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OBSTETRIC ANESTHESIA (LR LEFFERT, SECTION EDITOR)

Drug Shortages in Obstetrics

Heather C. Nixon[1]

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Abstract

Purpose of Review This review highlights the patient safety and practice management concerns surrounding drug shortages in obstetric anesthesiology. Given the lack of evidence-based strategies for managing shortages, this review was created to provide societal consensus suggestions and practical guidance to assist clinicians in creating safe systems for medication administration in the obstetric unit.

Recent Findings Drug shortages occur for a variety of reasons but may pose significant risk to patients as they may be more likely to receive suboptimal therapy or even experience harm due to medication errors.

Summary Minimizing the potential patient harm that may occur on the obstetric floor secondary to drug shortages requires a rigorous and time-consuming multi-disciplinary approach to ensure unit organization and provider education. Standardization of medications, pharmacy preparation of medications, conservation strategies, contingency planning, bar-coding technology, and effective communication to end users are all necessary components to creating a safe system for patients.

Keywords Obstetric anesthesiology · Medication errors · Patient safety · Drug shortages · Pharmacy

Introduction

Scope of Problem

The American Society of Health-System Pharmacists (ASHP) defines a drug shortage as "a supply issue that affects how a pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative agent [1]." National drug shortages in the United States have been reported with increasing frequency since 2009 and have been attributed to a variety of factors in the supply chain. Changes in financial drivers, material availability, manufacturing capacity and quality problems, industry consolidation, lack of manufacturing redundancy, inventory practices, and current distribution systems may all create drug shortages [2–4]. Despite implementation of legislation from the Food and Drug Administration (FDA) to promote both the proactive reporting of potential shortages and governmental resources to promote production, drug shortages continue to plague the field of anesthesiology. In 2018, the American Society of Anesthesiologists conducted an informal survey of its membership to determine the impact of drug shortages to anesthesiology providers. Results indicated that more than 95% of the 2500 respondents reported that drug shortages were impacting the care of patients [5].

Patient Safety Concerns Due to Shortages

Drug shortages may pose a significant patient safety concern. When a medication is on shortage, patients may receive less effective therapies, no therapy secondary to lack of alternatives, or therapies with significantly higher side effect profiles [6–8]. For anesthesia providers, other patient consequences may include the cancelations of elective procedures, increased surgical time or delays in patient discharge from recovery units due to suboptimal pain, nausea, or vomiting treatment [9]. In addition, drug shortages may increase the risk of medication errors. In a national survey by the Institute of Safe Medical Practices (ISMP) in 2012, 1 in 3 respondents reported their institution had experienced a near miss or medication error due to drug shortages [6]. A 2013 survey of pharmacy directors revealed between one to five institutional medication

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✉ Heather C. Nixon
hnixon1@uic.edu

[1] Department of Anesthesiology, University of Illinois Hospital and Health Sciences System, 1740 W. Taylor Ave, Suite, Chicago, IL 3200, USA

errors associated with drug shortages in addition to increases in patient complaints [10].

The increased risk for medication errors occurs for several reasons. When a shortage occurs, hospital pharmacies may procure medications from alternate suppliers which package medication differently. This lack of standardization in the drug manufacturing industry could lead to look-alike errors or wrong dose errors due to changes in medication packaging or availability of certain concentrations. For example, when methylergonovine maleate was changed on our unit from our standard ampule (Akorn, Inc.) to a 2 mL vial (American Regent, Inc.), it was visually similar to ondansetron (West Ward Pharmaceuticals). Although this change provided a consistent supply of the medication to the labor and delivery floor, we experienced several near-miss situations where methylergonovine was almost administered to patients instead of ondansetron (Fig. 1). Providers must recognize that at this time, there is no mandated standardization of medication labeling to ensure consistency of packaging colors or containers between manufacturers.

Drug Shortages in Obstetric Anesthesiology

The mainstay of obstetric anesthesiology is the provision of neuraxial analgesia and anesthesia which rely heavily on sterile preservative-free injectable medications. Unfortunately, compared to other medications, the manufacturing of these medications is more susceptible to contamination and quality issues which are the most common contributors to drug shortages. Due to financial consideration, these generic medications have no redundancy in production between manufacturers as there is no competition in the market for these drugs and generally, there are few available appropriate substitutes. Overall, generic drugs are also more susceptible to shortages as generic medication productions lines are typically used to produce several generic drugs specific to the type of formulation. This means that if a particular production line becomes compromised, other production lines are not fitted to be used as an alternative [2]. In 2013, there were only seven suppliers of generic sterile injectables in the USA and reports indicate that 90% of sterile injectables produced in the USA come from one of three manufacturers [11].

