Systemic Causes of In-Hospital Intravenous Medication Errors: 
A Systematic Review

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Objectives: Delivery of intravenous medications in hospitals is a complex process posing to systemic risks for errors. The aim of this study was to identify systemic causes of in-hospital intravenous medication errors.

Methods: A systematic review adhering to PRISMA guidelines was conducted. We searched MEDLINE (Ovid), Scopus, CINAHL, and EMB reviews for articles published between January 2005 and June 2016. Peer-reviewed journal articles published in English were included. Two reviewers independently selected articles according to a predetermined PICO tool. The quality of studies was assessed using the GRADE system and the evidence analyzed using qualitative content analysis.

Results: Eleven studies from six countries were included in the analysis. We identified systemic causes related to prescribing (n = 6 studies), preparation (n = 6), administration (n = 6), dispensing and storage (n = 5), and treatment monitoring (n = 2). Administration, prescribing, and preparation were the process phases most prone to systemic errors. Insufficient actions to secure safe use of high-alert medications, lack of knowledge of the drug, calculation tasks, failure in double-checking procedures, and confusion between look-alike, sound-alike medications were the leading causes of intravenous medication errors. The number of the included studies was limited, all of them being observational studies and graded as low quality.

Conclusions: Current intravenous medication systems remain vulnerable, which can result in patient harm. Our findings suggest further focus on medication safety activities related to administration, prescribing, and preparation of intravenous medications. This study provides healthcare organizations with preliminary knowledge about systemic causes of intravenous medication errors, but more rigorous evidence is needed.

Key Words: patient safety, medication safety, intravenous medications, medication errors, systemic cause, risk management, systematic review

Intravenously administered drugs are associated with the highest medication error frequencies and more serious consequences to the patient than any other administration route.1–3 The bioavailability of intravenously administered medication is high, therapeutic dose range is often narrow, and effects are hard to undo. Many intravenously administered drugs are high-alert medications, bearing a heightened risk of causing significant patient harm if used in error.4 For example, in intensive care, the most serious medication errors are associated with intravenously administered high-alert medications, such as catecholamines, insulin, electrolytes, opioids, and parenteral nutrition.5,6

Intravenous medication administration is a multistep process involving specific administration devices, information systems and many healthcare professionals with different work tasks and skills. This complex delivery process poses to safety risks if appropriate systemic defenses are not in place.7–10 Identification of the systemic causes of medication errors (e.g., the possibility to make mistakes in infusion pump programming or confusion between similar drug names and packages) highlights the weaknesses of current intravenous medication practices. This enables the development of medication processes by implementation of effective systemic defenses to prevent medication errors (e.g., smart infusion pumps with error-reduction software or effective means to prevent confusion between similar drug names and packages).

However, the systemic causes of errors throughout the intravenous medication process have not been systematically reviewed. Previous systematic reviews have focused on types and incidence of intravenous medication errors5 or the effectiveness of smart infusion pumps as a systemic defense.11–13 These studies present important knowledge of the frequency of errors and effectiveness of a systemic defense, but they do not focus on medication safety issues throughout the in-hospital intravenous medication process. The aim of our study was to explore recent evidence of systemic causes of in-hospital intravenous medication errors to inform medication safety improvement activities.

METHODS

Study Design

A systematic review of recent evidence on systemic causes of in-hospital intravenous medication errors was carried out following the PRISMA guidelines for undertaking and presenting systematic reviews.12 The quality of included studies was assessed according to the GRADE system.13 The included articles were analyzed using qualitative content analysis.14,15

Search Strategy

A systematic literature search was performed in June 2016 on MEDLINE (Ovid), Scopus, CINAHL, and EMB reviews covering the period from January 2005 to June 2016. This period was chosen to focus on the most recent evidence published in peer-reviewed journals. An example of the search strategy is presented in Table 1.

We divided the search terms into two themes (“intravenous medication therapy” and “medication errors”), both of which needed to appear in the included articles. The theme “medication error” was chosen according to our study objectives to explore preventable adverse drug events, which occur as a consequence of errors in the medication process caused by omissions or commissions.5,16 The search strategy was completed with other terms...
Inclusion and Exclusion Criteria

We applied a predetermined PICO tool (participants, interventions, comparison, and outcomes) to select studies for inclusion. A study was included if participants were hospitalized patients or the study used a patient scenario in a simulated hospital environment, and patients received intravenous medication. We decided to exclude studies conducted in ambulatory settings, such as home infusion chemotherapy, because we wanted to focus on in-hospital intravenous medication process. We also excluded studies focusing on multiple administration routes, if the findings related to intravenous administration route could not be reliably identified and extracted from the results. Comparison was not required. Studies applying measures associated with systemic causes resulting in medication errors or assessment of a system defense to prevent medication errors were included. Studies exploring unpreventable adverse drug events or only incidence and types of medication errors were excluded. Only English language articles were included. Peer-reviewed journal articles using all methods and study designs were included.

