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Shortage of perioperative supplies and drugs: Theory and practical implications

Desabastecimiento de insumos y medicamentos de uso perioperatorio: teoría e implicaciones prácticas

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Abstract

During the past three decades the world has been witness to an alarming increase in the shortage of drugs and biomedical products in the field of anesthesia and surgical care. This situation can be particularly challenging when there are no therapeutic alternatives available, as is the case with some supplies and drugs for perioperative use. Anesthesiologists, who play a crucial role in the preparation of the drugs they administer, are particularly aware of these shortages. The reasons for these shortages are diverse and involve problems in supply, demand and government regulation. Among the causes identified are the increase in demand, bidding systems and the sustainability challenges faced by pharmaceutical companies. It is essential to understand these causes in order to seek strategies to reduce the risk of shortages of medicines and supplies. Addressing this challenge requires improving supply chain management, fostering transparency in information on stock-outs, promoting local production of medicines, and strengthening procurement and distribution regulations and policies. The solution to this problem requires a comprehensive and collaborative approach, with multiple stakeholders working together to ensure adequate access to needed medications in the anesthesia and surgical care setting.

Key words: Anesthesia; Analgesia; Resource shortage for health; Economics, pharmaceutical; Equipment and supplies; Drugs, generic; Intellectual property of pharmaceutical products and process.

Resumen

Durante las últimas tres décadas, en el mundo se ha observado un alarmante aumento en el desabastecimiento de medicamentos y productos biomédicos en el ámbito de la atención anestésica y quirúrgica. Esta situación puede resultar especialmente problemática cuando no existen alternativas terapéuticas disponibles, como ocurre en algunos casos de insumos y medicamentos de uso perioperatorio. Los anestesiólogos, quienes desempeñan un papel crucial en la preparación de los medicamentos que administran, son particularmente conscientes de estos fenómenos de desabastecimiento. Las causas de estos desabastecimientos son diversas e involucran problemas en la oferta, la demanda y la regulación estatal. Entre las causas identificadas se encuentran el aumento en la demanda, los sistemas de licitación y los desafíos de sostenibilidad que enfrentan las empresas farmacéuticas. Es fundamental comprender estas causas para buscar estrategias que reduzcan el riesgo de desabastecimiento de medicamentos e insumos. Para abordar este desafío se requiere mejorar la gestión de la cadena de suministro, fomentar la transparencia en la información sobre desabastecimientos, promover la producción local de medicamentos y fortalecer las regulaciones y políticas de adquisición y distribución. La solución a este problema exige un enfoque integral y colaborativo, en el que múltiples partes interesadas trabajen conjuntamente para garantizar un acceso adecuado a los medicamentos necesarios en el ámbito de la atención anestésica y quirúrgica.

Palabras clave: Anestesia; Analgesia; Escasez de recursos para la salud; Economía farmacéutica; Equipos y suministros; Medicamentos genéricos; Propiedad intelectual de productos y procesos farmacéuticos.

INTRODUCTION

Over the past 30 years, medical and surgical care has endured significant consequences as a result of the shortage of medicines and other biomedical products. (1-3) Drug shortages can have a reduced impact on healthcare when it comes to drugs with limited indications and suitable therapeutic options available. However, their impact may be significant on public health, especially in the case of drugs such as vaccines or when there are no alternative therapeutic options. Anesthesiologists, who frequently prepare the drugs they administer, are particularly aware of stockouts when they occur. (4) Determining a single cause responsible for drug shortages is often difficult due to the interaction of the different stages of the production and distribution process, which may contribute concurrently to the problem. (5) The purpose of this review is to analyze and summarize the current scientific literature on shortages of medications and supplies for perioperative use, delivering a detailed theoretical vision and exploring the practical implications resulting from this issue.

CONTEXT

Shortages and stockouts

Shortages and stockouts are two fundamental economic concepts. Shortages refers to the fact that limited resources are insufficient to meet the needs or the demands of the people (which are unlimited). In contrast, stockout or lack of supply refers to a situation in which the market demand exceeds the availability of products at a particular point in time. (6)

There are so-called "free resources" of which there is such a quantity that they will always be available; the classic example is air. These free resources may, however, one day become scarce, as has been the case with land for cultivation; these resources are called economic resources. The characteristic of economic resources is

that they are scarce for the needs of human beings and therefore have alternative uses from which to choose: they have an opportunity cost. (7). It is usual to use the term shortage to describe the reality that resources are not enough to satisfy all needs, one of these resources is time. (8)

