

Risk Assessment and Management of Drug Inventory in Hospitals during COVID-19 Pandemic in Taiwan

Li-Yao Lee

Kaohsiung Medical University Hospital

Ying-Hao Lu (✉ yhlu@kmuh.org.tw)

Kaohsiung Medical University Hospital <https://orcid.org/0000-0002-5885-4469>

Ya-Ling Wang

Kaohsiung Medical University Chung Ho Memorial Hospital

Mei-Chen Chen

Kaohsiung Medical University Chung Ho Memorial Hospital

Deng-Chiung Shih

Kaohsiung Medical University Chung Ho Memorial Hospital

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Abstract

Background

The COVID-19 pandemic has caused the suspension of active pharmaceutical ingredients (APIs) production in China, the source of the global largest medication supply chain, resulting in the potential risks of hospital insufficient drug stocks affecting clinical treatment. If all drug inventory of the hospital increased, the short-term drug shortage risk can be reduced, but the inventory costs will be increased. Therefore, the purpose of this study is to establish a risk assessment mechanism for inventory management of APIs from China, to identify the medical priorities affected by drug shortages, and to plan different countermeasures to achieve the best effect of inventory management.

Methods

In this study, the tables of "Incidence of Drug Shortage" and "Impact Level of Drug Shortage" related to the risk of drug inventory were developed, which were evaluated in four levels respectively, and "Drug Shortage Risk Assessment Matrix" was designed according to the probability of drug shortage and impact according to the model data of Reproductive Number (R_0) value and pandemic prediction. Each drug requiring APIs from China was evaluated and ranked according to the hazard index, so as to increase the different inventory and to find alternatives.

Results

We have evaluated the inventory risk level of drugs requiring APIs from China through the risk assessment mechanism, and increased the different backup stock according to the levels. The total increasing purchase amount was NTD 4.85 million, which could reduce the stock cost by about 2/3 compared with NTD 14.61 million of the total inventories for three months.

Conclusions

The study shows that there are significant differences between scientific inventory management and general method during COVID-19 pandemic. It can provide a reliable reference for other hospitals to adjust drug stocks in the face of other emerging infectious diseases or major emergencies by using the innovative mechanism.

Background

Medications are indispensable in the treatment of diseases, so the stable medication supply is the core of drug inventory management in hospitals. Joint Commission International (JCI) conducted a document review and field visit on the medication supply chain in order to ensure the quality and safety of

medication for patients [1]. The source of the medication supply chain is active pharmaceutical ingredients (APIs). However, due to factors such as weather (earthquake, hurricane and other disasters) and human factors (strikes, capital turnover, etc.), the production of APIs will be affected. As a result, pharmaceutical factories have no raw materials to produce drugs, and therefore cannot support drugs to medical institutions.

According to the U.S. Food and Drug Administration (FDA), a total of 1,079 factories in the world can produce 370 essential medicines listed by the World Health Organization (WHO), 166 of which are located in China (15%) [2]. However, in terms of production capacity, China and India are the major suppliers of APIs in the world, and 70% of the APIs in India pharmaceutical factories come from China [3]. Therefore, China is the main supplier of APIs in the global pharmaceutical industries, providing key raw materials for drugs such as antibiotics, diabetes drugs, analgesics and antiretroviral drugs. In early 2020, due to the continuous spread of the SARS-CoV-2 virus in China, China implemented large-scale lockdown and traffic restriction, and many factories in some cities (such as Wuhan and Zhejiang) were shut down. As a result of the Covid-19 pandemic, it has a great impact on the supply of medicines in the global pharmaceutical industries and increases the risk of global chain broken. It also puts the Hospital to be taken to prepare and handle drug shortages [4, 5].

During the COVID 19 pandemic, our APIs from China are at the greatest risk of supply disruption. The Hospital has a total of 90 APIs supplied by China. If the inventory of all these APIs is increased for three months, the inventory cost will be increased by about NTD 14.61 million (14,607,340). An undifferentiated increase in the stock of these drugs would certainly reduce the risk of a short-term drug shortage, but it will significantly increase the inventory space and cost, so it is not the most suitable inventory management measure. Therefore, the purpose of this study is to establish a risk assessment mechanism to identify the medical priorities affected by drug shortage during the outbreak of COVID-19 in China, so as to individually increase the inventory days of different stocks to achieve the best effect of inventory management.