Study Selection

After the removal of duplicates, the search produced 1417 potentially relevant publications (Fig. 1). Two reviewers (S.K., I.N.) independently selected studies based on the titles. In case of disagreement, the article was included in the next phase in which the reviewers (S.K., I.N.) independently selected studies based on the abstracts. Disagreements were resolved through discussion and consensus with a third reviewer (A.R.H.). The reviewers (S.K., I.N.) independently selected studies based on full texts of the remaining publications. The articles fulfilling inclusion criteria by both reviewers were included (n = 36). Disagreements were resolved through discussion and consensus with the third reviewer (A.R.H.), which led to the inclusion of nine more articles. A total of 45 publications met the inclusion criteria. After this, reference lists of the included articles were searched manually for relevant articles (n = 12), giving us a total of 57 included studies.

We identified two major themes among the selected articles: systemic causes of in-hospital intravenous medication errors and systemic defenses to prevent errors (Fig. 1). The articles focusing on systemic causes of intravenous medication errors (n = 11) are reported in this publication. Articles focusing on systemic defenses to prevent intravenous medication errors are discussed in another publication.

Data Extraction and Analysis

Data extraction and analysis were carried out by one of the authors (S.K.), and the results were carefully reviewed by the other authors (I.N., A.R.H., M.A.). Study characteristics, country and setting, objectives, study design, materials and methods, key findings, and quality of evidence were extracted to a table (Supplementary File 1, http://links.lww.com/JPS/A243). We assessed the quality of evidence using the GRADE system, which has the following four levels of evidence: very low, low, moderate, and high.13 Evidence from randomized controlled trials (RCTs) was graded as high quality and evidence that included observational data was graded as low quality. Factors that decreased the quality of evidence (e.g., study limitations and inconsistency of results) or increased the quality of evidence (e.g., large magnitude of effect) were also taken in account. Measures used in the articles concerning systemic causes of in-hospital intravenous medication errors were extracted to Table 2.

We analyzed the contents of the included articles using qualitative content analysis to identify systemic causes, examples of errors, and suggested systemic defenses for error prevention (Table 3).10,14,15 We used Leape’s classic analysis of medication errors as a foundation of our taxonomy.15,16 Because of the fast development in medication safety research during the past decades and the most important medication safety issues arising from the studies included in our systematic review, we had to make some modifications to the categorizations (Table 3, Table 4). Because we wanted to identify the most crucial systemic risk factors causing errors in the intravenous medication process, we defined a systemic cause as a system failure or an iterative error-prone process step or task, which can be replaced with safer system modifications (e.g., calculation tasks related to preparation can be removed by using standard concentrations of prefilled syringes). The findings were extracted and classified according to the error type and medication process stage, in which the error happened or could have been prevented.
The systemic causes affecting more than one process stage were identified and presented in Table 4.

**RESULTS**

**Characteristics of the Included Studies (n = 11)**

This systematic review is based on 11 peer-reviewed original articles (Supplementary File 1, http://links.lww.com/JPS/A243). The studies were conducted in the United Kingdom (n = 4), United States (n = 3), Spain, France, Republic of Korea, and Canada. All studies were carried out in hospital setting. Three studies were conducted in neonatal intensive care units and three in adult oncology.

All of the included studies applied an observational study design (Supplementary File 1, http://links.lww.com/JPS/A243). Four of the studies were retrospective analyses of medication error reports, three were observational studies involving analyses of infusion concentrations, two were interview studies, one was a prospective analysis of medication orders, and one was a direct observation study. The three studies investigating infusion concentrations to detect preparation errors used a controlled study design. More than one error detection method was used in two studies, of which one combined a video...
analyses of preparation technique and revision preparation protocols with analysis of infusion concentrations, and the other used interviews to complement direct observation. Six studies used self-reporting methods, such as voluntary medication error reporting and interviews. The study limitations were not reported and their influence was not assessed in three studies. None of the included studies applied RCT design, which is why they were graded as low quality.