When the supply of a product is equal to its demand, that is, when at a certain price (called the market equilibrium price) there are no suppliers willing to sell at a lower price and no buyers willing to pay a higher price, there is no shortage. All those willing to pay the market price have access to the product or service they need. (6)

Criteria for defining shortages

In the medical scientific field, the lack of a standardized definition for shortages and stockouts is evident. This shortcoming results in variability in the definitions used by different regulatory authorities. Some of these authorities approach drug shortages from a supply perspective, while others consider them from a demand perspective. Additionally, some authorities define shortages with regards to its position within the drug supply chain, either due to a lack of supply or an increase in demand. On the other hand, some definitions are time-based or depend on the duration of the shortage, such as the inability to supply a drug to a patient within a specific time frame. Moreover, there are some authorities that adopt a definition in accordance to its position in the medications chain of supply, whether because of shortage in supplies or increased demand. On the other hand, some definitions are based on time or the duration of the shortage, such as the inability to deliver a drug to a patient within a specific time frame. (3,9). Minor variations in this definitions have important implications on the way the medication shortages index is estimated. Such discrepancies arising from the different criteria and methods used to evaluate the availability of medications result in wide range of results obtained. (3)

The pharmaceutical industry

The aspects that describe the business model of the pharmaceutical industry have been characterized. (10) The pharmaceutical and medical supply industry is no different in its objectives from other industries in the economy that must be accountable to their stakeholders. (11) With the exception of the giant Chinese state-owned company Sinopharm, the world's largest pharmaceutical companies are private, for-profit and publicly traded. (12) In this respect, the pharmaceutical industry is no different from, for example, the microprocessor industry, with similar issues of dependence on innovation, high costs, global competition, variable demand, and supply and logistics challenges. (13)

An important difference is that, since these products are associated with something as sensitive as health, their relationship with the State is different from that of other industries, and this is where a large part of both their sources of profit and their problems lie, including issues leading to shortages. (13) In order to stimulate research and production of new drugs and medical supplies, States allow pharmaceutical companies to maintain an artificial monopoly for a few years through patents. The purpose of this is that the possibility of high profitability resulting from these monopolies will encourage companies to innovate. (14,15)

But, on the other hand, the monopolistic position is of concern to governments, which see high prices, not subject to competition, as an unfair impediment to access to medicines and supplies. For this reason, it is common for price control laws to be established or for governments to act as a buyer with a dominant position, able to enforce their conditions on pharmaceutical companies. (16)

Opportunity cost

Performing any activity always entails the cost (not necessarily economic, but no less

real) of not doing another activity (7). This cost is called opportunity cost (forgone benefit that would have been derived from an option other than the one that was chosen) and this explains why making a choice is difficult. Moreover, even if it is not always visible, using resources for one thing implies not using them for something else. Resources are scarce for the existing needs, and this leads us to the need to choose. (8)

The problem is that there are multiple, partially conflicting objectives. Ideally, society would like innovative, completely effective, always available, totally safe and very low-cost drugs. These objectives cannot be met simultaneously, so it is necessary to choose what to compromise on and how far to go. Possibly, always having all drugs and medical supplies available to everyone would be possible if one were willing to bear the cost. This cost has to be paid by the individual patient or by society as a whole through the health system, but this implies allocating fewer resources to other needs. However, this cost is often so high that no society is willing to take it on.

Price control

A special situation arises when there is price control; i.e., when market prices are fixed by government regulation at a lower level than they would be in the equilibrium of supply and demand. Controlled prices affect the supply side by removing from the market those suppliers with costs higher than the controlled price, since under these conditions they experience losses, which leads to a lower supply than would otherwise be the case. On the demand side, demand increases when there are lower prices. (17)

The combination of these two reactions, lower supply and higher demand, leads to shortages: there is no product available for those who are willing to pay the controlled prices. This shortage leads to bizarre behaviors that aggravate the problem: hoarding, excess inventories, black market, corruption and waste (18). Hoarding,

because sellers prefer not to offer (at these low prices) their merchandise; hoarding, because consumers try to protect themselves against future shortages; black market and corruption, because of the possible extraordinary profits; and waste, because the lower price causes resources to be used in activities for which they were not really needed. (18)

Necessary products

It is common knowledge that the higher the price of a product, the less quantity of it will be purchased. There are, however, products such as drugs for which demand is less sensitive to price, i.e. increasing the price only slightly reduces consumption. (19)

The combination of monopoly and high demand products leads to a special situation, since there are practically no barriers to price increases. Neither competition from other producers nor substitutes allow price regulation. This is where governments intervene again, either by setting price controls or by exercising their great purchasing power. (20)

