Medication errors in critical care: risk factors, prevention and disclosure

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The case

Mr. S, a 63-year-old man with a recent history of peptic ulcer disease who is taking proton pump inhibitor therapy (his only medication) as an outpatient, is admitted to the intensive care unit (ICU) with respiratory distress. Community-acquired pneumonia is diagnosed, although pulmonary embolism was considered in the differential diagnosis. Treatment with both antibiotics and intravenous heparin is initiated. Over the next 24 hours, the patient's clinical condition improves, and his care is transferred to the medical teaching unit. Before discharge from the ICU, a computed tomography chest scan with contrast confirms the absence of a pulmonary embolism. On day 4 after admission, hematemesis, hypotension and respiratory distress develop. The patient is intubated, readmitted to the ICU and given 6 units of blood. Endoscopy shows an actively bleeding peptic ulcer. The patient's intravenous heparin therapy is stopped. Protamine is administered because his partial thromboplastin time is greater than 150 seconds, and a proton pump inhibitor is prescribed.

Why did this medication error occur? What could have been done to prevent this error? How should the medical team proceed?

Key points

- Medication reconciliation may improve patient safety in the intensive care unit, and an updated list of medications should be maintained, including long-standing medications, the reasons for starting new medications and their planned stop dates and the reasons for discontinuing or holding old medications.
- Engaging pharmacists in inpatient rounds in the intensive care unit may decrease the risk of adverse drug events.

Medication errors in critical care

Critically ill patients admitted to an ICU experience, on average, 1.7 medical errors each day, and many patients suffer a potentially life-threatening error during their stay.[1,2] Medication errors are the most common type of error and account for 78% of serious medical errors in the ICU.[3] Providing 1 critically ill patient with a single dose of a single medication requires correctly executing 80–200 steps.[4] The medication process involves 5 broad stages: prescription, transcription, preparation, dispensation and administration.[5] Medication errors, defined as any error in the medication process regardless of whether a patient experiences an adverse consequence, can occur at any step.[6] It is important to have an understanding of the risk factors for medication errors and the evidence base for preventing medication errors and disclosure, should an error occur.

Although the medication process is similar for all patients in hospital, we have restricted our review to studies focused on critically ill adult patients because the environment, patient characteristics and medications used in the ICU are substantially different from those in other hospital units.[7] The ICU brings together high-risk patients who require urgent, complex interventions from multiple health care professionals in a complex environment where patients are exposed to twice as many medications as those in general medical wards.[7,8] In addition, critically ill patients differ from most other hospital patients because they have limited ability to participate in their medical care and lack the physiologic reserve to tolerate additional injury.

Methods

Our search strategy (Appendix 1, available at www.cmaj.ca/cgi/content/full/180/9/936/DC1) resulted in the identification of 1168 citations: 870 from MEDLINE, 262 from EMBASE and 36 from Evidence-Based Medicine Reviews. Of these, 57 full-text articles met our initial inclusion criteria and were retrieved for assessment (Appendix 2, available at www.cmaj.ca/cgi/content/full/180/9/936/DC1). An additional 5 articles were selected from the reference lists of the retrieved articles. After assessment, 17 articles[3,7,9–23] remained for review. These articles were published between 1950 and 2008. We extracted key elements from the selected studies, including study design, study population, recruitment and sampling, blinding, attrition rates and statistical methods (Appendix 3, available at www.cmaj.ca/cgi/content/full/180/9/936/DC1).

What is the incidence of medication errors in the intensive care unit and what are the risk factors?

From 49 of the articles retrieved in our search, we identified and categorized potential risk factors for medication errors in the ICU (Box 1). Only 6 of these studies satisfied our inclusion criteria. The first used a survey of nurses and physicians

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to examine the point prevalence of sentinel events and their risk factors in 205 ICUs in 29 countries.[9] Medication errors were the second most frequent sentinel event, with a point prevalence of 10.5 medication errors per 100 patient-days. The frequency of medication errors was similar during the prescription (54%) and administration (46%) phases of the medication process. Multiple variable logistic regression analysis revealed that the patient-to-nurse ratio in the ICU (range 1.3:1 to 2:1), exposure time to medications, organ failure and the high level of care provided to each patient were independent risk factors for sentinel events including medication errors.

The second was a prospective cohort study of 4031 medical and surgical patients admitted to 5 ICUs and 6 general care units over 6 months.[7] Adverse drug events and medication errors were identified by direct reporting, investigator visits to each care unit and chart review. In this study, 2 physician reviewers independently evaluated all potential adverse drug events, and structured interviews were performed to determine the circumstances of the adverse event. The number of preventable and potential adverse drug events per 1000 patient-days was higher in ICUs than in general care units (19 v. 10, $p < 0.01$), but the number was similar after adjustment for the number of medications prescribed (1.27 v. 1.07 per 1000 patient-days per prescribed medication). The rate of preventable and potential adverse drug events was higher in medical ICUs (25 per 1000 patient-days) than in surgical ICUs (14 per 1000 patient-days) ($p < 0.05$) with similar numbers of medications prescribed in both types of ICU. A similar finding was reported in the third article, a multicentre prospective trial of safety incidents.[10] This study reported that medication errors were more frequent in medical ICUs than in surgical ICUs (13% v. 6%; $p \leq 0.001$).[10] Cullen and colleagues[7] also found that most medication errors occurred during either the administration (44%) or ordering (38%) phase of the medication process. Interviews suggested that most errors occurred during what caregivers perceived as normal working conditions.

