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CRITICAL MEDICATION SHORTAGES: EFFECTIVE STRATEGIES TO MAINTAIN CONTINUOUS MEDICATION AVAILABILITY FOR EMERGENCY MEDICAL SERVICES

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ABSTRACT

Objective: Critical shortages of generic injectable medications are an ongoing challenge for Emergency Medical Services (EMS) systems. Mitigation strategies have been proposed to address the issue, but a limited amount of data exists quantifying the scope of the problem or describing strategies being used to ensure access to essential medications for prehospital care. In this study, we sought to quantify specific medication shortages and to determine the most frequently employed mitigation strategies to maintain medication availability in a large, regional EMS system. **Methods:** A survey was distributed to the 30 public advanced life support (ALS) provider agencies in Los Angeles County (LAC) to assess the prevalence of specific medication shortages and types of shortage mitigation strategies implemented. Survey responses were reviewed and presented using descriptive statistics. **Results:** Survey responses were received from

29 of 30 (97%) provider agencies. All but one of the responding agencies reported being impacted by medication shortages. Strategies to maintain the supply of medications included use of alternative vendors 20/28 (71%), rotating medications from low to high volume units (54%), utilizing expired medication FDA-approved extensions (50%), substituting medications (43%), borrowing medications from the LAC EMS Agency (39%) or other EMS provider agencies (32%), utilizing expired medications with medical director approval (29%), diluting medications to obtain desired concentration (18%), reducing minimum periodic automatic replacement (PAR) levels (14%), and using alternate medication concentrations/formulations (14%). The medications most frequently reported to have shortages included epinephrine (0.1 mg/mL), morphine, dextrose 10%, and normal saline. None of the provider agencies self-reported adverse events due to the shortages. **Conclusions:** Critical medication shortages remain a problem for many EMS systems. EMS medical directors need to implement multiple mitigation strategies to maintain supply of critical medications for prehospital patient care. **Key words:** critical medication shortage; emergency medication shortage; drug shortage; medication supply; mitigation strategies

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M. Gausche-Hill conceived of the study. D. Whitfield, N. Bosson, and M. Gausche-Hill reviewed the data and performed the analysis. M. Eckstein and C. Kazan assisted with data acquisition for analysis. J. Telmos and G. Watson designed the survey. J. Telmos supervised study enrollment, reviewed all survey submissions for concordance, and compiled data. D. Habrat and D. Whitfield completed literature review. D. Whitfield drafted the manuscript and all authors contributed substantially to its revision.

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INTRODUCTION

Critical medication shortages are an ongoing concern in the United States (U.S.) and can impact clinical care in both hospital and prehospital settings (1, 2). At the height of the U.S. medication shortage crisis in 2011–2012, over 250 individual medications were reported to the Food and Drug Administration (FDA) to be in short supply (3, 4). During that time, it was estimated that 40% of medication shortages affected the delivery of emergency care (5). While the annual number of medications in shortage has decreased as a result of FDA reporting requirements and federal legislation (4, 6, 7), critical medication shortages, particularly of generic injectable medications, continue (8). These shortages have potential to seriously impact emergency medicine and emergency medical services (EMS) (2, 9).

To our knowledge, there are no data published that quantitatively describe the extent of critical medication shortages in U.S. EMS systems or document successful strategies that can be implemented

TABLE 1. Los Angeles County Emergency Medical Services (EMS) Agency pharmaceutical mitigation strategy policies used for pharmaceutical shortages listed in hierarchical order (top strategies to be implemented first)

Los Angeles County EMS Medication Shortage Mitigation Strategies

1. Provider agencies may attempt procurement from other pharmaceutical vendor resources.
2. Provider agencies may request to temporarily reduce their drug inventory by contacting the EMS Agency's Medical Director.
3. The EMS Agency may elect to contact county-operated pharmacies to seek assistance in replenishing current pharmaceutical restock.
4. The EMS Medical Director may temporarily reduce minimum inventory periodic automatic replacement levels.
5. Provider agencies may redistribute their current inventory amongst their own advanced life support (ALS) units from low volume to high volume utilizers.
6. Provider agencies may request use of medication identified by Food and Drug Administration (FDA) for extension of use.
7. Provider agencies may request blanket use of expired medications for up to 6 months.
8. The EMS Agency may deploy available pharmaceuticals from the disaster preparedness pharmaceutical cache to provider agencies most in need.
9. Provider agencies may request use of alternative medication.
10. Provider agencies may request alternative formulations of the medication.
11. Provider agencies may request to dilute medication.