In 2019, Haggerty and Nixon surveyed academic obstetric anesthesiology directors regarding drug shortages. Almost 83% of respondents reported experiencing a drug shortage on their obstetric anesthesiology unit in the year prior. Over 30% of the represented units reported a medication error or near miss event that was considered to be directly related to drug shortages [12]. Drug shortages in obstetric anesthesiology may also resort to unsafe medication practices in order to increase the supply of medications. Many academic institutions in 2018 reported that sterile single-dose medications were being divided into multiple doses at the bedside by anesthesiology providers under non-sterile conditions in order to conserve medications [12]. Therefore, obstetric anesthesiology providers may experience more drug shortages than other fields of medicine, and management strategies should be employed to mitigate the potential for harm secondary to shortages [13].

Managing Drug Shortages Managing drug shortages in obstetric anesthesiology properly and safely requires significant system organization and the utilization of institutional resources. Not only does the culture need to support efforts to improve

Fig. 1 Look-alike errors due to Drug Shortages

safety, but leaders need to be willing to dedicate significant time, financial resources, and personnel to address this ever moving target.

In order to provide an algorithm to approach the management of drug shortages, the American Society of Hospital Pharmacists (ASHP) put forth guidelines with an included algorithm in 2009 and revised guidelines in 2018 (Fig. 2) to provide management strategies to assist institutions struggling with drug shortages [14]. These guidelines outline best practices in multi-disciplinary organizational structure, monitoring and assessment of the institutional consequences of individual drug shortages, and distribution and administration practices to improve both availability and safety. Below, we will discuss each step of this algorithm, and then, we will present a drug shortage management example and how providers may approach this situation utilizing the algorithm to manage drug shortages on the obstetric anesthesiology unit.

Organizational Planning

In order to mitigate some of the impact drug shortages, the Federal Food, Drug, and Cosmetic Act (FD&C Act) section 506(c) provides legislation that mandates manufacturers notify the FDA when there are interruptions in production or a planned discontinuation of a medication. Likewise, the Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012 was created to improve early notification to the FDA when manufacturers have production disturbances or problems [4]. However, unexpected quality issues, including contamination of production lines or raw material shortages due to natural disasters, may contribute to shortages and these often do not allow for advanced notification. Therefore, although there may be expected shortages of medications, often the unexpected medication shortage leaves little room for contingency planning. Health care systems need to have a structure in place to safely and quickly address unexpected shortages.

Pharmacy Planning (Situation Assessment)

Managing drug shortages relies on the significant allocation of pharmacy personnel resources, with the annual labor costs associated with drug shortage management in the USA estimated to be $216 million [15, 16]. Pharmacy personnel must monitor shortages and initiate measures to manage shortages. Initially, the pharmacy personnel must verify the suspected or actual shortage of the medication, and assess the operational and therapeutic implications. Information gathered would include the patients or units affected, projected length or severity of shortage, current usage and stocks available, and the possible alternative manufacturers or therapies. Armed with this information, pharmacy providers can then create possible strategies to discuss with a multi-disciplinary team.

Multi-Disciplinary Planning (Shortage Impact Analysis)

Many institutions rely heavily on pharmacy personnel, including drug purchasing agents and pharmacy managers to navigate drug shortages. While these personnel are integral to procuring and distributing medications to the end-users at the bedside, a team approach to managing drug shortages includes proactive planning for shortages with continued communication and feedback.

In some practices, pharmacists are employed by the anesthesiology department to participate in drug education as well as provide expertise regarding drug storage and distribution to help create compliant and safe medication systems. These individuals are vital when planning for drug shortages as they may provide a valuable bridge between pharmacy leadership and the anesthesiology service. In most institutions, however, anesthesiology departments may need to communicate with pharmacy personnel directly with concerns. In such cases, a *designated drug manager* position should be appointed for the anesthesiology group. This anesthesiology provider would be responsible for multi-disciplinary planning regarding any new drug shortages (anticipated or actual) and would provide input to pharmacy providers regarding how to best allocate the drug, the patients or service lines most affected, and the possible patient safety ramifications for any proposed management plan based on the anesthesiology workflow.

