



Current Situation and Management of Drug Shortage in Some Western Countries and Its Enlightenment to China

Dong Sixu, Lian Guiyu*

(School of Business Administration, Shenyang Pharmaceutical University, Shenyang 110016, China)

Abstract

Objective To analyze the current situation of drug shortage in some western countries and their management strategies, and to put forward feasible suggestions for drug shortage management in China. **Methods** The methods of literature research and comparative study were used to collect policy information and related data from official government websites and news websites, then, the current situation and management of drug shortage in some western countries were compared and studied to summarize their effective experience in dealing with drug shortage. **Results and Conclusion** The current situation and influencing factors of drug shortage in these western countries are different, but the management system established to deal with drug shortage is good, including the support of policies and regulations, the early warning of monitoring platform and the construction of organizational system. Drawing lessons from their experience, China should strengthen cooperation and consultation among stakeholders and rationally allocate powers and responsibilities. The transparency of drug shortage data disclosure should be increased. The important role of pharmacists should be played to strengthen the management. Further optimizing the drug shortage management system in China can ensure the safety of drug supply.

Keywords: drug shortage; shortage current situation; management

The World Health Organization says that drug shortage is a complex global challenge^[1]. The shortage of drugs will directly increase patients' economic burden, and seriously threaten their lives and health. The shortage of varieties of essential drugs in the World Health Organization's list is more likely to have a serious negative impact on the treatment results. The causes of drug shortage are complicated, including factors such as economy, production quality, logistics and supervision. At the same time,

it is also affected by factors such as unreasonable internal system, mechanism and policy design of the medical and health system, which is closely related to all stakeholders. At present, many countries are still facing serious drug shortages and need to formulate long-term strategic responses.

In recent years, some western countries have taken systematic measures to solve the drug shortage problem, establishing an effective policy system and implementation path to solve the problem, which has achieved certain results. This paper makes a comparative study on the current situation and management of drug shortage in foreign countries,

* Corresponding author: Lian Guiyu, associate professor. Major research area: Medical industry development, production and operation management. Tel: 18698849647, E-mail: lianguiyu@163.com.



draws lessons from their management experience in dealing with drug shortage problem, and puts forward feasible suggestions for perfecting the management mechanism of drug shortage in China to ensure drug supply.

1 Current situation of drug shortage in some western countries

The developed countries, such as Europe and the United States, facing drug shortage earlier, have established relatively perfect and systematic medium- and long-term strategies. In addition, they have successively issued a series of management methods in public health emergencies, and the implementation effect was well verified, effectively alleviating the shortage.

Through the search, we find that the United States is in a leading position in the research of drug shortage. It has a good intermediary center, and has formed a stable and good cooperation network with other countries or regions. The research in the member countries of European Union (EU) and Canada is also fruitful. The EU's hierarchical treatment mechanism and Canada's classified treatment method have also achieved good results. In addition, these countries have clearly defined the definition and concept of drug shortage. They have well-established data platform for drug shortage that can update data timely. The wide coverage and mature handling mechanism have determined effective management methods based on system legislation and unified management^[2]. They have more perfect early warning mechanism and management measures than other countries in Asia and Africa, which has strong reference significance.

In this paper, the research progress of the current situation of drug shortage supervision and the difficulty of data collection are comprehensively considered, the United States, EU and Canada are selected as typical countries to study the drug shortage problem.

1.1 The United States

Because there are some differences in the

definitions in different countries and regions, unifying the definition of drug shortage is an important way to manage drug shortage effectively.

Food and Drug Administration (FDA) defines drug shortages as disruptions in the total supply of all clinically interchangeable FDA-regulated drugs that are in insufficient supply or are expected to be insufficient to meet anticipated demand^[3].