Industry reaction

This being the case, the pharmaceutical industry, as would be the case for any other industry or even an individual, will look for ways to lower its costs or increase its sales in order to achieve the profitability necessary to survive. These strategies involve: 1) going to political bodies (lobbying) with the purpose of extending the validity of the; 2) increasing the duration of patents; 3) doing research only on diseases of rich or numerous populations; 4) reducing the suppliers costs; 5) centralizing production; 6) downsizing inventories. All of these practices jeopardize product availability; or, in other words, all of the practices necessary to increase availability involve increasing the cost and, consequently, the price. (21)

For the practicing physician these problems do not make any sense; a patient

who needs a drug or a medical device must have it regardless of the cost. (13) It is how it should be and how we want it to be if you are the patient. (22)

Perspectives on the perioperative context

In the surgical area, an increased demand for surgical services is expected in the medium and long term. More than 300 million surgical procedures were conducted around the world in 2012. (23) According to the data collected from Individual Healthcare Services Records (RIPS), it has been estimated that in 2016 in Colombia, approximately 1.4 million surgeries were conducted in operating rooms. This represents between 2,690 and 3,090 procedures per every 100,000 inhabitants. This number is below the goal established by the Lancet Commission which requires an increase in the volume of surgeries of 5,000 surgical interventions per every 100,000 inhabitants for 2030. (24)

Causes of shortages of supplies and medications

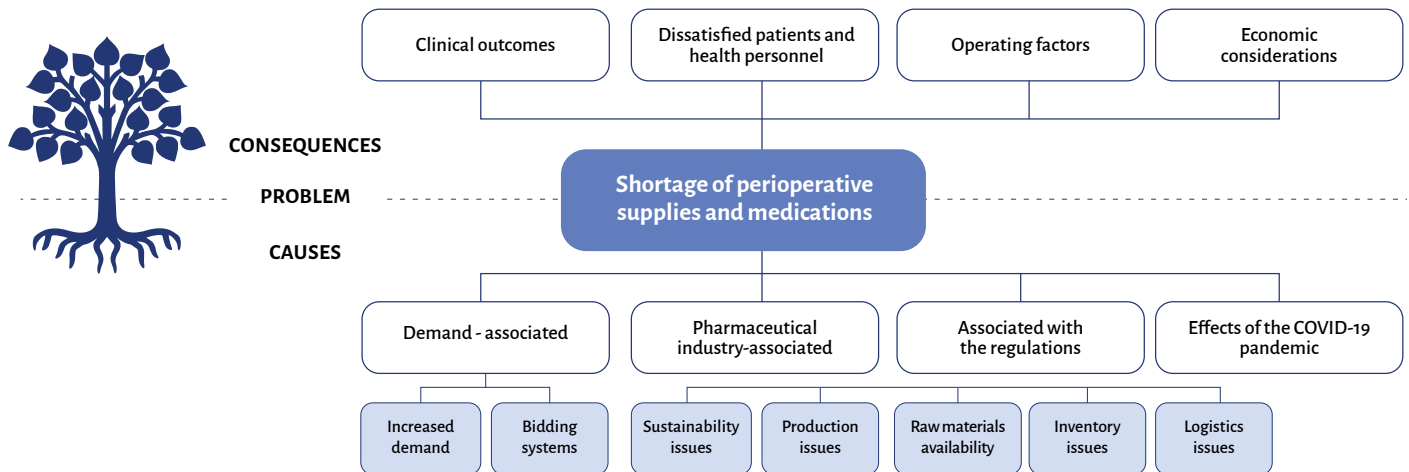
It is important to understand the causes in order to find a solution to lower the risk of shortages of medicines or supplies (Figure 1). Overall, the lack of availability of medicines may be attributed to several factors that may be classified into: 1) supply issues, 2) demand issues, or 3) regulatory issues.

CAUSES ASSOCIATED WITH THE DEMAND

Increased demand

The problems associated with the demand comprise both the epidemic and seasonal demand, and may be both predictable and unpredictable. A properly established system is capable of foreseeing the average

Figure 1. "Problem Tree" diagram.



The analysis of the shortage of perioperative supplies and medications was conducted using the problem tree diagram, with a view to identifying the nature and the context of the problem. It is represented graphically where the key issue is in the trunk of the tree, the causes are distributed from the trunk to the roots, and the consequences are represented from the trunk to the branches. This visual approach facilitates the breakdown of the problem, the identification of its causes and the understanding of its impacts, hence improving the comprehensive analysis.