Multi-disciplinary teams consisting of drug purchasing agents, pharmacy managers, and a designated drug manager from the anesthesiology department should create drug shortage and resource allocation committees that will define processes to intervene when shortages arise. Ideally, a drug shortage team and a resource allocation committee would act to determine the impact of a shortage, the patients and procedures most affected, and how possible alternative formulations or therapies may impact patient outcomes and safety. When a drug shortage arises, the group will meet and discuss how the drug is normally used at bedside and the possible patient safety concerns. Strategies to limit waste, restrict use, and employ alternative safe therapies should be discussed, while the anesthesiology designated drug manager highlights possible safety and workflow concerns (Fig. 3).

Specific Strategies to Manage Drug Shortages (Fig. 3)

Limit Waste Techniques to limit waste include only drawing up medication for immediate use and utilizing pharmacy services to provide dose-specific aliquots in a ready to use form.

Eliminating the *routine* preparation of medication may be challenging in the obstetric anesthesiology unit where

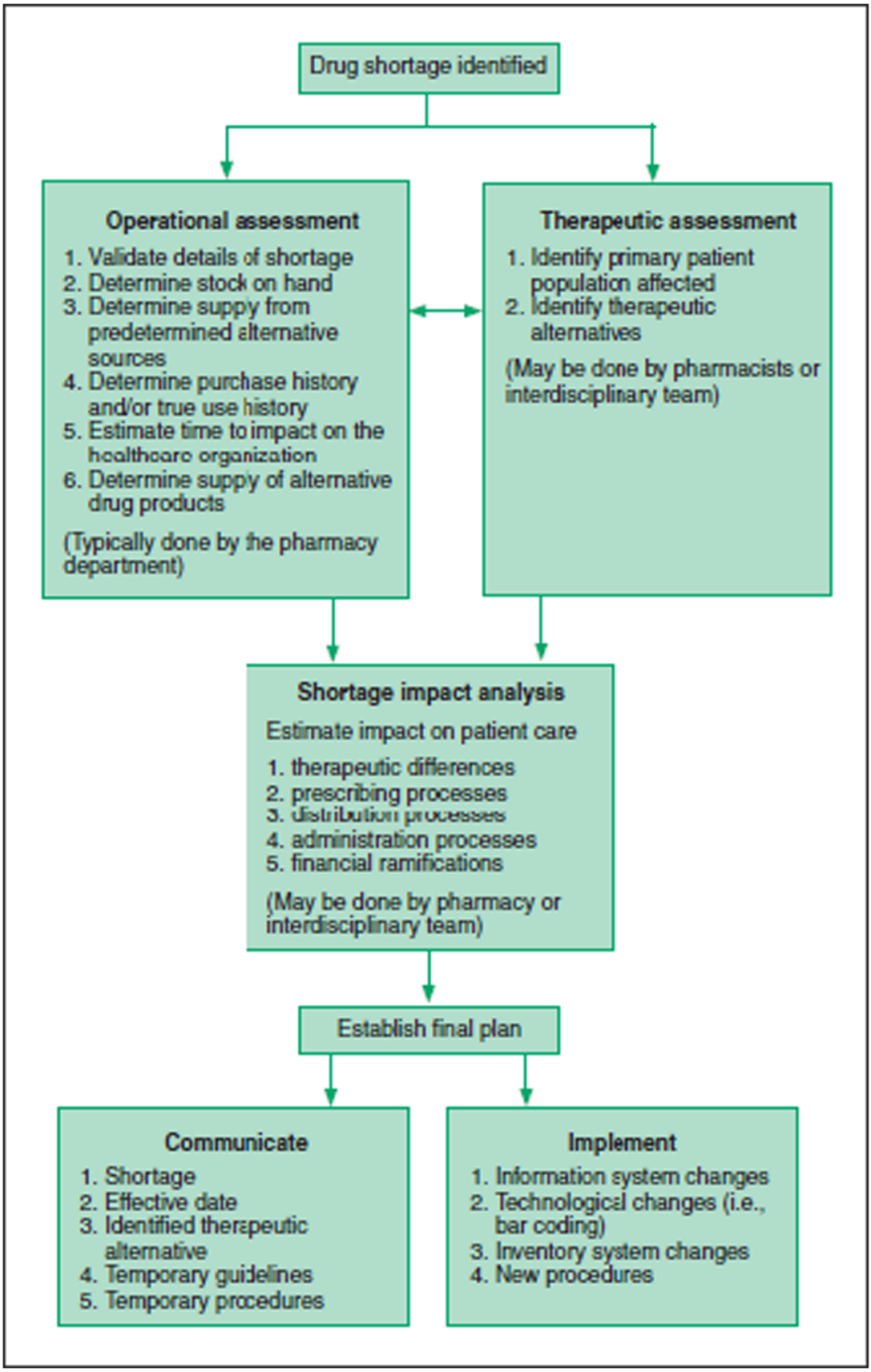

Fig. 2 ASHP Guidelines on the Management of Drug Shortages

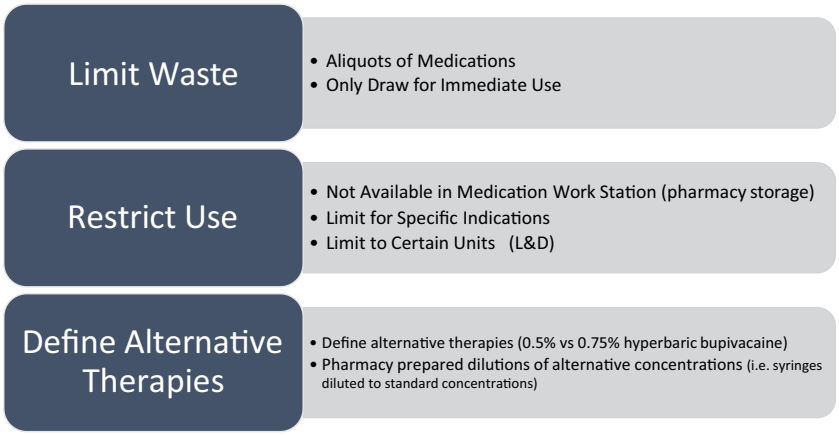

Fig. 3 Multi-disciplinary Planning and Strategies during Drug Shortages

providers may routinely prepare medications in advance for emergency use such as succinylcholine, propofol, or chloroprocaine [17]. This leads to daily waste if the medication is not used. If available, it may be prudent to obtain color-coded pre-filled ready to use syringes that