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Why the Utilization of Ready-to-Administer Syringes During High-Stress Situations Is More Important Than Ever

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ABSTRACT

The COVID-19 pandemic has led to a high-stress environment causing a significant impact on frontline workers, including pharmacists and nurses. In addition to the increased workload, scarcity of resources, and emotional challenges, the frontline health care workers are required to wear additional personal protective equipment that can further limit their range of movement and decrease efficiency. The potential for errors can increase in these types of high-stress situations. One way to reduce the risk of errors is to use manufacturer-prepared, ready-to-administer (RTA) prefilled syringes, when appropriate. The use of RTA prefilled syringes is supported by literature evidence, recommendations, and guidelines from various professional organizations and societies.

Key words: coronavirus disease 2019, COVID-19, intravenous push medication, intravenous push medication errors, prefilled syringes, ready-to-administer, ready-to-use syringes, RTA

Any crisis situation can exacerbate stress levels and create an extra burden for health care professionals. The global COVID-19 pandemic has caused a significant psychological, emotional, and physical impact on health care workers, including pharmacists and nurses. Hospital pharmacists have been playing a crucial role during the pandemic. They face stressors such as working extra hours, ensuring sufficient medication supply to support intensive care units while implementing strategies and patient care plans to mitigate drug shortages and avoid disruptions in the supply chain. This in turn can help reduce nursing time spent in COVID-19 patient isolation rooms for medication administration.[1-3] Nurses are the frontline health care workers who face patient suffering and death, ethical issues, work overload, and scarcity of staffing resources. A diversion of clinicians to unfamiliar care areas has led to significant nurse burnout.[4,5] Moreover, due to the contagious nature of the virus, clinical staff are required to wear extra personal protective equipment (PPE) that can limit their movement and speed of action. This increases

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Financial support for this manuscript was provided by Fresenius Kabi USA, LLC. The authors are employees of Fresenius Kabi.

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DOI: 10.1097/NAN.0000000000000451

the chance of errors during preparation and administration of drugs.[6] One of the ways to reduce the burden on clinicians and minimize complex steps for drug preparation is to use ready-to-administer (RTA) products.[7] RTA products, such as prefilled syringes, can play a significant role in increasing efficiency while reducing errors and potentially related patient harm.[6,8]

This review provides a cumulative summary of the current literature and demonstrates that the use of manufacturer-prepared RTA prefilled syringes is an ideal option for the administration of intravenous (IV) push medications in the inpatient setting, especially during the COVID-19 pandemic and in times of heavy workload and high stress. This review article includes published literature, recommendations, and guidelines related to the use of RTA syringes in the hospital setting over the last 10 years and can be used as a reference tool to support the adoption of RTA prefilled syringes. Articles that were unrelated to the topic (eg, technical reviews, premix infusion bags or other RTA products, outpatient settings) were excluded.

DEFINITIONS OF RTA

The Institute for Safe Medication Practices (ISMP) defines *RTA* as "an injectable product containing the active drug in solution at the required concentration and volume, presented in the final container (syringe, infusion bag, or elastomeric device) and ready to be administered to the patient."[9] The World Health Organization (WHO) defines *RTA* as "an injectable medicine that requires no further dilution or reconstitution and is presented in the final container or device, ready for administration or connection to a needle or administration set."[10]

CHARACTERISTICS OF AN IDEAL RTA

In 2015, a multidisciplinary expert panel was convened to provide an assessment of current IV push medication delivery systems.[11] One of the objectives of the conference was to identify the characteristics of an ideal RTA device or system for IV push medications.[11] The expert panel identified 7 characteristics of an ideal RTA system:

- Prefilled standard single dose
- Manufacturer-prepared under current good manufacturing practices (cGMPs)
- Single-patient-use only
- No assembly required (ie, no needles, plunger, or labeling needed at the point of care)
- No drug manipulation required (eg, no need for further dilution)
- Labeling information consistent with ISMP labeling guidelines (including clear, easily understood, readable, and unobscured labels and easy-to-read gradations showing best contrast [vertical gradations preferred])
- Label and barcode on the outside of the tamper-evident package.[11]

BACKGROUND

According to published studies and recommendations, the use of manufacturer-prepared RTA syringes can reduce errors and the potential for patient harm. Additionally, RTA prefilled syringes provide benefits related to nursing workflow, pharmacy workflow, and cost containment initiatives.[7,12-15]