to mitigate medication supply chain deficiencies. Both the medication shortages and the mitigation strategies themselves have the potential to lead to adverse patient care outcomes. Understanding specifically how EMS is affected, what strategies are currently being used, and how effective such strategies are in alleviating the shortage are important first steps in determining how to reduce the negative impact of critical medication shortages on pre-hospital patient care.

In response to recurrent critical medication shortages, the Los Angeles County EMS Agency (LAC EMS) approved standardized mitigation strategies (10) based on consensus recommendations (5) with the intent of limiting the impact of such medication shortages on prehospital care in Los Angeles County (LAC). In this study, our objective was to describe the extent of critical medication shortages in this large, regional EMS system as experienced by public Advanced Life Support (ALS) EMS provider agencies through a web-based survey. We sought to quantify the frequency of specific medication shortages and to determine the most frequently employed mitigation strategies to maintain medication availability.

METHODS

This was a cross sectional study conducted among all public ALS provider agencies operating within a regional EMS system. The Los Angeles Biomedical Research Institute at Harbor-UCLA Institutional Review Board approved the study.

Study Setting and Population

ALS 9-1-1 EMS response in LAC is fire-based, with service delivered locally by 30 individually

managed public provider agencies operating within the county. LAC has a population of over 10 million residents living in a 4,084 square mile geographic area. There are 4,005 state licensed, locally accredited public provider agency paramedics practicing in the county that respond to over 600,000 9-1-1 dispatched ALS calls annually. LAC EMS is a regional EMS agency with authority from the State of California to implement EMS policy in the county of Los Angeles, providing regulatory and statutory oversight. The medications utilized during ALS responses are purchased, resupplied and managed by the responding provider agencies such that each fire-based, ALS provider agency is individually responsible for maintaining ALS medication inventory. Some agencies have agreements with local hospitals for resupply, though most manage their own inventory purchase, stock, and resupply exclusively.

From 2017-2018, LAC ALS provider agencies experienced several critical medication shortages while supporting continued prehospital care needs, administering over 130,000 doses of FDA defined shortage medications (11) in 2017. LAC EMS supported the sustainment of uninterrupted medication availability for county ALS providers by authorizing specific strategies for implementation by provider agencies (Table 1). These strategies were deployed in a hierarchical order with the latter strategies employed only if others did not alleviate the shortage. This approach was taken to reduce risk of adverse events due to latent safety threats inherent with the use of the strategy (e.g., dosing errors associated with dilution of medication).

Selection of Participants

Public ALS provider agencies in LAC were eligible for participation in the study on a voluntary basis.

1. Which of the following best describes your agency?
 - Aeromedical services only
 - Private ALS and/or SCT
 - Private, special events only ALS
 - Public, fire based 9-1-1
2. How many paramedics does your agency employ?
3. During 2017/2018 has your provider agency been impacted by drug shortages?
 - Yes
 - No
4. What strategies has your provider agency implemented in order to address drug shortages? (check all that apply)
 - Reduce PAR levels
 - Used FDA identified lots of expired medications with extensions
 - Used expired medications with provider agency Medical Director's approval for up to 6 months
 - Rotated medications from rescues/squads with less frequent runs to those with a greater number of runs
 - Changed medications to an alternate medication with better availability
 - Borrowed medications from Los Angeles County EMS Agency
 - Borrowed medications from another EMS provider agency
 - Reached out to different vendors in order to obtain medications
 - Diluted medications to create the correct formulation of medication (epinephrine)
 - Changed formulation of medication
 - Other strategies not listed
5. Which of the following medications did you have to use one or more of the alternate strategies listed in the previous question?
 - Atropine 1mg/10mL
 - Calcium chloride 1gm/10mL
 - Dextrose 10%
 - Epinephrine 0.1mg/mL
 - Epinephrine 1mg/mL
 - Fentanyl
 - Morphine
 - Sodium Bicarbonate
 - Other drugs not listed (please specify)
6. Has your agency experienced any adverse patient events associated with the use of alternate drug strategies?
7. Since you answered yes to the previous question, may EMS Agency staff contact you to discuss details of the adverse event? If you answer yes, the EMS Agency will use the contact information you provide at the end of the survey, otherwise, we will not contact you.
8. If indicated, may EMS Agency contact you to discuss your responses?
9. Please provide the following information.
 - Name of agency you are responding for
 - Your name
 - Your title
 - Your contact information

FIGURE 1. Medication shortage survey administered to advanced life support emergency medical services (ALS EMS) provider agency representatives.

