

Causes, Impact and Management of
Drug Shortage Crisis

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Abstract

The number of new and continuing drug shortages has continued to be on the rise for last ten years. Drug shortages not only reduces the quality of patient care but also contributes to the indirect costs on the healthcare systems by requiring additional time and money to be spent finding alternatives, rescheduling procedures, or modifying drug usage protocols. In order to better understand the dilemma of this crisis, this review article will focus on the specific causes, impact, and most importantly, management strategies of the drug shortage crisis.

Introduction

Over the recent years, drug shortages have been on a significant rise and have created difficulties within the United States (U.S.) healthcare system [1,2]. According to the U.S. Department of Health and Human Services, shortages of key cardiovascular, anesthetic, analgesic, anti-infective, and sterile injectable drugs have quadrupled within the last six years. It is estimated that nearly forty percent of the drug shortages affect the delivery of emergency care, which in turn hinders effective patient care and burdens healthcare providers [3,4].

Causes of Drug Shortages

There are multiple reasons for why drug shortages occur. The main cause of these recent shortages is the lack of an advanced warning system. This is because the drug manufacturers are required to notify the Food and Drug Administration (FDA) only six months in advance of when they plan to stop producing a particular drug [5] however; there is no penalty for failing to report this particular required notification [6]. Without an advanced warning of an impending drug discontinuation, there is not an ample opportunity for the healthcare systems to prepare for all the implications associated with drug shortages [5-7].

Other factors that contribute to drug shortages include drug-manufacturing difficulties due to non-compliance with good manufacturing practices, shortage of raw materials, voluntary recalls, natural disasters, supply and demand issues, and business and economic issues [1,3,5]. These drug shortages are very problematic when only one manufacturer who is the sole-source producer of a particular drug delays or discontinues its production due to any of the reasons mentioned above [5].

Impact of Drug Shortages

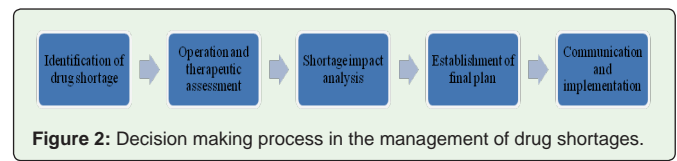
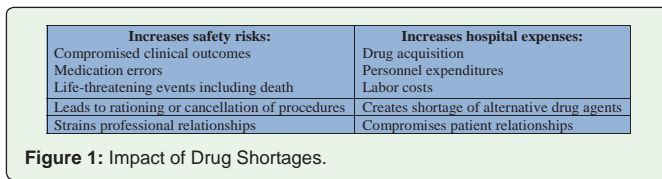
As mentioned previously, drug shortages can have a profound impact on the quality of healthcare and can create significant obstacles for the healthcare systems. Figure 1 lists the consequences associated with drug shortages [1,7,8].

Management of Drug Shortages - FDA's Role

A coordinated effort is often required between the drug manufacturers and FDA to manage drug shortages [9]. The FDA has limited authority in assisting manufacturing companies with the management of drug shortages however, once a shortage has been verified, both of the entities work together in order to resolve the identified problem [5,9]. Based on the bylaws, the FDA does not have the authority to mandate drug manufacturers to resume or increase production of a particular drug but it can definitely provide assistance in resolving drug shortages [6].

There are several ways in which the FDA can help alleviate different manufacturing issues. If a new manufacturing site or supplier needs to be established, the FDA can expedite a data review to approve such changes. Additionally, it can also expedite the review of new or generic drug applications to approve medications that are alternatives to those that are experiencing manufacturing difficulties. This particular strategy was implemented when the FDA expedited approval of generic injectable penicillin when penicillin G sodium for injection was on critical shortage.

The FDA can also assist in establishing a substitute or alternative source for the product by



encouraging other drug manufacturers to initiate or increase production of the drug to meet demands [9]. It can also request a drug manufacturer to not suspend drug production until an alternative source has been made available [5].

The FDA may also help a manufacturer establish an allocation program for remaining product inventory until a shortage is resolved. In the past, it has helped set up allocation programs for caspofungin acetate and betamethasone sodium phosphate-betamethasone acetate [9]. In rare cases, the FDA may allow emergency importation of a product from a foreign manufacturing source until that shortage is resolved [5,9]. So far, the FDA has allowed foreign importation of six drugs, including propofol and few chemotherapy agents [9].

Management of Drug Shortages-Healthcare Systems' Role

Given that the FDA's efforts to prevent or resolve drug shortages are not standardized, healthcare systems must act rapidly to obtain the original drug or therapeutically-equivalent alternative product to help avoid interruptions in patient care [5]. Although it may be impractical to prepare for every potential drug shortage, strategies for dealing with shortages should be defined well in advance. The healthcare systems can follow the recommendations made by the American Society of Health-System Pharmacists (ASHP) and the Institute for Safe Medication Practices (ISMP) to help manage this complex problem [2,5]. Figure 2 summarizes the key steps in this management process.

The first step in the management of drug shortages is identification. There are several avenues to knowing about these shortages. Signs

of an impending shortage such as partially filled orders or specific strengths of drugs that are difficult to obtain, should always be considered [2]. Additionally, the FDA and ASHP websites should be utilized on an ongoing basis for investigating drug shortages. Both of these websites provide information about current and resolved shortages. Additionally, the ASHP website also provides additional information regarding recommendations on possible therapeutic equivalents and patient safety [10,11].