The measures used to identify and describe systemic causes of medication errors in the studies varied, but some shared measures were identified (Table 2). Actual or potential systemic causes of errors were used in studies focusing on a larger scale of errors in multiple process stages. Concentration accuracy of prepared infusion solution was used to identify preparation errors in studies comparing different ways of preparing intravenous medications to identify error risk factors. Three of the studies also focused on contributing factors to medication errors.

**Systemic Causes of Medication Errors and Potential Systemic Defenses for Error Prevention**

The studies identified systemic causes of intravenous medication errors related to prescribing (n = 6 studies), preparation (n = 6), administration (n = 6), dispensing and storage (n = 5), and treatment monitoring (n = 2) (Table 3). The process stage with the most systemic error causes identified was administration. The manual adjustment of infusion rates for each patient is an especially high-risk task, which can lead to wrong dose errors. An infusion pump programming error can occur as a consequence of confusion between hours and minutes, weight and volume, decimals, and program time and volume. In all of the studies, potential systemic defenses for intravenous medication error prevention were suggested (Table 3). Error prevention strategies were presented in discussion sections of the articles; thus, their effectiveness was not measured. Overall, activities related to process standardization, replacement of error-prone tasks with technological solutions and staff education were suggested to decrease possibilities of errors and improve error detection.

Some systemic causes enabled medication errors in more than one process stage (Tables 3, 4). Insufficient actions to secure safe use of high-alert medications and lack of knowledge of the drug were identified as the two causes, which affected the most process stages, followed by calculation tasks and confusion between look-alike, sound-alike medications (LASAs). The studies also pointed out that absence of a systemic defense, or an existing defense breaking down, can enable errors. For example, failure to review orders after prescribing or to double-check during the preparation and administration stages can let errors actually reach the patient.

**DISCUSSION**

To the best of our knowledge, this is the first systematic review to summarize systemic causes of intravenous medication errors in hospitals. We found a limited number of studies, all of them being observational studies not providing the most rigorous evidence. Current intravenous medication systems remain vulnerable, which can result in patient harm. According to the included studies, administration, prescribing, and preparation are the process phases most prone to systemic errors. We found insufficient actions to secure safe use of high-alert medications and lack of knowledge of the drug two leading error causes in multiple process stages, followed by calculation tasks, failure in double-checking procedures, and confusion between LASA medications.

Considering the issues related to high-alert medications, the Institute for Safe Medication Practices recommends standardizing the ordering, storage, preparation, and administration of high-alert medications and improving access to information about these drugs. Furthermore, healthcare organizations should use multidisciplinary teams to review more carefully and standardize the use processes of high-alert medications through risk management strategies, such as failure mode and effects analysis and root cause analysis of reported errors.
### TABLE 3. Systemic Causes of Intravenous Medication Errors and Potential Systemic Defenses for Error Prevention Identified in the Included Studies (N = 11)