have longer expiration dates and may decrease waste. Alternatively, pairing a clean and empty syringe with attached drawing needle next to emergency medications may encourage providers to limit routine drawing of medications as it is more quickly available for use.

Depending on a drug's therapeutic and toxicity window as well as manufacturing packaging, it may be prudent to advocate for pharmacy personnel to prepare ready to use single-dose medication syringes. Although this requires pharmacy personnel resources, a cost analysis of anesthesiology provider only versus a mixed anesthesiology provider and hospital pharmacy prepared medication structure, there appears to be a financial benefit to utilization of hospital pharmacy services in assisting in medication preparation [18]. An example of a medication that may be appropriate for this preparation is 0.5% isobaric bupivacaine which is packaged in 30 mL vials yet would be administered in much smaller volumes in a spinal anesthetic for cesarean delivery or for combined spinal-epidural analgesia for labor. When prepared following the USP chapter 797 guidelines in a sterile hood in the pharmacy, single dose medications can be divided into aliquots that may be used for several patients and therefore conserve valuable medication while meeting CDC compounding standards. By partnering with pharmacy to advocate for this practice, systems can eliminate the risk that bedside providers will perform this technique under non-sterile conditions in order to conserve medication [12]. According to the CDC, this bedside division may increase the risk of contamination and subsequent patient harm although the veracity of this assertion has been challenged [19, 20].