In November 2018, the Third Consensus Conference on the Safety of Intravenous Drug Delivery Systems convened in Chicago, Illinois. It included an expert panel with representatives from The Joint Commission (TJC), American Society of Health-System Pharmacists (ASHP), and ISMP. The purpose of this conference was to examine the available IV drug delivery systems and assess their benefits and concerns, as well as the ongoing threats to the safety of IV drug delivery. The consensus panel rated manufacturer-prepared RTA products as the safest option of the available IV drug delivery systems due to their continuous quality assurance during product production. The panel also mentioned that sometimes the lack of availability of preferred systems might pose a challenge in adoption.[16]

There has been an increased awareness and guidance around the use of manufacturer-prepared RTA prefilled syringes. Organizations, including TJC, ASHP, and the Centers for Medicare & Medicaid Services (CMS), have released similar guidelines and recommendations regarding the use of medications in RTA form.[17-19]

Table 1 is a representative timeline of relevant guidelines, recommendations, and pertinent articles related to RTA prefilled syringes. The guidelines and publications have evolved from a pharmacy-centered workflow to include the nursing medication administration workflow in order to support safe IV push medication practice. The 7 ideal characteristics of an RTA IV push medication system were identified by a multidisciplinary expert panel.[11] Researchers continue to evaluate the impact of RTA prefilled syringes on patient safety, clinical workflows, and overall cost.

ISMP SURVEYS AND RECOMMENDATIONS RELATED TO IV PUSH MEDICATION ADMINISTRATION

In response to the COVID-19 pandemic, ISMP published recommendations for facilities to plan for the anticipated shortage of smart infusion pumps and dedicated administration sets in April 2020.[28] They advised hospitals to consider IV push administration instead of infusions when appropriate and to consult hospital-specific IV push guidelines along with the *ISMP Safe Practice Guidelines for Adult IV Push Medications* before considering this alternative. To

TABLE 1

Timeline of Relevant Guidelines, Recommendations, and Published Articles Regarding RTA

Author/year	Title	Key highlights/recommendations
ISMP[20] (2010)	*Survey Shows Recession Has Weakened Patient Safety Net*	One third of 848 survey respondents reported that economic conditions have greatly impacted their practice including less safe drug purchasing decisions, such as switching to multiple-dose vials instead of using single-use vials and prefilled syringes.
Eichhorn[21] (2010)	*APSF Hosts Medication Safety Conference: Consensus Group Defines Challenges and Opportunities for Improved Practice*	Consensus group of 100 stakeholders from many different backgrounds defined challenges and opportunities for improved practice in the OR. High-alert drugs should be available in standardized concentrations/diluents prepared by pharmacy in RTA (bolus or infusion) form that is appropriate for both adult and pediatric patients. RTA syringes and infusions should have standardized fully compliant machine-readable labels.
De Giorgi et al[22] (2010)	*Risk and Pharmacoeconomic Analyses of the Injectable Medication Process in the Paediatric and Neonatal Intensive Care Units*	Risk and pharmacoeconomic analyses in their local setting revealed clinical pharmacy involvement, and the introduction of ready-to-use syringes for selected drugs appear as the most promising safety tools in connection with the injectable medication process.
ISMP[23] (2012)	*ISMP Survey Reveals User Issues With Carpuject Prefilled Syringes*	Many nurses reported using Carpuject prefilled cartridges as single- and multiple-dose vials withdrawing all or part of the medication from the cartridge into a syringe, often unlabeled, prior to administration.
Adapa et al[12] (2012)	*Errors During the Preparation of Drug Infusions: A Randomized Controlled Trial*	Providing drug infusions in syringes prefilled by pharmacists or pharmaceutical companies would reduce medication errors and treatment delays and improve patient safety.
ASHP[18] (2013)	*ASHP Guidelines: Minimum Standards for Pharmacies in Hospitals*	Whenever possible, medications should be available for inpatient use in single-unit packages and in RTA form. Manipulation of medications before administration (eg, withdrawal of doses from containers, reconstitution of powdered drug products, labeling of containers, and splitting of tablets) by final users should be minimized.
The Joint Commission[17] (2014)	*Standards BoosterPak for Safe Medication Storage 03.01.01*	Medications in patient care areas should be available in the most RTA forms commercially available or, if feasible, in unit doses that have been repackaged by the pharmacy or a licensed repackager.
ISMP[24] (2014)	*Survey: Some IV Medications Are Diluted Unnecessarily in Patient Care Areas, Creating Undue Risk*	Survey of registered nurses revealed that 83% of the nurses were further diluting IV push medications for adult patients prior to administration.
ISMP[9] (2015)	*ISMP Safe Practice Guidelines for Adult IV Push Medications*	Commercially available, prefilled syringes of medications that are already labeled should be used, when possible. To the greatest extent possible, provide adult IV push medications in RTA form (to minimize the need for manipulation outside of the pharmacy sterile compounding area).
Gorski et al[25] (2016)	*Infusion Therapy Standards of Practice*	In adults, use IV push medications in RTA form (to minimize the need for manipulation outside the pharmacy sterile compounding area).
Benhamou et al[13] (2016)	*Ready-to-Use Pre-filled Syringes of Atropine for Anaesthesia Care in French Hospitals - A Budget Impact Analysis*	The budget impact analysis shows that, although atropine prefilled syringes are more expensive than atropine prepared by conventional methods, its use would lead to significant cost savings. Savings would mainly be due to fewer medication errors and their associated consequences and the absence of wastage when atropine syringes are prepared in advance.
Fanikos et al[11] (2017)	*An Assessment of Currently Available IV Push Medication Delivery Systems*	Identified the 7 characteristics of an ideal RTA system.
Hertig et al[7] (2018)	*A Comparison of Error Rates Between IV Push Methods: A Prospective, Multisite, Observational Study*	The RTA group demonstrated a statistically significant lower observed error rate when compared with IV push traditional practice, suggesting that the use of this product is associated with fewer observed preparation and administration errors in the clinical setting.

