic medications and switching between therapeutic options. Examples here include the switching from neuromuscular blocking agent cisatracurium, on shortage due to increased demand, to rocuronium. Another example is switching between the intravenous analgesic fentanyl to remifentanyl. Such changes while they may seem simple involve a crucial role for the pharmacist in educating other members of the healthcare team on the appropriate use and other associated ordering and administration information to avoid the medication errors that we previously discussed. Other strategies include using adjuvant medications to spare the use of those in high demand as well as supplementing with oral or transdermal formulations to stretch the supply of the intravenous ones. Examples here include utilizing dexmedetomidine, and the use of oral formulations of lorazepam through feeding tubes for those with a functional gastrointestinal tract to attempt weaning propofol and midazolam. In addition, the use of transdermal fentanyl has the potential to help lower the rate or completely stop the intravenous infusion. Pharmacists are involved in designing specific algorithms to successfully implement these strategies utilizing their knowledge of the pharmacologic and pharmacokinetic properties of these agents.

Physicians and nursing deployment from their routine practice sites to other areas as a result of the pandemic will increase the dependence of these healthcare providers on the clinical pharmacists who will find themselves being relied on, even more than ever, as the medication experts on the team. While clinical pharmacists may practice in a specific setting or serve a specific population are generally familiar with the institutional medication policies, formulary, computerized order entry, drug information resources and guidelines. This will allow them to significantly support other providers in their newly assigned tasks and help relieve overall provider anxiety and secure patient safety.

Other than the shortages caused by increased demand for repurposed drugs, the fact that many medications and raw materials are sourced from countries like India and China has also caused direct shortages. The pharmacist is able to navigate alongside other members of the healthcare team alternative therapeutic options until the shortages are resolved. It is important for the pharmacist to be aware of general guidelines to mitigate shortages such as those published by the American Society of Health-System Pharmacists.<sup>19</sup> This is in addition to the pharmacist being entrusted to provide frontline medical staff with answers to drug information questions and participating in clinical trials. Pharmacists are also encouraged to collaborate at a global level to share experiences on strategies to mitigate drug shortages as well as overall innovations as they relate to academic, institutional, and community pharmacy practice during the pandemic. [Table 1](#), outline the potential role of the pharmacists in drug shortages.

**Table 1**  
Role of the pharmacist in COVID-19 related drug shortages.

Pharmacist Role
<ul style="list-style-type: none"> <li>● Design overall most evidence-based treatment guidelines.</li> <li>● Conduct drug demand analysis to identify medications of interest in context of the pandemic.</li> <li>● Secure medications on compassionate use basis.</li> <li>● Design specific electronic best practice alerts to ensure proper prescribing of identified COVID-19 therapies.</li> <li>● Advocate for appropriate prescribing and use of therapies.</li> <li>● Formulate special approval procedures for certain medications.</li> <li>● Design appropriate alternative medications and therapeutic options.</li> <li>● Design algorithms to successfully implement medication sparing strategies using pharmacologic and pharmacokinetic knowledge.</li> <li>● Support other providers who are deployed from their routine practice site due to the pandemic.</li> <li>● Collaborate at a global level to share experiences on strategies to mitigate drug shortage.</li> </ul>

## Role of the policymakers in COVID-19 related drug shortages

Policymakers working at the national and institutional levels should act proactively to tackle this issue. National policymakers should work to preserve the drug supply by all means. Several examples have been proposed in the literature in order to preserve the drug supply, including the creation of a list of drugs that could potentially be in shortage due to this pandemic. This entails drugs that have no generic alternative and are solely manufactured in locked-down countries.<sup>20</sup> It is extremely crucial to create a freely available warning system to alert all stakeholders about potential drug shortages. They should ensure that national health care institutions are not working in silos during these times by generating channels for rapid communication between all local healthcare institutions. This will guarantee the availability of certain lifesaving drugs with significant demand.<sup>21,22</sup>

Moreover, policymakers should require manufacturers to disclose the location of drug production publicly in order to provide drug purchasers with enough time to be prepared for any impactful consequences and locate a local alternative if possible. Policymakers should work to incentivize local manufacturers to optimize their supply to meet the demand without contravening the good manufacturing practices, especially those that have profit margins not high enough to keep manufacturing these drugs during the pandemic. An extensive amount of drugs requires specific devices to prepare and administer them safely. Policymakers should work to grant enough custody of these devices and make sure to distribute them to institutions in need.<sup>20</sup> Also, they should educate the public to be extra vigilant in procuring shortage drugs through online sourcing. Policymakers should work to implement adjustable policies that govern the preparation plan of any potential drug shortage and investigate the outcomes of these policies.<sup>23,24</sup>

Institutional policymakers should institute and implement several internal policies and procedures to ensure the wise utilization of all drugs but mainly the ones that are not locally manufactured during these times. They should also establish a step-wise approach to transition patients to alternative bioequivalent generics that could be nationally manufactured. Also, they could work to assign an appointed person or task force to deal with drug shortage during these times. Moreover, they could create an internal electronic communication system to warn prescribers regarding any potential shortages and the available alternative therapy. This is in addition to reallocating internal financial resources in order to deal with any potential shortage.

Communication is key in any pandemic and the task force involved in handling the drug shortage situation at any institution should aim to provide regular updates on these shortages to all involved entities. As previously mentioned, many healthcare providers may be practicing in settings outside their comfort zone at the time of the pandemic, and thus the duty of task forces is to communicate with these providers as well as with appointed educators for each unit to ensure the proper dissemination of knowledge and updates. Moreover, a regularly scheduled virtual or on-site conference call or webinar is important for each multidisciplinary team to provide their overall updates and concerns including those related to drug shortages.

## Conclusion

Almost all global sectors have been affected by the emergence of COVID-19. Global drug shortages are a potential problem that is emerging on the horizon as a result of the global lockdown policies. The ultimate consequences could be detrimental and difficult to predict, and it might affect patient outcomes. Pharmacists and policymakers should be proactively engaged in alleviating the effects of this threat to patient care and outcomes.

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## Declaration of competing interest

Authors have no competing interests to declare.

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## Appendix A. Supplementary data

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