Restricting Use In addition to limiting waste, it is important to conserve the hospital supply of drugs on shortage. Restricting use by removing the medication from the anesthesia medication station and requiring release from pharmacy, limiting use by imposing specific use indications, or restricting use to certain units are all viable options. In 2015, Ladha et al., reported that by simply replacing pharmacy prepared syringes of ephedrine with ephedrine that required provider preparation, there was a significant change in provider administration patterns, where providers administering less overall ephedrine relative to phenylephrine which was provided in a ready to use syringe [21]. From this observation, it can be extrapolated that adding procurement barriers to the administration of medications such as physical distance or indication based allocation, providers will use less overall restricted medication. However, when decisions regarding restricting use are being considered, an evaluation of current use and potential for harm must be considered. Restricting or creating physical barriers to life-saving medications may have serious and morbid consequences. Therefore, it would not be advisable to remove epinephrine from the anesthesiology medication drawer, but a medication such as labetalol could be removed as long as other antihypertensive drugs were available. This removal discourages routine use, but the medication would still be available if necessary. The above example highlights why clinician input should be valued in any medication restriction planning.

Alternative Therapies Identifying potential alternative medication therapies is a valuable strategy for teams handling drug shortages. In some instances, a reasonable alternative may be available (i.e., ropivacaine vs bupivacaine for epidural infusions). In other circumstances, a second line agent may need to be utilized or there may not be an appropriate alternative. Sometimes when a shortage occurs, there may not be information available regarding the efficacy or ideal dosing regimen of an alternate drug. For example, during the preservative-free morphine shortage in the USA in recent years, many providers were hesitant to utilize hydromorphone neuraxially as research was lacking for its use in obstetric patients. Although many studies have now defined the utility

of neuraxial hydromorphone in this population, units may elect to avoid alternate therapies without guidance from the literature [22–24].

In any decision regarding changes in clinical protocols, it is very important that bedside providers who understand system constraints and workflow are involved in decision-making and an analysis of the potential for harm is performed. Clinicians may provide insights into clinical differences between therapies (i.e., 0.5% isobaric bupivacaine vs 0.75% hyperbaric bupivacaine) which may impact delivery of a fetus in emergent situations. Evidence suggests that the use of hyperbaric bupivacaine provides a faster onset and is more reliant on patient positioning when compared to isobaric bupivacaine for cesarean delivery [25]. Failure to appreciate these clinical differences may result in inadequate sensory blocks with subsequent patient discomfort, the use of anesthetic adjuncts or the need to convert to general anesthesia. When considering appropriate alternatives, it is important to understand the staffing models of the unit, provider familiarity with new therapies and the potential for poor outcomes. Prior to implementation of changes, the designated drug manager must communicate effectively with end-users and provide tools to help guide changes.

Implementation

Careful multidisciplinary planning should be performed prior to implementation of medication storage or stocking changes due to drug shortages. Often alternate formulations and medications may be visually similar to other commonly used drugs in obstetric units. As aforementioned, drug substitutions due to shortages may lead to medication errors including wrong drug, wrong dose, or inappropriate substitutions. This is especially hazardous for neuraxial medications which have a narrow therapeutic and toxicity window [26]. There are some technological systems and provider education strategies that may reduce the potential for errors.

Technology The practice of anesthesiology is unique in that one provider typically independently obtains, prepares, and administers all medications to their patients. Other health care providers are typically mandated to have some mechanism to limit drug accessibility and to double check medications prior to administration. When other providers are administering high risk drugs, hospital protocols often require a second provider to verify the drug and dose. This double check by a second provider acts as safety check to pause and verify the drug is correct. An analogous system in anesthesiology would be the use of bar-coding devices which have become more popular in anesthesiology practices. These systems serve as the second check of medications prior to provider administration. When the drug is scanned, the name and dose of the medication flashes on a monitor and in some instances, the name of the drug is verbally announced. Although little research has been conducted regarding the efficacy of bar-coding technology to prevent error by the anesthesiologist in the operating room, there is support the system reduces medication errors in the intensive care arena [27–29]. In addition, several bar-coding technology systems also print color-coded medication labels with drug names, doses, and expiration dates which is a practice supported by the Anesthesia Patient Safety Foundation to prevent error. However, several studies have noted that a barrier to the usefulness of bar-coding technology in the operating room is correct usage by providers which includes the scanning of medications *prior* to administration as scanning medications after administration does not prevent error [30]. Likewise, disabling the voice function may limit its utility to act as a second check system.