Once a drug shortage is identified, the next step is to validate it. When a back order or other notice is received, it is important to verify the suspected drug shortage with either the distributor or drug manufacturer. The reasoning behind the shortage should be determined and estimated time for resumed product availability should be obtained. All of this information is helpful for the healthcare systems in developing management strategies and determining the ability to sustain this drug shortage [3-5].

After confirming a particular drug shortage, the pharmacy leadership of the healthcare systems should take charge in evaluating the current in-house supply. Additionally, they should provide projected timeframe on how long the current supply would last based on the current usage patterns of the drug in shortage. This information will help the healthcare systems assess if the shortage is sustainable [3,5].

If a drug shortage is not feasible, the pharmacy leadership and the Pharmacy and Therapeutics committee members of the healthcare systems need to identify therapeutically-equivalent alternative product(s) and perform inventory of the current supply of these

Table 1: Examples of Management of Drug Shortages.

Drug on Shortage	Current Restriction(s) and/or Alternative Therapies
Calcium Chloride Calcium Gluconate	<ul style="list-style-type: none"> ○ Ionized calcium <0.9 + contraindication to PO calcium + one of the following: neurological symptoms, cardiac abnormalities, coagulopathic bleeding requiring transfusion, emergent parathyroidectomy = 1 g one time order ○ Hyperkalemia + proven peaked T waves on EKG = 1 g one time order ○ Known or suspected calcium channel blocker toxicity/overdose for patients with hemodynamic instability = 1 g one time order
Dobutamine	<ul style="list-style-type: none"> ○ Heart failure patients waiting for transplant or left ventricular assist devices (LVADs) ○ Home inotropic support for end-stage heart failure patients ○ Patients who cannot tolerate milrinone (alternative therapy) based on: severe renal dysfunction (CrCL ≤ 10) OR any renal dysfunction + hypotension despite renal dosing adjustment OR platelet count ≤ 20,000 OR undergoing a stress ECHO
Fosphenytoin	<ul style="list-style-type: none"> ○ Status epilepticus + poor peripheral access (defined as feet or hands) and/or cardiac instability ○ All others should receive phenytoin (alternative therapy)
Intralipid	<ul style="list-style-type: none"> ○ Parenteral nutrition on Mondays, Wednesdays, and Fridays = max of 50 g on days listed ○ No lipids if receiving from other sources such as propofol or clevidipine
IV Furosemide	<ul style="list-style-type: none"> ○ Boluses: < 40 mg; > 40 mg in only solid organ transplant patients only. All others converted to bumetanide (alternative therapy). ○ Drips: Converted to bumetanide
IV Sodium Bicarbonate	<ul style="list-style-type: none"> ○ Liver disease patients OR sepsis and liver disease OR pH ≤ 7.15 ○ Use PO sodium bicarbonate, IV sodium chloride, IV sodium acetate, or acetazolamide as alternative therapies
Potassium Acetate	<ul style="list-style-type: none"> ○ Not added to regular parenteral nutrition unless chloride > 120 + non-functioning ileus + potassium < 2.5 with arrhythmias
Potassium Phosphate	<ul style="list-style-type: none"> ○ Not added to regular parenteral nutrition ○ Refeeding syndrome: 15 mmol one time order ○ Phosphorous ≤ 1.5 = 15 mmol or ≤ 1 = 30 mmol one time order
Sodium Phosphate	<ul style="list-style-type: none"> ○ Not added to regular parenteral nutrition ○ Potassium ≥ 5 + phosphorus ≤ 1.5

product(s) [2,3,5]. Additionally, new restrictions to the current practice guidelines or development of new practice guidelines should also be set in place in order to control the usage of these products. During these times, the healthcare systems should also discuss the options of obtaining the shortage drugs from avenues other than the drug manufacturers, such as in-house compounding or other specialty compounding pharmacies [2]. In all of these discussions, the ethics committees of every organization should also be involved in order to ensure safe and appropriate utilization of these alternative resources [2]. Table 1 lists examples of the management of drug shortages.

Decisions regarding managing a drug shortage need to be made in a timely manner in order to allow for proper implementation of an education plan [2,3]. In order for these decisions to be effective, strong communication needs to occur between the pharmacy staff and the rest of the healthcare team. Communicating essential information related to a drug shortage is crucial to ensure patient safety and prevent medication errors that can arise secondary to new changes in current standards of practice [3,5].

One of the biggest challenges that can arise during a drug shortage is inventory management. Healthcare systems should resist the temptation for stockpiling drugs in anticipation of a particular drug shortage because it can result in a feared shortage, which can deplete existing inventory and worsen the current shortage by diverting supplies away from other facilities and patients in need [2,3,5].

In order to avoid this dilemma, the healthcare systems within the vicinity of each other should join forces together in an effort to provide the best available patient care during the midst of a drug shortage [2]. This can include sharing of the new restricted guidelines as well as sharing of the actual drugs in shortage and/or therapeutically-equivalent alternatives [2,3-5].

Conclusion

Drug shortages significantly burden the health care system and can lead to failure in providing high-quality and cost-effective

medical care to the patients. Drug shortages are caused by many factors and can have significant consequences if appropriate actions are not taken in a timely fashion. Sustainable management strategies that include clear policies and procedures for information gathering, decision-making, collaboration, and timely communication should be established in order to effectively handle these drug shortages.

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