(*continues*)

TABLE 1

Timeline of Relevant Guidelines, Recommendations, and Published Articles Regarding RTA (*Continued*)

Author/year	Title	Key highlights/recommendations
ISMP[26,27] (2018)	*Surveys Part 1 and 2: Unsafe Practices Persist With IV Push Medications and Action Is Needed to Improve Safety With Adult IV Push Medications*	When possible, dispense IV push medications in ready-to-administer RTA prefilled syringes in the correct concentration and volumes needed for common or patient-specific doses. The use of saline flush syringes should be eliminated for dilution and administration of medication. Avoid unnecessary dilution of RTA syringes by establishing proper procedures for IV push administration.
CMS[19] (2018)	*State Operations Manual Appendix A – Survey Protocol, Regulations and Interpretive Guidelines for Hospitals*	Whenever possible, medications are dispensed in the most RTA form available from the manufacturer or, if feasible, in unit doses that have been repackaged by the pharmacy.
Hansen et al[14] (2018)	*Insourcing RTA Syringes With IV Robotics*	Authors reviewed the benefits of RTA syringes along with the evaluation of insourcing RTA syringes during national drug shortages.
Gabay et al[16] (2020)	*Third Consensus Development Conference on the Safety of IV Drug Delivery Systems*	The panel was convened to assess the benefits and concerns of the available IV drug delivery systems and to examine ongoing threats to the safety of IV drug delivery. The panel reaffirmed that manufacturer RTA products remain the safest IV drug delivery system.
Degnan et al[8] (2020)	*Risk of Patient Harm Related to Unnecessary Dilution of Ready-to-Administer Prefilled Syringes: Literature Review*	Literature review concluding that unnecessary dilution of IV push medication in RTA syringes is an unsafe practice that occurs routinely and increases the risk of patient harm through errors related to incorrect dose, improper labeling of syringes, and the potential for microbial contamination.
ISMP[28] (2020)	*Planning for Anticipated Shortage of Smart Infusion Pumps and Dedicated Administration Sets*	Because of the COVID-19 pandemic, there is a significant increase in critically ill patients admitted to hospitals, and organizations are already experiencing shortages of smart infusion pumps and dedicated administration sets. Administering medications via IV push instead of a secondary infusion can be considered when appropriate. To support adult IV push administration, prefilled and/or RTA syringes of medications should be dispensed whenever possible.
Hertig et al[29] (2020)	*A Continuous Observation Workflow Time Study to Assess Intravenous Push Waste*	The availability of more precise clinically relevant vial and prefilled syringe drug product sizes (eg, vials and RTA prefilled syringes) may help address diversion by limiting the need for product waste and delays related to documentation and wastage.
Ludwin et al[6] (2020)	*Place of Prefilled Syringes in COVID-19 Patient Based on Current Evidence*	In emergency medicine, especially during cardiopulmonary resuscitation of patients with suspected/confirmed COVID-19, emergency staff should consider a combination of intraosseous access and drugs in prefilled syringes to reduce the time of infusion and the risk of infection. In emergency situations when treating COVID-19 patients wearing additional PPE can potentially increase mistakes during drug preparation and administration due to challenges related to limitation of movement range, speed of action of clinicians, reduced visibility, and fatigue resulting from working in high-stress environment. Best methods such as use of prefilled syringes should be sought to reduce potential errors, needlestick injuries, risk of infections, and increase in efficiency.
ISMP[30] (2020)	*ISMP Survey Provides Insights Into Preparation and Admixture Practices Outside the Pharmacy*	Survey in August 2020 of 444 practitioners of various backgrounds and settings was done to gather insights into preparation and admixture practices outside the pharmacy. Eighty-three percent of the respondents reported preparing IV push medications outside of the pharmacy at least 50% of the time. Lack of staff training was identified as a significant challenge, and 31% reported awareness of or personally experienced errors when preparing or admixing outside the pharmacy. The biggest safety challenge cited is rushing, especially during emergencies.
Gorski et al[31] (2021)	*Infusion Therapy Standards of Practice, 8th Edition*	INS recommends, in adults, using IV push medications in RTA form to minimize the need for manipulation outside the pharmacy sterile compounding area.