The main reasons for the shortage in the United States include lack of willingness to produce low-margin drugs, low market incentives for manufacturers with more mature GMP systems, and logistical and regulatory difficulties caused by the complexity of the supply chain. In 2011, the number of drugs in shortage in the United States was more than 200, and in 2019, there were 126 new drugs in shortage, involving antibacterial drugs, chemotherapy drugs, cardiovascular drugs, and central nervous system drugs. In February 2023, there were 121 varieties on the shortage list in the United States, and the drugs most vulnerable to shortages were usually small-molecule drugs that had been on the market for a long time and were the most widely used. In June 2023, FDA released its 10th annual "Drug Shortage Report", which noted that the FDA has effectively prevented shortages of 222 drugs by using a range of available tools. The number of new drug shortages tracked was 49, a nearly five-fold decrease from 2011^[4].

FDA used drug shortage management tools early, including working with manufacturers to address manufacturing and quality issues that lead to supply shortages, expediting FDA's inspection and review of manufacturer submissions, identifying and working with manufacturers who are willing to increase production to fill anticipated supply gaps and exercise regulatory flexibility and discretion while ensuring there is no therapeutic risk to patients^[5]. While requiring manufacturers to report disruptions in the production of essential drugs, and speeding up the regulatory review process for new drug suppliers, manufacturing locations, manufacturing changes, FDA also requires rigorous and clear reporting of product shortages so that authorities can address shortages from an early stage accordingly. In addition, they



generally allow the import of foreign drugs that are not currently approved by the FDA for treatment in the United States.

Novel corona-virus infection in 2019 exposed the shortage of global drug production and distribution, aggravated many original restrictions and unfairness of drug supply, caused new shortages. In the United States, the import of raw materials was restricted, and the supply of some key drugs was also affected, including antibiotics, respiratory system, sedation and anesthesia. In this regard, FDA has been paying close attention to the supply chain of pharmaceutical products and predicting the possible impact due to the outbreak of COVID-19. At the same time, pharmacists were encouraged to evaluate and find substitute generic drugs, explored new prescriptions that matched the indications of patients, which would shorten the clinical improvement time of patients with severe symptoms and optimize the overall treatment. With the increasing infection of COVID-19, FDA kept close contact and cooperation with pharmaceutical manufacturers and gave full play to the important role of pharmacists, published the information of drug shortage on the website, effectively alleviating the drug shortage in public health emergencies.

It can be seen that FDA's management of drug shortage is usually based on coordination and rarely takes administrative measures. Through the implementation of incentives and regulatory measures to optimize drug production and improve drug quality, FDA explores the monitoring and early warning mechanism, cooperating with various departments to seek new measures to solve drug shortages.

1.2 EU

EU defines drug shortage as that the existing or calculated drug demand is not enough to meet the needs of end users. At present, some European countries, such as Belgium, Italy, and France are short of drugs to varying degrees, including antibiotics, antipyretic and analgesic drugs and antitumor drugs, among which the shortage of anti-infection and

nervous system drugs is more serious. Up to now, the public data of European Medicines Agency (EMA) website shows that there are 21 drugs in persistent shortage, and 25 varieties have been solved.

The factors affecting the shortage of drugs in Europe include economy, commerce, production and supply chain. Economic challenges and austerity, drug price reduction and medical insurance expenditure reduction, international reference pricing, delayed payment and bidding directly determine the business decisions of all stakeholders in the pharmaceutical industry, thus aggravating the structural problem of drug shortage to some extent^[6]. In addition, the low market price has obviously reduced the incentive effect on the listing of new drugs. For example, due to market policies some products that have already been listed are not on sale in the market, including innovative drugs. Medical insurance and policies related to drug sales may lead to drug shortages, manufacturers streamlining production plants and processes, drug price inflexibility and supply chain compression also affect drug supply.