<table>
<thead>
<tr>
<th>Error Type</th>
<th>Systemic Causes and Examples of Errors</th>
<th>Potential Systemic Defense for Error Prevention</th>
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<tr>
<td><strong>Prescribing (ordering, transcription and order verification)</strong> (n = 6)&lt;sup&gt;18,19,21–23,25&lt;/sup&gt;</td>
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<td><strong>Wrong drug</strong>&lt;sup&gt;22,23&lt;/sup&gt;</td>
<td>LASA medications; communication errors: choosing a wrong drug (e.g., a sound-alike drug), confusion with drug name because of verbal prescription&lt;sup&gt;22,23&lt;/sup&gt;</td>
<td>Incorporating medical consultation and multidisciplinary reports to CPOE&lt;sup&gt;22&lt;/sup&gt;</td>
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<td><strong>Wrong dose</strong>&lt;sup&gt;19,21–23&lt;/sup&gt;</td>
<td>CPOE and CDSS: not taking CPOE alarms into account, “alarm fatigue,” inappropriate adaptation (e.g., 10 mg/kg instead of 15 mg/kg), weight (e.g., 64 kg instead of 74 kg), or unit (e.g., 3 mg instead of 3 g)&lt;sup&gt;22,23&lt;/sup&gt;</td>
<td>Standardized procedures for high-alert medications and emergencies&lt;sup&gt;23&lt;/sup&gt;</td>
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<td><strong>Wrong route</strong>&lt;sup&gt;25&lt;/sup&gt;</td>
<td>CPOE and CDSS: the possibility to choose wrong route (e.g., IT instead of IV)&lt;sup&gt;25&lt;/sup&gt;</td>
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<td><strong>Wrong choice</strong>&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Lack of knowledge of the drug: failure to adjust dose to comorbidities (e.g., renal impairment, sleep apnea) or other drugs (e.g., opioid and multiple CNS drugs)&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Pharmacists' analysis of prescriptions and duplication of previous order in CPOE&lt;sup&gt;22&lt;/sup&gt;</td>
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<td><strong>Multiple error types</strong>&lt;sup&gt;18,19,22&lt;/sup&gt;</td>
<td>CPOE and CDSS: failure in documentation (e.g., wrong patient identity or treatment setting identification, incomplete or illegible prescription, contradictory or duplicated orders, prescription forgotten, or documented in wrong place)&lt;sup&gt;19,22&lt;/sup&gt;</td>
<td>Increasing vigilance and adapting alarms to the needs of prescribing physicians&lt;sup&gt;22&lt;/sup&gt;</td>
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<tr>
<td><strong>Dispensing and storage</strong> (n = 5)&lt;sup&gt;18,19,21,23,25&lt;/sup&gt;</td>
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<td><strong>Wrong drug</strong>&lt;sup&gt;18,19,21,23,25&lt;/sup&gt;</td>
<td>LASA medications; high-alert drugs: e.g., morphine and HYDROMorphine or two sound-alike medicine during product shortage, misfills of automated dispensing devices (e.g., wrong concentration or wrong product in machine's pocket)&lt;sup&gt;18,19,21&lt;/sup&gt;</td>
<td>Full training of practitioners before they participate in high-risk processes (e.g., prescribing PCA)&lt;sup&gt;19&lt;/sup&gt;</td>
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<td><strong>Preparation</strong> (n = 6)&lt;sup&gt;18,19,24,26–28&lt;/sup&gt;</td>
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<td><strong>Wrong drug or diluent</strong>&lt;sup&gt;18,24&lt;/sup&gt;</td>
<td>Similar looking equipment: preparing multiple medications at the same time and storing them in close proximity (e.g., incorrect labeling)&lt;sup&gt;18,24&lt;/sup&gt;</td>
<td>Education, training, and increased access to supportive resources&lt;sup&gt;18&lt;/sup&gt;</td>
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<td><strong>Wrong dose</strong>&lt;sup&gt;19,24,26–28&lt;/sup&gt;</td>
<td>Calculation tasks: no standard concentrations (e.g., other strength of replacement infusion, using standard volumes makes doses unique)&lt;sup&gt;19,26&lt;/sup&gt;</td>
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<td><strong>Wrong technique</strong>&lt;sup&gt;26–28&lt;/sup&gt;</td>
<td>Lack of knowledge of the drug: incorrect mixing or insufficient reconstitution time (e.g., overdose or too low dose because drug was not uniformly distributed in the syringe or infusion bag)&lt;sup&gt;24,26,27&lt;/sup&gt;</td>
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<td><strong>Multiple error types</strong>&lt;sup&gt;18,24&lt;/sup&gt;</td>
<td>Failure to double-check: staff shortage, busy shift, inadequate staff mix, only visual inspecting look-alike products after reconstitution or not checking thoroughly when tasks were carried out with a trusted colleague&lt;sup&gt;18,24&lt;/sup&gt;</td>
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<tr>
<td>Administration (n = 6)</td>
<td><strong>LASA medications: similar looking equipment:</strong> several injection lines on a single fluid hanger, confusion between LASA medications</td>
<td><strong>Barcode medication administration systems</strong></td>
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<td><strong>Wrong drug</strong>&lt;sup&gt;18-21,23,25&lt;/sup&gt;</td>
<td><strong>Independent double-checks of products by two individuals</strong>&lt;sup&gt;19&lt;/sup&gt;</td>
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<td><strong>Calculation tasks:</strong> products supplied in different concentrations (e.g., pump not reprogrammed when starting replacement infusion), 10-fold errors, confusion between weight and volume (e.g., 1 mg ordered, 10 mg/mL used, 1 mL given)&lt;sup&gt;19,21&lt;/sup&gt;</td>
<td><strong>Smart pumps including a drug library and safety-alerts</strong>&lt;sup&gt;20&lt;/sup&gt;</td>
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<td><strong>Wrong dose</strong>&lt;sup&gt;19-21,23&lt;/sup&gt;</td>
<td><strong>Documenting independent double-checks for right pump settings</strong>&lt;sup&gt;19,20&lt;/sup&gt;</td>
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<td><strong>Wrong route</strong>&lt;sup&gt;0,21,23,25&lt;/sup&gt;</td>
<td><strong>Restricting the number of PCA medications to avoid confusion in drug selection from PCA screen</strong>&lt;sup&gt;19&lt;/sup&gt;</td>
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<td><strong>Extra dose</strong>&lt;sup&gt;18&lt;/sup&gt;</td>
<td><strong>Awareness of the possibility of tubing misconnections, tracing the origin of tubing to insertion or connection to ascertain the proper location of each tube</strong>&lt;sup&gt;21&lt;/sup&gt;</td>
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<td><strong>Missed dose</strong>&lt;sup&gt;19,20&lt;/sup&gt;</td>
<td><strong>Documenting pump inspection and validation of infusion rates at shift change</strong>&lt;sup&gt;20&lt;/sup&gt;</td>
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<td><strong>Equipment failure</strong>&lt;sup&gt;20,23&lt;/sup&gt;</td>
<td><strong>Separating two drugs with different routes in time, location and appearance (e.g., IV vinca alkaloids prepared in mini-bags to avoid accidental IT administration)</strong>&lt;sup&gt;25&lt;/sup&gt;</td>
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<td><strong>Multiple error types</strong>&lt;sup&gt;18&lt;/sup&gt;</td>
<td><strong>Not reported</strong></td>
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<td><strong>Inadequate monitoring</strong>&lt;sup&gt;18,23&lt;/sup&gt;</td>
<td><strong>Not reported</strong></td>
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**Abbreviations:** ADD, automated dispensing device; CDSS, clinical decision support system; CPOE, computerized physician order entry; IT, intrathecal; IV, intravenous; LASA, look-alike sound-alike; PCA, patient-controlled analgesia.
Calculation tasks were identified as a cause of wrong dose errors in multiple medication process stages. Pediatric and neonatal populations are at the highest risk for life-threatening calculation errors because of weight-based dosing and inadequate commercial products. Standard concentration procedures are an important way to improve intravenous medication safety. Calculation tasks can also be eliminated or secured by successful implementation of other systemic defenses, such as smart infusion pumps using error-reduction software, dose conversion charts, and decision support systems. In addition, smart infusion pumps can reduce errors related to manual pump programming, which we identified as a particular high-risk task. Manual independent double-checks are widely used in error identification, but the frequent poor quality of these procedures can enable medication errors. Safety of procedures relying on accuracy and awareness of an individual is easily jeopardized. Likewise, procedures that lack sensitivity to all potential error types are problematic. Some manual double-checks could relatively simply be replaced with more reliable technological solutions (e.g., barcode scanning) or even by eliminating using error-prone process steps (e.g., reducing preparation errors by using pre-prepared syringes or sealed systems requiring minimal manipulations). Calculation tasks can relatively simply be replaced with more reliable technological support systems would be an optimal strategy for error reduction.

