



## Evaluation of an intravenous preparation information system for improving the reconstitution and dilution process



Yun Hee Jo<sup>a,b</sup>, Wan Gyoon Shin<sup>a,\*</sup>, Ju-Yeun Lee<sup>c</sup>, Bo Ram Yang<sup>d</sup>, Yun Mi Yu<sup>a</sup>, Sun Hoi Jung<sup>b</sup>, Hyang Sook Kim<sup>b</sup>

<sup>a</sup> College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University, 103 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea

<sup>b</sup> Department of Pharmacy, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea

<sup>c</sup> College of Pharmacy, Institute of Pharmaceutical Science and Technology, Hanyang University, Ansan 15588, Republic of Korea

<sup>d</sup> Division of Clinical Epidemiology, Medical Research Collaborating Center, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea

### ARTICLE INFO

#### Article history:

Received 10 November 2015

Received in revised form 1 July 2016

Accepted 6 July 2016

#### Keywords:

Electronic medical record  
Intravenous preparation information system  
Interrupted time series analysis  
Proper reconstitution rate  
Proper dilution rate

### ABSTRACT

**Background:** There are very few studies reporting the impact of providing intravenous (IV) preparation information on quality use of antimicrobials, particularly regarding their reconstitution and dilution. Therefore, to improve these processes in IV antimicrobial administration, an IV preparation information system (IPIS) was implemented in a hospital.

**Objective:** We aimed to evaluate the effect of improving reconstitution and dilution by implementing an IPIS in the electronic medical record (EMR) system.

**Methods:** Prescriptions and activity records of nurses for injectable antimicrobials that required reconstitution and dilution for IV preparation from January 2008 to December 2013 were retrieved from EMR, and assessed based on packaging label information for reconstituting and diluting solutions. We defined proper reconstitution and dilution as occurring when the reconstitution and dilution solutions prescribed were consistent with the nurses' acting records. The types of intervention in the IPIS were as follows: a pop-up alert for proper reconstitution and passive guidance for proper dilution. We calculated the monthly proper reconstitution rate (PRR) and proper dilution rate (PDR) and evaluated the changes in these rates and trends using interrupted time series analyses.

**Results:** Prior to the initiation of the reconstitution alert and dilution information, the PRR and PDR were 12.7 and 46.1%, respectively. The reconstitution alert of the IPIS rapidly increased the PRR by 41% ( $p < 0.001$ ), after which the PRR decreased by 0.9% ( $p = 0.013$ ) per month after several months. However, there was no significant change in the rate or trend of the PDR during the study period.

**Conclusions:** This study demonstrated that the provision of reconstitution alerts by the IPIS contributed to improving the reconstitution process of IV antimicrobial injection administration. However, providing passive information on dilution solutions was ineffective. Furthermore, solutions to ensure the continuous effectiveness of alert systems are warranted and should be actively sought.

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**Abbreviations:** CPOE, computerized physician order entry; EMR, electronic medical record; IPIS, IV preparation information system; IPIS.R, IPIS reconstitution set; IPIS.RD, IPIS reconstitution and dilution set; IV, intravenous; PDR, proper dilution rate; PRR, proper reconstitution rate; SNUH, Seoul National University Hospital.

\* Corresponding author.

**E-mail addresses:** [jobright@snuh.org](mailto:jobright@snuh.org) (Y.H. Jo), [wgshin@snu.ac.kr](mailto:wgshin@snu.ac.kr) (W.G. Shin), [jypharm@hanyang.ac.kr](mailto:jypharm@hanyang.ac.kr) (J.-Y. Lee), [bebe77@snu.ac.kr](mailto:bebe77@snu.ac.kr) (B.R. Yang), [yupharm@snu.ac.kr](mailto:yupharm@snu.ac.kr) (Y.M. Yu), [shojjung@snuh.org](mailto:shojjung@snuh.org) (S.H. Jung), [hyangsook0716@hanmail.net](mailto:hyangsook0716@hanmail.net) (H.S. Kim).

<http://dx.doi.org/10.1016/j.ijmedinf.2016.07.005>

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### 1. Introduction

Proper reconstitution and dilution, which ensures the correct concentration and stability of intravenous (IV) drugs, are essential to optimizing the efficacy and safety of administered medications. However, the process of IV preparation of some medications for administration to patients is complex and error-prone [1–4]. Previous studies reported that IV preparation errors occurred in 20 [1] and 26% [2] of IV medication orders. In addition, reported wrong dilution error was as high as 49% in Germany hospital wards [3].

In Korea, pharmacy departments of general hospitals do not dispense all IV drugs in the form of ready-to-use IV bags except for cytotoxic drugs and total parenteral nutrition mixtures. Instead, they have adopted a floor stock system for fluid distribution due to the shortage of pharmacists. Therefore, most injectable medications are distributed to wards in their original vials or ampules. While injectable drugs provided in solution form can be administered to patients without reconstitution or dilution, injectable drugs provided in powder form should be either simply reconstituted or also diluted following reconstitution with fluids stocked in wards, prior to administering them to patients. Reconstitution is the process of changing a medication from powder form to an injectable, solution form, and dilution is the process of reducing the concentration of the reconstituted solution to a lower concentration that could be directly infused into patients. Errors resulting from the process of reconstitution or dilution can create stability problems such as inadequate dissolution and inactivation or precipitation of chemicals that might cause harm to patients, such as thrombus formation and even death, in some cases [3,5]. The provision of insufficient information to medical teams or lack of knowledge of medication characteristics is a well-known source of medication errors [6–8].