Methods

1. Assessment of the Severity and Duration of COVID-19 Pandemic

Before exploring how to assess drug supply risks, it is important to know how long the COVID-19 pandemic may last. The Basic Reproductive Number (R_0) is an important indicator of the severity of Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). $R_0 > 1$ means that the number of infected people may increase; $R_0 < 1$ means the spread of the pandemic is likely to disappear. The research results show that the COVID-19 pandemic in Wuhan, China has an R_0 value of 2.68, which indicates that COVID-19 is difficult to control in a short period of time [6]. In addition, a recent study published in The Lancet mentioned that the COVID-19 pandemic would peak around April 2020,

and then slow down after May until the pandemic was under control in June [7]. Therefore, under the pressure of inventory costs, the stock of drugs should be limited to three months at most.

In addition, the worst-affected region of this outbreak is Wuhan, China, and many raw material and pharmaceutical factories are located in Hubei Province and Zhejiang Province. Therefore, it was conducted among drug suppliers required to reply whether the raw materials of their drugs came from China or not, and whether there might be drug shortage within three months.

2. Risk Assessment Mechanism of Drug Inventory

In this study, Table 1 and Table 2 were developed for the "Incidence of Drug Shortage" and the "Impact Level of Drug Shortage". In Table 1, the probability of drug shortage is divided into four categories (Frequent, Occasionally, Uncommon and Remote), and the drug supplier's prediction of stock shortage within three months and the frequency of stock shortage are used as the evaluation criteria. In Table 2, the impact level of drug shortage is evaluated in three aspects, and the average monthly dosage of the drug is one of them. High amount was defined as above the monthly mean of each pharmaceutical form: (1) more than 18,000 oral tablets, (2) more than 880 injections, and (3) more than 600 for drug of external use. In addition, the availability of an alternative drug with the same ingredient and whether the drug shortage is widely reported by the official sources, such as FDA or EMA are the two other criteria. The cases with three of the evaluation criteria were listed as Serious (level 4); the cases with two of three were listed as Severe (level 3); the cases with one of them were listed as Medium (level 2); the cases with none of three were listed as Light (level 1). In addition, according to the probability and the impact level of drug shortage, "Drug Shortage Risk Assessment Matrix" (Table 3) was designed [8]. According to the research prediction from The Lancet and the reference of R_0 value (2.68) of Wuhan, China, the pandemic will last for up to three months.^{4, 5} Therefore, taking the backup inventory days of 12 weeks (three months) as the upper limit, the drug at Levels 13 to 16 of the hazard index in the risk assessment matrix should increase the backup stock of 12 weeks; nine weeks for Levels 9 to 12; six weeks for levels 5 to 8; three weeks for levels 1 to 4. Finally, according to the hazard index ranking of the risk assessment result of each drug, the action strategies of increasing the backup stock of different weeks and searching for alternatives were carried out.

Results

After importing 90 drugs with raw materials from China into the risk assessment model of drug inventory designed in this study, it was found that the risk assessment level of none of the drugs was within the range of 12-week backup stock according to the risk matrix ranking. The total cost of drug purchase increased by NTD 4.85 million (4,851,501) based on the number of additional orders for each drug after evaluation. The data of evaluation are shown in Table 4 (see Appendix for details). According to the model analysis of this study, it is found that most drugs (about 67.8%) only need an increasing stock of three weeks. 22.2% of the drugs need an increasing stock of six weeks. Only 10.0% of the drugs need an increasing stock of nine weeks and there are no drug needs to increase stock of 12 weeks (three months).