Abbreviations: APSF, Anesthesia Patient Safety Foundation; ASHP, American Society of Health-System Pharmacists; CMS, Centers for Medicare and Medicaid Services; COVID-19, coronavirus disease 2019; INS, Infusion Nurses Society; ISMP, Institute for Safe Medication Practices; IV, intravenous; OR, operating room; PPE, personal protective equipment; RTA, ready-to-administer.

support adult IV push administration, prefilled and/or RTA syringes of medications should be dispensed whenever possible.[28]

Between 2010 and 2020, ISMP conducted multiple surveys of health care professionals regarding patient safety issues related to IV push medication administration. In 2010, ISMP published survey results on assessing how the recession and economic downturn negatively affected medication safety.[20] One third of the total 848 respondents in the survey reported that the economic conditions have resulted in less-safe drug purchasing decisions, such as switching to multiple-dose vials instead of using single-use vials and prefilled syringes.[20] In 2012, another survey assessed safety issues regarding use of the Carpuject (Hospira Inc, a Pfizer company, New York, NY) cartridge syringe system.[23] Many of the 540 surveyed nurses reported using Carpuject prefilled cartridges as single- and multiple-dose vials by withdrawing all or part of the medication from the cartridge into a syringe, often left unlabeled, before administration to the patient.[23] This practice presented many potential safety issues and risks of errors, including microbial contamination, use of unlabeled or mislabeled syringes, dosing or measurement errors, needlestick injuries, and risk for drug diversion.[23] The 2014 survey had 1773 respondents and assessed the undue risk of unnecessarily diluting IV medications in patient care areas.[24] In 2018, ISMP published a 2-part follow-up survey to the 2014 survey.[26,27] The survey included 997 respondents and the results identified several unsafe practices that continued to persist, such as further diluting IV push medications prior to administration (84%), including manufacturer's prefilled syringes (16%); withdrawal of medications from prefilled syringes or cartridges to be transferred to another syringe for IV push administration (66%); and rarely or never labeling syringes (28%).[26] The second part of the survey provided recommendations to improve patient safety with adult IV push medications. It was determined that further action was needed to improve safety with adult IV push medications.

One recommendation was for facilities to dispense IV push medications in RTA prefilled syringes in the correct concentration and volumes needed for common or patient-specific doses, when possible. Additionally, a gap analysis tool was also created for institutions to assess their adult IV push medication practices.[27]

In a 2020 ISMP survey of clinicians that included 444 participants (85% included advanced practice nurses, certified registered nurse anesthetists, and anesthesiologists), rushing during emergency situations and interruptions/distractions were reported as the biggest challenge related to the preparation/admixing of these medications. Many respondents reported a concern of feeling ill-prepared to follow the standard routine processes during critical and time-sensitive conditions.[30] In many instances, they also reported having to rely on their memory to complete the required task. Concerns regarding the sterility of the preparation area, admixing processes, and the end product were also mentioned. Almost one third of the participants reported personally experiencing errors during preparation/admixing medications/infusions.[30] These conditions can be exacerbated during the COVID-19 pandemic, where clinicians face increased pressures and scarcity of resources during emergency situations.[6]