In Europe, the responsibility for avoiding shortages is shared by the EMA, the heads of pharmaceutical institutions and distributors. Article 81 of Directive 2001/83 states that drug Marketing Authorization Holders and distributors should ensure the appropriate and continuous supply of drugs to pharmacies and hospitals to meet the needs of patients^[7]. The European Association of Hospital Pharmacists (EAHP) began to investigate the shortage of drugs in 2012 because of the increasing difficulty in finding drugs. In 2019, EMA issued "Guidance on Detection and Notification of Shortages of Medicinal Products for Marketing Authorization Holders in the Union" and "Good Practice Guidance for Communication to the Public on Medicines Availability Issues", which laid the foundation for the improvement and coordination of drug reporting and communication in the EU. The guideline contains good communication practice cases that should be followed when sharing information on drug shortage with the public, patients and health care professionals. Besides, it emphasizes the need



for timely, accurate and up-to-date information on usability issues to ensure the continuity of care ^[8]. In 2022, EMA issued the announcement “Towards Better Prevention of Medicine Shortages in the EU”, which stipulated the main principles of drug shortage management from the perspectives of patients and medical institutions to support patients and health care professionals to organize the prevention and management of human drug shortages. In 2023, EMA announced the newly established solidarity mechanism of the Medicine Shortage Steering Group (MSSG), which was based on the informal setting during COVID-19. This voluntary mechanism enabled EU countries to support each other in the face of serious drug shortages.

Besides, EU has adopted more effective regulatory policies for drug manufacturers through regulations, established a monitoring and reporting system for drug shortages, and reported the shortages through manufacturers, pharmacists and hospitals. In order to realize supply diversification, EU work with all stakeholders to promote the production of key drugs and solve the fragility of the drug supply chain. Active measures have been taken from the aspects of organizational structure and policies to alleviate the shortage of drugs in EU, which have achieved results.

1.3 Canada

Canada defines drug shortage as the inability of manufacturers to meet the demand for drugs that have been approved in Canada ^[9].

Since 2017, in order to monitor the severity of drug shortage, Health Canada has asked manufacturers to report the situation of drug shortage, and issued a multi-stakeholder toolkit to clarify the reasons for the shortage and the management tools to increase the understanding and transparency of drug shortage. Previously, the data of drug shortage in Canada were not complete and reliable. The main reasons for the shortage of drugs in Canada include enterprises stopping production, single supplier and low profit in the drug market. Shortages are more likely to occur

when drug prescriptions and production processes are complicated. According to the report of drug shortage in Canada, at present, the third-class drug shortage has the most serious impact, and there are 33 kinds of drugs classified into third-class shortage varieties.

According to the drug supply chain, Canada divides the drug shortage into four stages for research and management. The possibility of drug shortage in the stage of drug approval is low. At this stage, the impact of drug shortage is mainly reduced through drug product database (DPD), accelerated review procedure and special access procedure (SAP) ^[10]. In the production stage, the factors affecting the shortage include the reduction and shutdown of manufacturers, the shortage of raw materials produced internationally and the delay in import and export caused by inconsistent supervision. Therefore, in the production stage, the toolkit issued by Canada involves multi-stakeholders. Some corresponding measures are put forward for the government and production enterprises from the aspects of supervision and compliance. At this stage, the rights and responsibilities of stakeholders are clearly defined, and drug production enterprises are required to provide accurate drug shortage information on the monitoring platform in time.

In the procurement and distribution stage, the reasons for drug shortage are concentrated in exclusive procurement and inventory management. Therefore, it is vital to guide planned drug buyers, centralized procurement organizations and organizations that have contractual agreements with drug manufacturers to reduce the procurement of exclusive varieties or exclusive production enterprises. Besides, it should formulate emergency plans, and continuously weaken dependence on exclusive and single suppliers. These methods include centralized price negotiation, market research in case of shortage and cooperation among stakeholders. The joint cooperation of all departments in the supply chain should be strengthened with terminal timely delivery. At the same time, pharmacists are encouraged to seek substitutes for medicines in short supply.



When delivering drugs to medical institutions or patients, the shortage of drugs in medical institutions and uneven geographical distribution may affect the accessibility of drugs for patients. At this stage, Canada pays attention to the role of pharmacists, regularly evaluates the drug situation, calculates and controls the inventory quantity, strengthens the use of alternative drugs to solve the temporary drug shortage by using combined strategies.

It can be seen that the management of drug shortages in Canada tends to be mature, and it actively cooperates with all parties to formulate more accurate and targeted strategies to alleviate drug shortage problem.