Source: Authors.

growth of the demand and any seasonal variations; however, outbreaks, epidemics and disasters are unpredictable situations. (25) Additionally, the irrational use of medications results in a waste of resources that generates a higher demand. (26) Other causes include the prescription practices and the unethical promotion of medicines by the pharmaceutical companies. (27)

Bidding systems

When a drug tender is awarded to a single supplier, there is a high risk of shortages, as any problem with that supplier can severely affect supply. In addition, the low price established through tenders has forced some manufacturers out of the market, resulting in decreased competition and higher prices. On the other hand, group procurement of drugs has also contributed to shortages, as it has altered the established purchasing pattern. (28)

Causes associated with the pharmaceutical industry

Drug supply difficulties refer to the inability or unwillingness of manufacturers to produce a sufficient quantity of drugs to meet the existing demand. (29)

Problems of sustainability of the companies

The shortage of generic drugs is mainly due to the relatively low market price, which makes it difficult for some manufacturers to compete against the established brands and modernize their infrastructures to meet the good manufacturing practices requirements. The lack of investment in industrial plants and inadequate maintenance of the facilities lead to inefficiency and lower the production capacity, which further contributes to the shortage of medications. (30)

Occasionally, companies decide to consolidate their manufacturing plants to minimize costs and obtain significant benefits. However, this consolidation leads to a reduction in the number of companies, which increases inflexibility in the supply chain and increases the risk of drug shortages. Inefficient procurement processes are also a common cause of shortages. (31)

Medications that have a small market, such as orphan drugs – including dantrolene – are particularly vulnerable to shortages, since manufacturers prefer to focus on higher demand products. (32,33)

Production Issues

In the pharmaceutical industry, priority conflicts arise when a manufacturer has the capacity to produce several products that compete with each other for resources such as raw materials, production lines

and markets. This scenario can influence manufacturers' motivation to invest in or produce drugs with lower profitability, such as generics and injectables. These drug categories require more stringent quality standards to be met during the manufacturing process, compared to those drugs that generate higher economic profits. (34)

Drug shortages are mainly attributed to quality problems in production, which are detected during quality control and post-manufacturing inspections, even after distribution to customers. These problems lead to the withdrawal of drugs from the market once they are discovered after launch. The causes of these problems include contaminating microorganisms, such as bacteria and fungi, endotoxins, disintegration of tablets, inclusion of foreign materials in the packaging, such as glass, metal or fiber, as well as the formation of precipitates or unexpected reactions between the products and the packaging used. (35)

Lack of availability of raw materials

Drug shortages can arise due to problems in the supply of essential raw materials for their manufacture, such as active pharmaceutical ingredients (APIs), excipients and packaging materials. The unavailability of these raw materials can be caused by a variety of factors. For example, there have been cases of drug shortages due to events such as Hurricane George in Puerto Rico in 1998 (36). India and China are recognized as the main suppliers of APIs in most economies. Therefore, it is considered desirable for a product to have at least three suppliers of raw materials to mitigate the associated risks. (37)

Inventory issues

Just-in-time inventory (JIT) is a management strategy that seeks to align raw materials or drugs provided by

suppliers directly with current scheduled requirements. In situations of budget constraints, stakeholders purchase a fixed amount of stock for a given period that only meets the immediate needs of the pharmacy or institution, without a back-up plan. This strategy is widely used to operate the system at minimal cost, but carries a higher risk of drug shortages due to the lack of safety stock in high-income countries. (38)

Logistics issues

Drug shortages can be attributed to logistical problems, including transportation difficulties and supply chain management deficiencies. Transportation challenges are often related to adverse weather conditions, traffic congestion and natural disasters. (32)

Long supply chains can represent a risk by making production chains more fragmented and less transparent, which can make it difficult to identify the source of drug production failures. (39)

Causes relating to legal regulation

Drug regulatory authorities play a key role in the effective regulation of medicines to ensure their quality, safety, efficacy and the accuracy of related information. However, one of the main regulatory challenges lies in the lack of a uniform definition, which creates gaps in assessing the severity of the problem and hinders mitigation strategies. (40) Additionally, there are several regulatory problems such as inflexibility of the regulatory processes, lack of clear policies and lack of effective communication among stakeholders. The implementation of new regulations, particularly with regards to Good Manufacturing Practices – GMP associated with the procurement and processing of raw materials, may cause delays in the production process and result in shortages of medications. (9)