The 2020 ISMP survey described above discussed the urgency faced by clinicians during emergency situations and not feeling prepared to follow the standard procedures.[30] The survey reported practices related to the frequency of medication preparation, including admixing and/or infusions outside the pharmacy setting, implementation of safe practices for these procedures, and the training and perceived safety challenges related to medication/infusion preparation and admixing. Previously noted, 85% of the participants were advanced practice nurses; the remaining 15% were pharmacists, technicians, physicians, supervisors, and others who prepare or admix medications and/or infusions outside the pharmacy in clinical areas.[30] The survey results showed that 24% of the participants reported a frequency of preparing/admixing IV push medications outside of the pharmacy as *always* (or >95% of the time), and 34% of the participants answered *often* (or 51%–95% of the time). IV push medications were also reported as one of the types of sterile injectables that is most frequently prepared outside the pharmacy. Survey respondents were in moderate agreement regarding establishing a standard process for preparing or admixing and labeling, but fewer respondents reported that these procedures are being followed.

The other ISMP surveys identified unsafe IV push practices, such as the use of prefilled cartridges as single- and multiple-dose vials and unnecessary dilution of IV medications, including manufacturer-prepared RTA prefilled syringes in patient care areas.[20,23,24,26,27,30] It could be anticipated that the risk of medication errors will increase if these unsafe practices of IV push medication preparation and administration arise in stressful environments such as the COVID-19 pandemic. The use of manufacturer-prepared RTA prefilled syringes, where appropriate, can play an important role in reducing errors and increasing efficiency.[6]

ISMP SAFE PRACTICE GUIDELINES FOR IV PUSH MEDICATIONS

In 2015, ISMP published *Safe Practice Guidelines for Adult IV Push Medications* in an effort to provide health care practitioners with relevant information that assists in identifying and managing the inherent risks with this form of parenteral medication administration, specifically with high-alert medications.[9] ISMP recommends, to the greatest extent possible, providing adult IV push medications in an RTA form to minimize the need for manipulation outside of the pharmacy sterile compounding area.[9] Furthermore, the ISMP guidelines recommend that all stakeholders re-evaluate current products that are administered by IV push and

standardize, as much as possible, the use of RTA formulations and concentrations. In turn, health care providers can avoid the unnecessary and error-prone complexity of IV push medication preparation and administration, the risk of contamination, and personnel exposure.[9]

INFUSION THERAPY STANDARDS OF PRACTICE

Similarly, the Infusion Nurses Society (INS) publishes the *Infusion Therapy Standards of Practice* every 5 years to provide a framework and guide safe practices that help ensure the best patient outcomes.[25,31] In the Compounding and Preparation of Parenteral Solutions and Medications Standard, INS recommends administering IV push medications in a safe manner by using an RTA form for IV push medications in adults, minimizing the need for manipulation outside of the pharmacy sterile compounding area.[25,31]

ERRORS RELATED TO IV PUSH ADMINISTRATION

Higher rates of errors (48%–81%) have been reported for IV medications compared with other routes of medication administration.[32] This can be attributed to the complexity of steps involved in the preparation and administration of IV medications.[7] IV medication errors pose an increased risk of patient harm due to the immediate bioavailability of the medication, narrow therapeutic window, and challenges involved in the reversal of systemic effects.[8,32] These errors can have a negative impact on both patients and nurses involved.[32]

Application of Human Factors: Implementation of RTA Products

Human factors and systems engineering analyze and consider human behavior, such as strengths, limitations, equipment, environments, and how they are interconnected within systems to deliver safe care.[33] Any change made to one of the components of the work system can negatively or positively impact the other. Using a systems approach, health care organizations can identify operational issues and optimize patient care and employee satisfaction.[33]

Studies have shown that errors have been reported throughout the medication preparation and administration processes, such as miscalculations, microbial contamination, and failure to properly label syringes.[7,11] Because these are educated and licensed health care workers, it must be asked what component of the system led to these negative outcomes? All too often, clinicians are required to complete complex drug calculations in a high-stress environment and experience fatigue from long shifts with high-acuity patients. Hertig et al[7] identified 10 individual tasks that are required to successfully prepare and administer an IV push medication. Because it is estimated that 44% of nurses who administer IV push medications do so >5 times per shift, this could lead to multiple opportunities for use errors to occur.[7] Leback et al[34] used the framework of the Systems Engineering Initiative for Patient Safety (SEIPS) model to evaluate barriers and facilitators for safe injection practices. The researchers categorized the results using 5 SEIPS elements: persons, organization, technologies and tools, tasks, and environment. A total of 106 injections using either a single- or multidose vial was observed, and 36 interviews were completed. The results of the study demonstrated how each of the 5 SEIPS elements could impact safe injection practices. For example, feeling rushed and high patient turnover was identified as one of the highest barriers during the workflow of completing all necessary steps for a safe injection, leading some clinicians to skip steps.