2 Current situation of drug shortage in China

China standardized the definition of drug shortage for the first time in the “Measures for the Administration of National List of Shorted Drugs (Trial)” (hereinafter referred to as the Measures), which refers to drugs that are clinically necessary and

irreplaceable or cannot be completely replaced and have insufficient or unstable supply in a certain period of time or in a certain region [11].

In the past few years, China experienced a shortage of various drugs, including the national list of essential drugs and emergency drugs. In order to solve the supply problem of “low-priced drugs” “life-saving drugs” and “orphan drugs”, in 2020, the National Health Commission issued the “Notice on Printing and Distributing the National List of Drugs in Shortage (Trial)”, and monitored the shortage of drugs from the aspects of production supply and clinical use. There were 6 kinds of drugs in the national shortage list this time, the dosage forms and indications are shown in Table 1. There are 57 national key monitoring varieties of clinically necessary drugs that are easily in short supply, which are mainly used for major diseases, emergency rescue, women and children’s specialties, public health and other fields, and injections used by medical institutions [12]. Since the number of manufacturers of these varieties is small, the clinical demand is small and uncertain.

Table 1 Dosage forms and indications of drugs in short supply in China

| Drug name | Dosage form | Indication |
|-------------------------------|-------------|--|
| Amethopterin | Injection | Anti-tumor, high-dose therapy, psoriasis chemotherapy |
| Posterior pituitary injection | Injection | Used for postpartum hemorrhage, pulmonary hemorrhage and diabetes insipidus, etc. |
| Benzathine penicillin | Injection | Used for long-term administration of mild to moderate infection, rheumatic heart disease and rheumatic fever caused by sensitive bacteria |
| Mitoxantrone | Injection | Breast cancer, malignant lymphoma, gastrointestinal cancer, leukemia, bladder cancer, ovarian cancer, primary liver cancer, multiple myeloma and diffuse pleural mesothelioma (malignant mesothelioma) |
| Neostigmine | Injection | Used for myasthenia gravis and intestinal paralysis after abdominal surgery |
| Sodium hyposulfite | Injection | Used for cyanide, arsenic, mercury, lead, bismuth and iodine poisoning |

The published data of drug shortage in some provinces and cities are shown in Table 2. At present, the shortage at the provincial level coexists with the shortage at the national level. Common drugs in most provinces and cities are in short, and fewer varieties of drugs are in short at the national level. The shortage of

clinical drugs in Jiangsu and Tianjin is more serious. The shortage of drugs is mainly concentrated in low-priced drugs, clinically necessary drugs (antibacterial agents, cardiovascular drugs, digestive system drugs, hormone endocrine drugs and psychotherapy drugs) and national essential drugs.



Table 2 Public data of drug shortage in some provinces and cities in China

| Province | National shortage list | National key monitoring varieties of clinically necessary drugs in short |
|----------|------------------------|--|
| Sichuan | 1 | 6 |
| Liaoning | 7 | 10 |
| Jiangsu | 7 | 31 |
| Tianjin | 14 | 67 |
| Shanxi | 4 | 7 |

The reasons for the inclusion of the six varieties announced in the national shortage list of drugs in short supply mainly include the shortage of raw materials, the low willingness to produce caused by the low price of drugs, and the lack of supply in local

areas. For emergency drugs, weak demand, low price and improper inventory management can lead to their shortage^[13]. From the perspective of drug supply chain, the reasons for drug shortage in China are summarized as shown in Table 3.

Table 3 Causes of drug shortage in China

| Supply chain link | Shortage factors |
|-------------------|---|
| Production link | Low willingness to produce low-priced drugs, shortage of raw materials, streamlining or stopping production in enterprises, and unsatisfactory GMP in enterprises |
| Circulation link | The low distribution capacity in remote areas, the vague supply and demand information, the monopoly of enterprises drives up the drug price |
| Use link | Drug discontinuation or recall, improper inventory management in medical institutions |

3 Problems of drug shortage in China

In recent years, China has taken some active measures to deal with these problems, including drug prices, production, import and export policies, monitoring and early warning. For example, pharmaceutical companies are allowed to decide the price of drugs purchased by pilot projects. Besides, production is strengthened by collecting drugs and encouraging the establishment of drug production bases with few substitutes and unstable supply. Some urgently needed drugs are imported by improving the relevant laws and regulations on drug import. Lastly, the supervision of drug use in medical institutions should be strengthened and essential drugs should be given priority to the purchase^[14].