In our study, absence of a standardized order review protocol was identified as a risk factor for inheritance of prescribing errors in later process stages. To support safe prescribing, an order review by a clinical pharmacist combined with clinical decision support systems would be an optimal strategy for error reduction. In addition, confusion between LASA medications can be particularly significant when high-alert medications are involved. To decrease errors related to LASA medications, use of Tall Man lettering (e.g., morphine and HYDROMorphine), safe storage, auxiliary labels, and barcode medication administration systems should be considered.

Our study was conducted in accordance with the PRISMA checklist. We included only peer-reviewed articles in the analysis and assessed the quality of selected studies using the GRADE system. The literature search was restricted to articles published in English; thus, studies published in other languages were excluded. Although intravenous medications are widely used in hospitals and associated with frequent and particularly serious errors, the number of studies included in our systematic review was limited. Many excluded studies focused on incidence and decision support systems. In addition, smart infusion pumps using error-reduction software, dose conversion charts, and decision support systems. In our study, absence of a standardized order review protocol was identified as a risk factor for inheritance of prescribing errors in later process stages. To support safe prescribing, an order review by a clinical pharmacist combined with clinical decision support systems would be an optimal strategy for error reduction. In addition, confusion between LASA medications can be particularly significant when high-alert medications are involved. To decrease errors related to LASA medications, use of Tall Man lettering (e.g., morphine and HYDROMorphine), safe storage, auxiliary labels, and barcode medication administration systems should be considered.

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and preparation of intravenous medications. Process standardization and implementation of effective systemic defenses are essential to improve medication safety. Our study provides healthcare organizations with preliminary knowledge about systemic causes of intravenous medication errors, but more rigorous evidence is needed.

REFERENCES