Effects of the COVID-19 pandemic

Analgesics, sedatives, and paralytics were all out of stock due to their increased demand during the COVID-19 pandemic (41). When a single supplier provides both APIs and excipients for a product, any problems with that supplier can result in drug shortages. During the COVID-19 pandemic, a global shortage of APIs, excipients, and drugs was experienced as API-producing countries, such as India, China, and the United States, stopped supplying certain products to other nations. This resulted in a generalized shortage of many drugs worldwide. (42) Furthermore, the pandemic presented numerous additional challenges, such as packaging material shortages, transportation disruptions, shipment delays, customer delivery delays, and restrictions on the import and export of APIs and drugs globally. (43)

Consequences

The consequences of shortages of supplies and drugs in the surgical context are many and varied, as illustrated in Figure 1. The consequences can be categorized into the following domains: 1) clinical outcomes, 2) patient and health personnel dissatisfaction, 3) operational aspects, and 4) economic considerations.

Clinical results

Drug shortages have been extensively investigated and have been shown to lead to various adverse clinical consequences. Among these are alterations in treatment, medication errors, prolonged hospitalizations and an increase in the mortality rate (25). It is essential to highlight that the lack of critical drugs can result in the cancellation of surgeries. Insufficient supply of protamine sulfate can lead to the cancellation of cardiac surgery, which has negative consequences for the patient. Cancellation of surgery can

aggravate the condition, prolong hospital stay and increase the risk of nosocomial infections. (44)

Patient and health personnel dissatisfaction

Drug shortages have various consequences on the work of health professionals. Studies carried out in several countries have shown that this situation generates complaints, frustration, dissatisfaction and psychological effects on patients and on health care human resources. (35) In addition, physicians are faced with difficult decisions in selecting which patients will receive the limited available drugs or seek alternative therapies. These shortages are especially critical for cancer patients, and health care professionals are challenged with increased levels of stress and frustration. (45) Drug shortages also affect patients' confidence in hospitals and raise concerns about the possible effects of alternative therapies. (46)

Operating aspects

Although initially described in the context of centrally controlled economies, János Kornai has proposed a theory that is useful in describing the different possibilities faced by buyers in the context of a shortage. The normal situation, according to Kornai, is that the buyer finds the product he wants and buys it (scenario 0). However, in a shortage scenario this situation rarely occurs. The other possibilities described by Kornai are: queuing up to buy the product (scenario 1), accepting a forced substitution (scenario 2), looking for the product elsewhere or postponing the purchase (scenario 3), or not buying the product at all (scenario 4). (47)

Hoarding and rationing are common phenomena observed in the context of shortages of medicines and supplies for perioperative use. Hoarding refers to the excessive accumulation of these products

by individuals or entities in order to ensure their availability and obtain economic or commercial benefits. Hoarding can exacerbate drug shortages in certain areas. (48) On the other hand, rationing involves the limited and controlled allocation of medicines and supplies, with the aim of addressing shortages and ensuring equitable use among patients and different health services. (49) Both practices have significant implications for perioperative care, as they can affect the ability of health professionals to provide optimal and safe care to patients.

Economic considerations

Drug shortages result in additional costs for all parties involved. Suppliers, distributors and health care providers are affected, as they have to incur extra expenses to cope with the unavailability of medicines. (50) These additional costs include the purchase of medicines at higher prices, the use of expensive alternative brands, as well as the implementation of awareness and training programs. (51) Also, the importation of medicines during periods of national shortages has a significant economic impact on governments. (52) The costs avoided are usually lower than the increased costs associated with shortages.

CONCLUSIONS

Drug and perioperative supply shortages are a growing problem worldwide in anesthesia and surgical care, especially when it comes to products without adequate therapeutic alternatives. There is no standardized definition of shortages in the medical field, which leads to variability in the definitions used by different regulatory authorities and makes it difficult to assess the availability of supplies and drugs. The pharmaceutical industry, like other industries, seeks ways to reduce costs and increase sales to maintain its sustainability, which can jeopardize

drug availability. The causes of shortages of supplies and medicines include supply-side problems, such as lack of manufacturer capacity, and demand-side problems, such as unpredictable increases in demand and inappropriate prescribing practices.

In addition, bidding systems and the lack of sustainability of pharmaceutical companies also contribute to shortages.

It is important to understand the causes in order to find a way to reduce the risk of shortages of supplies and medicines.

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Contributions by the authors

DAR and CG participated in the conception of the manuscript, search and analysis of the information, preparation, revision, discussion and correction of the manuscript.

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