Surveys were distributed electronically to all ALS provider agencies in LAC. Because only public and fire-based provider agencies perform 9-1-1 ALS response in LAC, surveys from private provider agencies and those that perform aeromedical services only were excluded from this analysis. Two public, fire-based agencies also provide aeromedical response, but we did not inquire separately about these units. Survey responses from individuals

identified by provider agencies as "paramedic coordinators" or "EMS coordinators" were included. Exclusion criteria included duplicate responses received from the same provider agency. If multiple responses were received from a single provider agency, only one response was included in the analysis with either concordance of responses or exclusion of less comprehensive surveys (i.e., skipped questions).

TABLE 2. Proportion of emergency medical services (EMS) provider agencies that employed specific strategies to mitigate the effects of the medication shortage

Mitigation Strategy	Frequency Utilized, % agencies (n)
Utilized alternate vendors	71% (20)
Rotated medications from low to high volume units	54% (15)
Utilized Food and Drug Administration (FDA) expired medication extensions	50% (14)
Substituted medication with better availability	43% (12)
Borrowed medication from Los Angeles County Emergency Medical Services (LAC EMS) Agency	39% (11)
Borrowed medication from other agencies	32% (9)
Utilized expired medication with Medical Director approval	29% (8)
Diluted medication to obtain desired concentration	18% (5)
Reduced minimum periodic automatic replacement (PAR) levels	14% (4)
Utilized alternate medication concentrations/formulations	14% (4)
Other strategies not listed	7% (2)

Data Collection

Participating public ALS provider agencies completed a web-based survey (Figure 1) designed to assess the extent of emergency medication shortages affecting provider agencies within LAC from January 1, 2017 to May 1, 2018. Surveys were sent electronically via SurveyMonkey® Team Advantage to individuals identified as “paramedic coordinators” or “EMS coordinators,” with a single response requested from each agency. The survey was available for completion on-line between May 14, 2018 and July 6, 2018. A total of 3 e-mail contacts were made to provider agencies to encourage response to the survey. Survey responses were reviewed by a study investigator (JT), LAC EMS Chief of Prehospital Care Operations, for response completeness, duplicate responses, and response concordance when applicable. Where there was a duplicate response from a single agency, the most complete response was retained for analysis, with any discrepancies clarified with respondents.

Key Outcome Measures

The primary outcome measures in this study were to identify the prevalence of medication shortages impacting public provider agency ALS operations in LAC and to quantify the prevalence of specific medication shortages experienced by provider agencies. In addition, we determined the strategies most commonly implemented to mitigate medication shortages.

Analytical Methods

This study utilized descriptive statistics including frequency and proportions to quantify and compare the key outcome measures assessed by the survey. Descriptive statistics were calculated using Excel

2016 (Microsoft, Inc., Redmond, WA). Results are reported numerically as frequencies and percentages.

RESULTS

Survey responses were received from 29 of 30 (97%) ALS provider agencies. One agency submitted 2 responses, for which an incomplete survey was excluded and the complete response retained for the analysis. Of the 29 responding provider agencies, 41% employed ≤ 30 paramedics, 45% employed 31–100 paramedics, and 14% employed ≥ 100 paramedics. Twenty-eight of the 29 respondents (97%) reported that they were impacted by medication shortages.