According to the results of the reply of the drug supplier on March 8, 2020, there were 90 drugs with raw materials from China, among which four drugs (Penicillin G injection/high dosage for 10MU, Vancomycin injection, Urea ointment and Epinephrine injection) were at risk of drug shortage within three months. Therefore, the Hospital immediately started to find alternative drugs with the same ingredients. We have found a stable supplier of alternative drugs with the same ingredients as Vancomycin injection, Urea ointment and Epinephrine injection. However, only this pharmaceutical factory (Taiwan YF Pharmaceutical Co., Ltd) in Taiwan produces Penicillin G injection, so we informed the clinicians to prescribe other drugs for treatment.

Discussion

The COVID-19 pandemic affected the stable supply and demand for drugs in the Hospital. For example, to cope with the pandemic situation, an increased cost of NTD 14.61 million would be required an increasing stock of three months for 90 drugs that require APIs from China. In this study, it is important to notice that no drug needs an increasing stock of 12 weeks. Therefore, according to the risk assessment level of each drug, it only needs to increase the purchase amount by NTD 4.85 million, which can reduce the inventory cost by 2/3 (66.8%). The results show that there are significant differences between scientific structured inventory management and general method.

In addition, R_0 is used to assess the severity and continuity of most infectious diseases, and the R_0 value varies at different times and locations. Therefore, the R_0 value in the middle (pharmaceutical production) and upper (raw material production) reaches of drug supply is closely related to the stability of the medication supply chain. In this study, the drug inventory was considered to be positively correlated with the R_0 value, so the R_0 value was taken into account in the risk assessment. Therefore, if the R_0 value varies, the backup stock of drugs will be adjusted simultaneously. However, there is no mathematical equation for the relationship between R_0 and backup stock of drugs. In the future, the mathematical model on the number of days of backup stock based on R_0 can be established for the situation of COVID-19 or other pandemic emerging infectious diseases.

Most of the potential drug shortage risks are difficult to detect when they do not occur. To predict the potential impact of drug shortage depends on the sensitivity and attention of the drug supervisor to the risk of drug shortage, as well as their accumulation of experience in the event of drug shortage. Therefore, the daily management of drug shortage risks can help to cope with more unpredictable drug supply problems. The following three daily management mechanisms can be used as a reference for other hospitals.

(1) Monitoring of the information on the medication shortages in real time

Due to the development of network information, the information about the shortage of APIs in the global drug market, contamination in the drug manufacturing process or defective products spread on the

Internet more quickly than ten years ago. Hospitals can establish a real-time monitoring mechanism of the medication supply chain to collect data. For example, it is to regularly update news about the international supply shortage, such as the substantial increase in the cost of blood preparation caused by the infection of bovine blood or the impact of African swine fever on the production process of Heparin in China. Only with real-time and sufficient information, hospitals can seek early response plans to resolve drug shortages [9].

(2) Principle of decentralized drug procurement

Based on the principle of risk spreading, even if a certain drug supplier has a complete range of drugs and the price is cheap, the hospital should not be centralized procurement from the manufacturer, it is advisable for the hospital to purchase different kinds of drugs from several drug suppliers instead of a single supplier to reduce the risk of drug shortage. In addition, when drugs with unstable supply are detected, other alternative suppliers should be found immediately. Take Hydroxychloroquine (formerly used to treat malaria and immunomodulators) which can be used for emergency treatment COVID-19 announced by FDA as an example [10], after the announcement, a large number of orders have been made from various countries and hospitals, resulting in the unstable supply of the drug. To avoid the impact caused by drug shortage, the Hospital purchased Hydroxychloroquine from another drug supplier for standby. Although purchasing drugs with the same ingredient from different suppliers increases the management cost, it can reduce the clinical treatment impact caused by the inability to supply of a single supplier.

(3) Contract management of low-alternative drugs

Low-alternative drugs can be listed through a comprehensive review of the standing drugs of the hospital. The definition of low-alternative drugs is that (1) drugs that must be used for clinical treatment such as Heparin and Digoxin; (2) exclusive drugs in the drug market, such as the Glypressin® (Terlipressin) for esophageal variceal bleeding, and the anticancer drug, Alkeran® (Melphalan). With regard to low-alternative drugs, we should not only take the price as the basis for judging whether to purchase or not, but also fully evaluate the supply status and raw material source of the drug supplier in the procurement negotiation, and we should sign a continuous supply contract, which can avoid or decrease the impact of the shortage. In addition, we can also increase the safety days of inventory for low-alternative drugs to avoid the impact of the short-term drug shortage.