Two previous studies reported that antimicrobials were the medications most prevalently associated with IV administration errors [9,10]. Many strategies have been implemented to promote quality use of antimicrobials [11]. In nurses' IV preparation processes, reconstitution and dilution errors were found not to be negligible [12,13]. Proper reconstitution and dilution, which ensures the correct concentration and stability could be one of such strategies and is critical to the efficacy and safety of treatment with injectable antimicrobial agents. Therefore, based on the decision of the Hospital Drug Committee, an IV preparation information system (IPIS) for injectable antimicrobial prescriptions was implemented in the electronic medical record (EMR) system to promote the clear description of medication orders and reduce IV medication preparation errors in our tertiary teaching hospital.

There are numerous previous studies on the effects of clinical decision support systems or medication information provision [14–19]. However, the impacts of error prevention programs involving IV reconstitution and dilution, as well as the continuation of the intervention effect have not been investigated. Therefore, we aimed to evaluate the effect of improving reconstitution and dilution by implementing an IPIS in the EMR system.

## 2. Methods

### 2.1. Setting and design

This study was conducted at a 1500-bed tertiary care Teaching Hospital of the Seoul National University Hospital (SNUH). SNUH initiated the computerized physician order entry (CPOE) system requiring daily medication orders by physicians in 1999 and implemented a comprehensive EMR system in 2004. Since the EMR system was initiated, the doctors and nurses employed in SNUH have been educated on using the EMR system and the new functions for clinical decision support. To prevent IV preparation errors, the Drug Committee of the SNUH made the decision, to implement a directive requiring doctors to prescribe reconstitution and dilution solutions for injectable antimicrobial orders, to record the medical orders clearly, and to provide IV preparation information to doctors and nurses.

Based on this decision, pharmacists built a database of proper reconstitution and dilution solution instructions for injectable antimicrobial drugs, and an IPIS was implemented in the EMR system of the SNUH comprising reconstitution alerts and dilution

information. However, the reconstitution alert and dilution information of the IPIS commenced sequentially in June 2010 and April 2011. Records of prescribed IV antimicrobials provided in powder form for adult patients from January 2008 to December 2013 were retrieved from the electronic records and reviewed by two pharmacists. They also reviewed the nurse's administration records. A retrospective interrupted time series design was applied in assessing whether the IPIS improved the reconstitution and dilution processes of IV antimicrobial administration.

### 2.2. Ethics statement

This study was approved by the Institutional Review Board of the Seoul National University Hospital (SNUH, H-1311-083-536, Republic of Korea). Because the study posed no more than minimal risk to the participants and involved no medical procedure, the review board agreed that written informed consent was not required. Patient records was anonymized and de-identified prior to analysis.

### 2.3. Implementation of the intravenous preparation information system

In June 2010, a pop-up information system for reconstitution solutions available at the point of injectable antimicrobial order entry was implemented in the EMR. For example, any medical doctor who prescribed amphotericin B injection would find pop-up-alert information conveying the pertinent message "Amphotericin-B is a powdered injection that requires reconstitution prior to administration. Would you like to prescribe 'water for injection, 20 mL' for reconstitution?" (Fig. 1).

The physicians in SNUH could accept or ignore the alert message. If the alert message was accepted, the suggested reconstitution solution was prescribed automatically. Otherwise, the doctors did not order the reconstitution solution, and nurses reconstituted the IV antimicrobial with a solution stocked in the floor according to IV preparation manual in the ward.

From April 2011, e-formulary containing dilution information that could be viewed easily in the EMR system by nurses, as well as doctors, was provided. Physicians and nurses in the SNUH could access some information regarding the prescribed drug in the e-formulary in the EMR by right-clicking the mouse on the prescription medical record. In addition, if they clicked the menu bar button and 'formulary' button in the EMR, they could see the e-formulary and search for the drug information (Fig. 2).

Dilution information is displayed as "Administer intravenously after reconstituting with water for injection and further diluting in 5% dextrose solution." (Fig. 2). The information for reconstitution was provided by a pop-up alert, while the dilution information was of a passive guidance type in this IPIS.

### 2.4. Definition of parameters determined

In this study, we included injectable antimicrobials that required reconstitution and dilution before administration (Table 1).

We classified these agents into two groups according to the required reconstitution solution. The P1 group involved the powdered form of the antimicrobials, which was reconstituted in saline solution to the final dilution. For example, if a physician selects 'ceftazidime' from the P1 group and 'normal saline 100 mL' for dilution purposes, it would be possible to reconstitute ceftazidime with 10 mL solution from 100 mL of normal saline and then dilute the reconstituted solution with same saline. However, the P2 groups consisted of antimicrobials requiring only water for reconstitution into the injected form; therefore, it was necessary

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