Additional barriers to safe injection practice included environmental concerns, such as small patient care areas and limited storage areas; organizational barriers, which included inadequate staff or training and financial constraints; patients' unsafe movements, potentially leading to a needlestick injury; and tools, such as glass vials and lack of safety needles.[34] These barriers can be further amplified in high-stress situations, such as during the COVID-19 pandemic.

In the context of the SEIPS model to facilitate safe injection practices, manufacturer-prepared RTA prefilled syringes are tools that can help improve a clinician's workflow by providing standard single unit doses that do not require assembly or further dilution and are labeled with a bar code and/or radio-frequency identification (RFID) technology. This is especially important in complex environments, where clinicians experience interruptions, distractions, time pressure, and competing activities during medication administration. Additionally, manufacturer-prepared RTA prefilled syringes remove the need for the users to rely on memory to identify unlabeled syringes and do not require dilution, as well as reduce the number of medication preparation steps.

RTA Syringes Versus Traditional Vial/Ampule and Syringe Method

In a randomized, controlled trial, Adapa et al[12] identified that the process of medication preparation and administration at the bedside could require up to 41 individual steps. Not only did it take a lot longer (a statistically significant mean time increase of 106 seconds) for nurses to prepare medications at the bedside, in a stressful environment (eg, critical care unit), causing a delay, and bedside preparation led to less accuracy (eg, several instances of patients receiving >4 times the prescribed dose and, in some cases, incorrect concentrations). The risk of medication error was 17 times greater for the medications prepared at the bedside

compared with RTA prefilled syringes. Another prospective, multisite, observational study by Hertig et al[7] compared the error rates between IV push methods. They observed the medication preparation and administration errors of the manufacturer-prepared Simplist (BD Rx Inc, later acquired by Fresenius Kabi, Lake Zurich, IL) RTA prefilled syringes compared with the traditional vial and syringe method (including cartridge-based syringe systems). The authors reported a 2.5% error rate in the RTA group compared with a 10.4% error rate in the traditional method group. This was a statistically significant difference that suggested that the RTA prefilled syringes were related to fewer errors when compared with traditional practice.[7] During the COVID-19 pandemic, the added complexity of modified workflows, additional PPE, heavy workload, and extra steps required can greatly increase the level of stress and potentially result in an increased number of errors.[6] Reducing the number of complex steps and manipulations by using manufacturer-prepared RTA prefilled syringes is one of the ways to reduce the risk of medication errors. Several institutions and societies have also provided guidance and recommendations to use RTA products when possible (Table 1).

Inaccurate and Missing Labels

Another risky practice that was discovered in the surveys conducted by ISMP was related to inaccurate and missing labels on IV push syringes prepared before administration. According to the 2018 ISMP survey, the syringes prepared away from the patient's bedside were labeled only 50% of the time.[26] Inaccurate label methods included taping vials to syringes and missing or incomplete labels, which made it challenging for nurses to differentiate between multiple syringes. Sodium chloride 0.9% flush syringes are not designed or approved by the US Food and Drug Administration for dilution of medications. When sodium chloride 0.9% flush syringes are used inappropriately for dilution, they are rarely relabeled. These situations forced the nurses to rely on volume, size, or any other notable physical differences in medications or syringes to distinguish between the medications, which is an unsafe practice.[26]

There have been various reports in the literature of patient harm related to the administration of incorrect medications attributed to missing or incomplete labels. Syringe swap cases are one of the most common causes resulting in medication errors. In a case reported by ISMP, a patient under general anesthesia received epinephrine from an unlabeled syringe instead of bupivacaine in his knee. That patient experienced severe cardiovascular events and died as a result.[35]