Conclusion

In view of the potential shortage crisis of drugs with raw materials from China during the COVID-19 pandemic, this study has detected the risk level of the drugs from China in the inventory management of the Hospital through the risk assessment mechanism, and ordered the drugs for the backup stock of different weeks according to the level, so as to effectively reduce the risk of drug disruption, achieve the best cost-effectiveness of inventory management and ensure the quality and safety of patients' medication. At the beginning of the study in February 2020, the outbreak of COVID-19 was limited to

China, but since March 2020, the outbreak has spread to the whole world, so the supply of raw materials is no longer a single regional problem. Therefore, based on the theoretical framework and experience of this study, we can fully explore all the drugs (about 1,300 items) in the hospital in the future, so as to find the best inventory management benefits. Finally, it is hoped that this study will provide a complete and reliable reference for other medical institutions or health authorities to adjust drug stocks in the face of other emerging infectious diseases or major emergencies by using the innovative methods and thinking of drug inventory risk assessment during the COVID-19 pandemic.

Abbreviations

APIs:active pharmaceutical ingredients;NTD: New Taiwan Dollar;FDA:Food and Drug Administration;WHO:World Health Organization;R0:Basic Reproductive Number;EMA:European Medicine Agency

Declarations

Ethics approval and consent to participate

Because this study did not involve the data of human subjects, the need for ethics approval and consent was waived by the IRB of Kaohsiung Medical University Hospital.

Consent for publication

Not applicable.

Availability of data and material

The data that support the findings of this study are available from the HIS of Kaohsiung Medical University Hospital.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LYL and YHL contributed equally to the conception and design of the work and to write the manuscript. YLW, MCC and DCS contributed in the literature review and collecting and analysis of the data/information. All authors have read and approved the final manuscript.

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Tables

Table 1 Incidence of Drug Shortage

Probability (P)

Classification	Score	Definition	Evaluation standard
Frequent	4	It is expected to happen again or several times a year in a short period of time.	<ol style="list-style-type: none"> The drug supplier replies that it will be out of stock within three months. One time of shortage in two years.
Occasional	3	It is likely to happen again or several times in one to two years.	<ol style="list-style-type: none"> The drug supplier replies that it will not be out of stock within three months. Over two times of shortage in three years.
Uncommon	2	In some cases, it may happen again or once two to five years.	<ol style="list-style-type: none"> The drug supplier replies that it will not be out of stock within three months. More than one time of shortage in three years.
Remote	1	It happens rarely, only in certain situations or once in 5 to 30 years.	<ol style="list-style-type: none"> The drug supplier replies that it will not be out of stock for three months. No shortage record in three years.

Table 2. Classification of Impact Level of Drug Shortage

Impact (I)

Level	Grade	(1) High amount	(2) No alternatives with the same ingredient	(3) News events	Evaluation standard
Serious	4	*	*	*	All the three items
Severe	3	*	*	*	Two of them
		*	*	*	
Medium	2	*	*	*	One of them
		*	*	*	
Light	1				None

Table 3. Drug Shortage Risk Assessment Matrix

Risk assessment (P*I)

Probability (P)	4	4	8	12	16
	3	3	6	9	12
	2	2	4	6	8
	1	1	2	3	4
		1	2	3	4
		Impact (I)			

Table 4. Results of Risk Assessment and Action Strategies

Risk assessment (P*I)	Number of items	Proportion (%)	(1) Increased backup stock		(2) Alternatives
			Increased weeks	Increased inventory cost (NTD)	
13~16	0	0%	X	0	X
9~12	9	10%	9 weeks	919,407	2
5~8	20	22.2%	6 weeks	1,654,742	2
1~4	61	67.8%	3 weeks	2,277,352	X

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