Education and Communication Drug shortages may necessitate providers to use alternative medications as well as different formulations or concentrations. Whenever possible, obstetric units should attempt to provide medications in standardized doses, but this is often difficult in the face of scarce medication stores. Therefore, it is extremely important to communicate any changes in formulation, concentration, or the discontinuation of a current therapy to providers in a timely manner. In obstetric units with trainees or providers who staff the unit infrequently, it is important to repeatedly communicate changes and provide clinical bedside resources to help guide the safe administration of medication. Protocols on acceptable doses and medication indications should be distributed to providers via multiple outlets. Departmental announcements, email blasts, pictures posted at the medication dispensing site, and other electronic modes of communication should clearly state the drug on shortage and the substitution. Pharmacy may also package drugs with labeling alerts such as "Alert: Medication Change," to visually alert providers to changes in drugs at the site of distribution. Finally, alerts and new protocols embedded in the electronic medical record may also cue providers to changes secondary to drug shortages.

Example Case

Management of a Drug Shortage

In order to understand how these organizational and management suggestions may be utilized in an actual drug shortage situation, the following section highlights the steps of drug shortage management via a case based approach.

Case

A potential shortage of 2 mL vials of preservative-free morphine (1 mg/2 mL) is identified by pharmacy.

Phase 1: Operational and Therapeutic Assessment

Pharmacy

- Verify the shortage and obtain information regarding projected duration
  https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm
  https://www.ashp.org/drug-shortages/current-shortages
- Assess current supply and possible alternative suppliers
- Identify the patients or units most affected

Resultant Information

- The shortage is real with no clear resolution timeline
- Current supply is adequate for 3 weeks of use through normal protocols
- Obstetric and regional anesthesia patients most affects

Phase 2: Shortage Impact Analysis and Multi-Disciplinary Planning

Drug Shortage Team Meets Attendees—Pharmacy Drug Manager, Anesthesiology Designated Drug Manager, Obstetric and Regional Unit Directors.

Discussion Regional Team—workflow

Staff

Faculty—4 members
Resident—1 per month

Clinical Considerations

using catheter techniques, so can use shorter acting agents
comfortable utilize hydromorphone in infusions and as bolus

Obstetric Team—workflow

Staff

Faculty—majority of faculty, some providers infrequently
Trainees—rotating residents and guest night and weekend call residents
Clinical Considerations—
catheter removed following surgery
short acting agents are suboptimal for post-op pain
Concerns—Providers who staff OB infrequently making errors if alternate therapies or different formulations used

Resultant Multidisciplinary Plan

1) Limit Waste—current stock of 1 mL (0.5 mg/mL)
   - aliquoted to single dose 150mcg doses
   - 24 h expiration date
2) Restrict use—allocate to OB service, regional team will use hydromorphone
3) Alternative Formulation:

   10 mL vial of (0.5 mg/mL) preservative-free morphine
   Continue vial availability for CD epidural use
   Contingency may need to pharmacy prepare both ready to use CD spinal and epidural use

Phase 3: Implementation

Communication with OB Anesthesiology Providers

Email blast with pictures of sample new aliquots
Notices placed in dispensing areas
Providers scheduled for OB shift in upcoming 2 weeks contacted
Shortage and plan posted on hospital pharmacy site

Feedback

Designated drug manager solicits feedback from end-users concerning availability, use, and safety concerns
Pharmacy manager solicits feedback from pharmacy techs regarding preparation and distribution

Phase 4: Surveillance and Reporting

Safety Issue Identified

Near miss event as preservative-free aliquot visually similar to already established aliquots of local anesthetic prepared for labor analgesia

Recommendation to add blue (narcotic) morphine label to the printed white label and to notify providers

Conclusion

Drug shortages have profound impacts on patient care and safety in the obstetric anesthesiology unit. In order to prepare for both expected and unexpected shortages, multidisciplinary teams should be assembled who are armed with both expertise in both pharmacy and end-user workflow and the ability to implement change. When a shortage occurs, limiting waste, restricting use, and defining alternative appropriate therapies can be useful planning strategies. Changes in formulations or concentrations can increase the chance of medication errors. Bar-coding technology and thoughtful communication with bedside providers are vital components of safe and successful implementation. Finally, a culture of safety, where anesthesiology providers are empowered, to report near misses or safety issues will help to shape safer systems.

Compliance with Ethical Standards

Conflict of Interest Heather C. Nixon has received compensation from Eton Pharmaceuticals for participating in a one-time focus group.

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