Microbial Contamination

There is an increasing awareness in recent years of microbial contamination-related errors involving unsafe practices around IV push medication preparation and administration.[8] Published literature has shown that there is a higher risk of microbial contamination involved in preparing and manipulating syringes in a nonsterile environment.[8,36] Various guidelines and recommendations have been issued to reduce the potential for microbial contamination resulting from the preparation and manipulation of sterile medications. United States Pharmacopeia (USP) Chapter <797> provides specific standards under which the sterile medications should be compounded.[37] The Association for Professionals in Infection Control and Epidemiology (APIC) also sheds light on risks of patient harm resulting from microbial contamination during the preparation and manipulation of sterile medications outside of International Organization of Standardization (ISO) Class 5 settings.[8,38]

COST-EFFECTIVENESS OF RTA

Patient harm attributed to medication errors can have a significant economic impact on the health care system.[15,22] A total cost of $21 billion has been estimated to result from preventable medication errors in the United States. Furthermore, it was estimated that, in the United States, injectable medication-related preventable adverse drug events (ADEs) contribute to an increase of $2.7 billion to $5.1 billion in annual costs to payers. An ADE resulting from a medication error is classified as a preventable ADE.[15]

In addition to the direct medical costs (increased hospital length of stay, treatment, and monitoring of the patient's condition) and clinical patient harm resulting from a preventable ADE, there are additional indirect (soft) costs involved. Indirect costs include an impact on the patient's financial, mental, and physical quality of life. The health care institution and its clinicians can also suffer from the substantial economic burden incurred from preventable ADEs due to lawsuits and provider medical liability claims.[15]

Significant cost savings can be achieved by using manufacturer-prepared RTA prefilled syringe products compared with the traditional vial or ampule methods. A budget impact simulation model for a French hospital demonstrated 1-year financial savings of €5,255,304 ($6,219,731 USD) by using atropine prefilled syringes rather than conventional methods of syringe preparation (CMP). Moreover, medication errors outweighed other costs (€9,425,448 or $11,154,687 USD) related to using CMP. Reduced product waste (prepared and unused) yielded significant savings of €1,167,323 ($1,381,485 USD). Although the RTA syringes may be more expensive than traditional vials and ampules, the overall economic impact of various factors, including product wastage, medical outcomes, and potential errors, must also be considered. The use of prefilled RTA syringes can result in a lower cost to institutions.[13]

Pharmacy Workforce Impact of In-House Compounding

Compounding any medication using traditional vial and syringe methods requires time, labor, and the proper

environment. For example, the reconstitution and dilution of a lyophilized drug powder can take >20 minutes to prepare a single dose. The overall cost of in-house compounding includes pharmacy workforce labor, time, supplies (diluent, syringes, needles, caps, labels, alcohol wipes), and compounding waste.[14]

Automation and additional technology might be required to prepare high-use RTA medications in the hospital pharmacy to ensure accuracy, minimize the risk of contamination, and reduce the likelihood of repetitive-stress injury for compounding technicians. Additional headcounts and storage space are typically required for any type of automation device in addition to a quality assurance program and training.[14]

Role of RTA in Reducing IV Push Waste and Drug Diversion Costs

During the COVID-19 pandemic, an increase in opioid and other substance abuse mortality rates has been reported at national, state, and local levels. More than 40 states have also reported ongoing concerns for those with a mental illness or substance use disorder.[39] Prescription drug diversion is a $25 billion-a-year industry according to Drug Enforcement Administration reports. Proper handling and disposal of controlled substances is an essential component that requires hospitals to invest time, money, and resources. Policies and procedures vary among various institutions, and disposal of controlled substances typically requires proper documentation in the presence of witnesses.[29]

A 2017 supply optimization study used 2 models to identify the annual cost and waste associated with controlled substances (IV hydromorphone and IV morphine) in an emergency department environment. The authors reported significant waste in both models. The price optimization model, where the most cost-effective vials were selected, yielded a waste cost of $139,563.10 (56,171 mg), and the waste optimization model, where vials were selected based on the least amount of possible waste, yielded $161,798.80 (16,612.99 mg) in waste cost.[29,40] A 2020 workflow time observation study by Hertig et al[29] assessed the total waste associated with IV push administration of controlled substances (fentanyl, morphine, and hydromorphone). The authors evaluated the total waste by observing the quantity of drug waste and the workforce time related to the disposal of waste. It was found that when using a fentanyl 100-mcg vial, at least half of the medication was wasted 50% of the time and three quarters of the medication was wasted 46% of the time. Similarly, for IV push hydromorphone when using the 1-mg vial, at least half of the medication was wasted 63% of the time and 80% of the medication was wasted 18% of the time. Limited morphine waste was identified, because the units that were studied had minimal morphine usage, and in instances where morphine was ordered, the full vial was utilized. The total annual cost of waste (product waste and workforce waste) was calculated to be $35,425.51. This study described that the availability of precise presentations, such as an appropriate size vial or RTA prefilled syringe, can minimize waste and have a significant impact on reducing the overall costs for the hospital. The availability of precise presentations also reduces the risk of drug diversion by limiting the opportunity of diverting medications that have not yet been wasted and minimizes delays caused by time required for the drug wasting process and required documentation.[29]