The 28 provider agencies reporting medication shortages implemented a variety of mitigation tactics to cope with limited medication supplies (Table 2), with the use of alternate vendors being the most frequently used strategy (71% of agencies). Other common strategies used included rotating medications from low to high volume units (54%), utilizing expired medication FDA-approved extensions (50%), and substituting medications with alternatives that had more consistent availability (e.g., changing from morphine to fentanyl, dextrose 10 to 50% in adults) (43%). Two provider agencies (7%) described “other strategies not listed” with both describing obtaining medications from a partnered hospital. Medications borrowed from LAC EMS included epinephrine and dextrose. FDA expired medication extensions were used for atropine, epinephrine, dextrose, and sodium bicarbonate, while medical director approved extensions were implemented for controlled substances. No agencies reported that adverse events occurred in association with the use of medication shortage mitigation strategies.

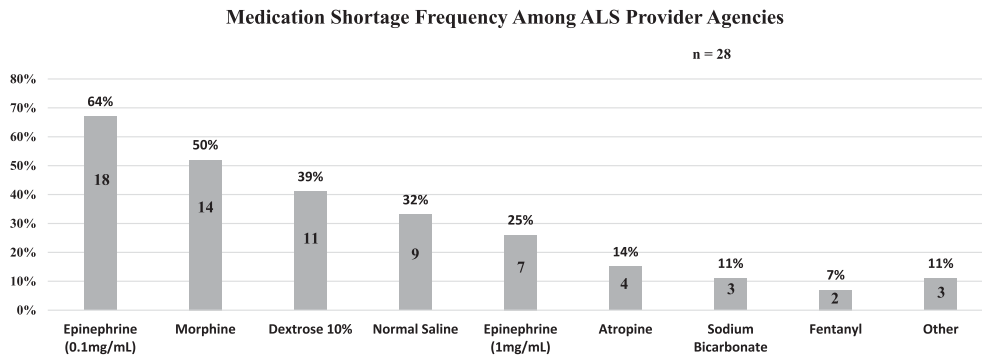


FIGURE 2. Proportion of emergency medical services (EMS) provider agencies that experienced shortages of specific medications requiring mitigation strategy implementation.

Agencies reported specific medications that required implementation of the strategies queried in the survey to maintain adequate supply. The most frequently reported shortage medications requiring implementation of any of the listed strategies are summarized in Figure 2. Epinephrine (0.1 mg/mL; 18 agencies, 64%) was the most commonly reported medication in short supply, followed by morphine (50%), dextrose 10% (37%), and normal saline (32%). Three provider agencies (11%) also reported other injectable medications (adenosine, glucagon, ondansetron, and midazolam) that were not listed on the survey, but required the implementation of LAC EMS approved strategies to maintain continuous supply.

DISCUSSION

In this study we demonstrated that critical medication shortages were experienced by nearly all public ALS EMS provider agencies in LAC during our study period. However, multiple strategies implemented by provider agencies across the county resulted in continuous medication availability for paramedic use despite the shortages. Medication shortages have been at the forefront of national discussion in recent years. In 2018, the FDA announced the formation of a drug shortages task force to identify long term solutions (7). Our study demonstrated that the effects of critical medication shortages go beyond patient care in hospitals, clearly impacting the emergency care of patients in the prehospital setting, as 97% of public ALS provider agencies in our county reported that their operations were affected.

Generic, injectable medications have been identified as a subset of medications that are frequently in short supply (8, 12, 13). Since most commonly used ALS medications fall into this class, it is anticipated that critical medication shortages will continue to be

problematic for EMS systems until long term solutions are identified and instituted. All medications reported to impact ALS provider agency operations in this study were of the generic, injectable class, supporting this assertion. Because production is limited to few manufacturers, generic injectables are particularly vulnerable to shortage due to supply chain limitations (14–16). Equipment needed to maintain quality is costly while products are typically sold with small profit margins (2, 8, 17). Profitability can only be attained with scaled production that limits markets to only the few manufacturers that are capable of producing at high volumes. When a gap in production occurs, oftentimes no alternate producers exist to fulfill market demand. Such a scenario likely resulted in our EMS providers reporting normal saline as a frequently shortaged medication. Normal saline is produced by only 3 manufacturers in the U.S., with significant shortages reported across the country in 2017 following Hurricane Maria (18). It is likely that limited production, suddenly disrupted by an unforeseen natural disaster, contributed to the shortage experienced in our EMS system, when provider agencies addressed the normal saline shortage in part by acquiring supplies from alternate vendors in alternate volume packaging. It is also reasonable to surmise that similar circumstances will result in shortages of comparably manufactured medications in the future.