However, there are still some problems in the implementation of drug shortage management in China, such as decentralized management, weak systematic policy, lack of a clearer division between provincial and national shortages. In addition, there

are decentralized supervision and management departments in all links. The transparency and public sharing of the shortage data reporting platform are low, and patients and medical staff have few channels to obtain drug shortage information. Most of the data are only available for inquiry and uploading by production enterprises. In public health emergencies, a complete emergency management system for drugs in short supply has not yet been formed. Besides, improper inventory management and failure to find alternative drugs for patients in time have aggravated the severity of the shortage.

4 Suggestions

Through the comparative study of drug shortage management at home and abroad, it is found that China started the management late, the policy implementation time is short, and the experience is insufficient. There are still some weaknesses in the implementation process. However, drug shortage



is a problem that needs to be dealt with for a long time. Learning from the international experience in managing drug shortage is conducive to improving China's drug supply system.

4.1 Strengthening the cooperation and consultation among stakeholders

These western countries pay attention to multi-party cooperation and consultation when dealing with drug shortage, and reform the supply chain involved in the whole life cycle of drugs. China should strengthen the communication among manufacturers, wholesalers and hospitals. Since wholesalers are the link between manufacturers and hospitals, they have the responsibility to strengthen the communication among the key parties in the supply chain. At the same time, the working group on drug shortage should strengthen the efficiency of coordinating the work of various departments, rationally allocate powers and responsibilities, build a platform for information exchange on drug shortage, which can improve the efficiency of joint law enforcement.

4.2 Increasing the transparency of drug shortage data disclosure

Judging from the channels of querying drug shortage data in EU and the United States, it has a more open and transparent data publishing platform than that in China. Besides, their data is updated in time with a wide coverage. At present, only some provinces and cities in China disclose the variety and quantity of drug shortage, and it is scarce to make national statistics on drug shortage data. Therefore, it is vital to increase the transparency of drug shortage data. A drug shortage information website and drug database led and managed by the drug shortage supervision department should be established, which can release the information of shortage varieties reported by hospitals or enterprises in real time. Besides, the channels for the public to inquire about drug shortage data should be broadened. It can not only protect the

public's right to know, but also alleviate the public's anxiety caused by the unavailability of drugs after the shortage.

4.3 Paying attention to the important role of pharmacists

Pharmacists provide patients with the most evidence-based drugs during public health emergencies, which shortens the time for clinical improvement of patients, optimizes the overall treatment with drugs, and avoids inappropriate prescriptions and drug hoarding. In addition, the guidelines published by the American Society of Health-System Pharmacists also encourage pharmacists to cooperate on a global scale, share the experience of strategies to alleviate drug shortages and the overall innovation related to academic, institutional and community pharmaceutical practice during the pandemic. Pharmacists can evaluate and switch to alternative generic drugs when they face drug shortages. Therefore, China should pay attention to the important role of pharmacists. Professional training for pharmacists must be strengthened, and the role of pharmacists in drug management should be given full play.

5 Conclusion

Ensuring drug supply is as important as ensuring the safety and effectiveness of drugs. The situation of drug shortage varies from country to country, but the management is the same. The reasons of drug shortage in China mainly include such factors as market, production, import and export policies. In the management of drug shortage, drawing lessons from international experience is necessary. Our government should call on all stakeholders to work together to formulate reasonable strategies to prevent drug shortages. Giving full play to the important role of pharmacists, strengthening cooperation and close contact among all parties, enhancing the openness and transparency of drug shortage data can ensure the safety of drug supply.



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