DISCUSSION

The use of RTA prefilled syringes, where possible, can simplify the drug preparation and administration process in high-stress emergency situations. Shortage of staff and the diversion of staff to unfamiliar care areas has resulted in an extra workload and added emotional stress for health care workers caring for COVID-19 patients.[5,6] Recent surveys have shown that the biggest challenge reported by the clinical staff was being rushed during emergency situations and during preparation/admixing tasks during critical and time-sensitive situations.[23,24,26,30]

The Environmental Protection Agency has issued recent regulations for the management of hazardous pharmaceutical waste by health care facilities, including hospitals. This new regulation prohibits the disposal of pharmaceutical hazardous waste, including controlled substances, down the drain, a practice more commonly referred to as *sewering*.[41] It will impact the workflows of disposing unused hazardous pharmaceutical waste in the hospitals (eg, after a surgical procedure in the operating room) and potentially require additional disposal equipment and new procedures. Minimizing waste by leveraging product optimization can help reduce the time and workload for nurses and staff.[29,41] Finally, RTA prefilled syringes can have a significant impact in reducing the time of infusion and the risk of infections, especially during the COVID-19 pandemic. Moreover, with the additional precautions required during the COVID-19 pandemic, PPE can limit the range of movement, reduce efficiency and visibility, and increase fatigue when compounded under stressful situations.[6] PPE can also prolong the medication preparation time and, in some cases, require temporary or permanent workflow changes. It can reduce the risk of needlestick injuries, which may cause additional stress and result in complications. Needlestick injuries requiring consultation or treatment in infectious disease wards can negatively impact an already stressed workforce.

Virus mutations of COVID-19 have occurred, and new variant strains have been reported around the world.[42] It is important to incorporate best practices as part of standard practice in facilities to better prepare for any future crisis situations. Safe IV push medication practices, guidelines, and recommendations, as mentioned above, support the use of prefilled RTA syringes, when possible, to help reduce errors and related patient harm and also help create an

efficient clinical workflow to reduce staff burden, especially during a high-stress crisis situation.

LIMITATIONS

This review article was not intended to answer a specific clinical question. The authors' research found that there is variability in types of evidence that are available (observational studies, surveys, case reports, and risk analysis). The impact of RTA prefilled syringes on the COVID-19 pandemic is continuing to evolve. Additional investigations are recommended to further understand the impact of manufacturer-prepared RTA prefilled syringes and to evaluate their impact on clinical workflow, cost savings, drug waste, drug diversion, reduction of microbial contamination, and medication errors.

CONCLUSION

The pandemic has brought additional challenges to health care, including changes in workflows, which may increase the chance of errors during bedside and in-house compounding of required medications and can lead to patient harm.[6] There are also several published reports of errors related to IV push administration leading to potential patient harm.[8] The errors highlighted in the ISMP surveys include unlabeled syringes, incorrect dose or concentration, measurement errors, risk of drug diversion, microbial contamination, and needlestick injuries, especially when nurses compound or manipulate medications at the patient's bedside prior to administration.[20,23,24,26,27,30] Other published studies have demonstrated that the preparation of IV medications at the bedside requires multiple steps, and reducing these complex steps and manipulations can reduce the number of errors.[7,12] Additionally, the use of prefilled RTA medication syringes can help reduce unnecessary wastage of medications and the risk of drug diversion by optimizing pharmaceutical product size.[29]

Manufacturer-prepared RTA prefilled syringes can play an important role in simplifying these processes and reducing errors and related potential patient harm. Moreover, the use of manufacturer-prepared RTA prefilled syringe products is supported by guidelines, recommendations, and published literature. Based on this review, they are an ideal option for safe IV push medication administration, especially in high-stress critical situations, such as the COVID-19 pandemic.

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