Provider agencies in our EMS system reported the use of 10 distinct strategies to maintain continuous medication supplies during the shortage. The Association of State and Territorial Health Officials (ASTHO) and the American Society of Health-System Pharmacists (ASHP) have published recommendations for healthcare systems managing critical medication shortages (5, 19). Specific strategies recommended by ASTHO that were implemented in LAC included broadening procurement options, sharing, using expired medications, and

substituting. In our study population, broadening procurement options by using alternate vendors was the most commonly implemented mitigation strategy, though borrowing, substituting, and extending the use of expired medications were strategies frequently used as well. The ASHP recommends an integrated strategy that incorporates assessments of the operational and therapeutic shortfalls that may result from a drug shortage (19). Integrated strategies utilized in our system included the rotation of medications from low to high volume units and the reduction of minimum periodic automatic replacement (PAR) inventory quantities required for provider agencies. Such frameworks encourage local identification of solutions to medication supply issues during times of shortage.

Our study demonstrates that recommended strategies can be implemented within a large EMS system to initiate a coordinated response. Such a response is likely to be a contributing factor to maintaining adequate medication availability as we were able to do in our system. Implementation of strategies in a stepwise order from least likely to impact safety (i.e., changing vendors, rotating medication within one provider agency) to strategies that are most likely to impact safety (i.e., changing formulation, dilution of medication) presumably allowed our system to safely maintain adequate medication availability throughout the study period and has the potential for applicable use in other EMS systems. Studies examining challenges encountered implementing specific strategies would be an area for future investigation.

In anticipation of future medication shortages, EMS systems should plan mitigation strategies that may be implemented in successive fashion to address critical shortages. The strategies should optimize safety and clinical practicality. Although many of the strategies implemented in LAC had the potential to lead to medication errors and subsequent adverse patient events, no agencies reported adverse events due to utilization of the mitigation strategies described in this survey. However, it is possible that adverse events were not recognized, were not recorded, or occurred later in the patients' clinical course such that they were not witnessed by our study population. In prior studies, medication substitutions during times of shortage have resulted in adverse patient outcomes (20, 21). In the hospital setting, one study found an association between periods of norepinephrine shortage and increased mortality from septic shock when patients were administered substitute vasopressors, even though norepinephrine was the drug of choice (22). The lack of availability of first-line medications remains a patient safety

concern (8). Additionally, many medication shortage mitigation strategies require changes in medication delivery methods. Such changes require anticipatory education initiatives discussing potential adverse consequences. It is important that provider agencies and regulatory authorities approach provider education during the implementation of these strategies to limit the incidence of adverse sequelae. Further study is needed to determine specific safety consequences of medication shortages on prehospital care including patient outcomes data. Additional research should also focus on targeted long-term solutions to fulfill U.S. generic medication production shortfalls.

This study has several limitations. Our results are based on survey data and are thereby limited by the validity of responses by survey participants, including limitations introduced by recall and response bias. Because this study only queried EMS providers in one county where the regulatory EMS authority provided recommendations on specific mitigation strategies, the prevalence of critical medication shortages reported and mitigation strategies implemented may not be generalizable to other systems. While we did provide respondents the option to describe other strategies implemented in addition to selecting the specific strategies listed, our list of mitigation strategies was not comprehensive. Two agencies commented on partnerships with hospitals to obtain medications. It is possible that additional agencies used similar or other strategies, but did not report these in the survey. No adverse patient events were reported to LAC EMS as a result of the mitigation strategies implemented, though it is possible that respondents may have been hesitant to report any adverse outcomes to survey administrators from a regulatory agency. In addition, an "adverse event" was not specifically defined in the survey, leaving the meaning to the interpretation of the respondent. Adverse events may have occurred that were not identified as such, or reported. Furthermore, provider agencies lack data on hospital outcomes; as a result, adverse outcomes that occurred later would not be detected.

CONCLUSION

Critical medication shortages impacted an overwhelming majority of ALS provider agencies in this regional urban-suburban EMS system. Mitigation strategies implemented by provider agencies allowed for continuous medication availability despite the shortages. EMS medical directors need to implement multiple mitigation strategies to maintain supply of critical medications for prehospital patient care during periods of medication shortage.

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