The study by Calabrese and colleagues[11] reported medication errors in a cohort of 851 patients admitted to 5 ICUs over 3 months. Pharmacists prospectively monitored each patient twice daily using direct observation and review of the administered medications. Medication errors were identified during 187 of the 5744 observations (3.3%). The most frequently reported errors were wrong infusion rate (40.1%), dose omission (14.4%), improper dose (11.7%) and wrong time (13.9%). The authors identified vasoactive medications (32.6%) and sedatives or analgesics (25.7%) as the medication classes most commonly associated with error.

In the fifth study,[12] pharmacists directly observed the preparation and administration process for 2009 prescriptions filled by nurses. They identified errors in 6.6% of the observations and characterized the most frequent errors as errors in

Box 1: Potential risk factors for medication errors in the intensive care unit (ICU)

Patients

- Severity of illness*[9]
  - Any organ failure (OR 1.13, 95% CI 1.00–1.29)
  - High intensity of care (OR 1.62, 95% CI 1.18–2.22)
- Lack of a usual medication list*[21] (for 94% of ICU patients, medication orders are changed after home medications are verified and medical records reviewed)
- Need for sedation and mechanical ventilation[5,24]
- Extremes of age[24–28]

Providers

- Inexperience[1,29–31]
- Lack of drug knowledge[32]
- Psychological state[33–37]
- Sleep deprivation[38–42]

Medications*[3,11] (% of medication errors)

- Cardiovascular medications (24%–33%)
- Sedative or analgesic (26%)
- Anticoagulant (11%–20%)
- Anti-infective (13%)

ICU environment

- Number of medications*[7] (on average, ICU patients receive 15 medications in the 24 hours before an adverse drug event)
- Frequent changes in substances and doses[27]
- Type of ICU*[7] (risk of preventable and potential adverse drug events is higher in medical ICUs than in surgical ICUs [unadjusted RR 1.74, 95% CI 1.17–2.62])
- Fast pace of medical care[43–49]
- Care is urgent and interventions often life-saving[27,28]
- Large number and complexity of interventions[1,26,27,50]
- Context of patient admission[28,51–53]
- Initiation of temporary medication therapies and lack of communication[33]
- Use of novel technologies and treatments[54,55]
- Failure to start recognized beneficial therapies[2,56–58]

Organization

- Patient-to-nurse ratio*[9] (increasing risk of error above 1.3 to 2.0 patients per nurse in the ICU; magnitude of risk unknown)
- Frequent changes in personnel and frequent handover of care[59,60]
- Difficult working conditions[60,61]
- Inadequate supervision[62]
- Premature and nighttime ICU discharge[63]

Note: CI = confidence interval, OR = odds ratio, RR = relative risk.
*Risk factors identified in articles that satisfied our search criteria included a summary of risk estimates.

the dose, wrong rate, wrong preparation technique, physicochemical incompatibility, wrong administration technique and wrong time.

The Critical Care Safety Study, performed by Rothschild and colleagues[3] as part the Harvard Work Hours and Health Study,[13] was a 1-year prospective observational study with multifaceted determination of adverse events, including adverse drug events, in a medical ICU and a coronary care unit of a tertiary care hospital. The authors reported a similar medication error rate in both units (ICU 127.8 errors per 1000 patient-days; coronary care unit 131.5 errors per 1000 patient-days, $p = 0.12$). Medication errors were most commonly associated with treatment, but errors were also found in prevention (e.g., prophylaxis), diagnosis (e.g., intravenous contrast agents) and monitoring (e.g., glycemic monitoring and insulin therapy). The most common medication errors were ordering or administering the wrong dose. Medication classes most frequently associated with errors were cardiovascular drugs (24%), anticoagulants (20%) and anti-infective agents (13%).

Our review of the literature highlighted 2 important findings. First, medication error rates vary widely among clinical settings (both ICU and non-ICU settings), patient populations and studies. The reasons for this variation are likely multifactorial, but the reasons may include different patient populations (illness severity, number and type of prescriptions) clinical practice variation, lack of uniformity of definitions, the processes under investigation (e.g., prescription, transcription), methods of reporting and the culture of the different centres reporting their data.[2,25,64,65] The lack of standard definitions and reporting techniques make comparisons across organizations, regions or countries difficult.[2] The single multicountry study included in our analysis did not report medication error rates across different countries.[9]

Second, although there are many potential risk factors for medication errors (Box 1), the strongest evidence that critically ill patients are at increased risk of a medication error are increased severity of illness; failure to document the patient's usual medication list; prescription of cardiovascular, sedative, analgesic, anticoagulant or anti-infective medications; prescription of each additional medication; admission to a medical ICU compared with a surgical ICU; and more critically ill patients per nurse (increasing risk above 1.3 to 2.0 patients per nurse in the ICU).

Box 2: Strategies for preventing medication errors in the intensive care unit (ICU)

Physicians

- Awareness of risk factors*
- Medication reconciliation† (resulted in 57% RR reduction in discharge orders being changed)[21]
- Pharmacology education[66–71]
- Prescribing vigilance among physicians caring for patients with renal or liver failure*
- Good handover technique*

Nurses

- Awareness of risk factors
- Pharmacology education[66–71]
- Second check*
- Good handover technique*

Pharmacists

- Medication reconciliation† (resulted in 1 medication order being changed for every 2.5 patients admitted)[21]
- Satellite pharmacy[72,73]
- Support for dose adjustments for patients with renal or liver failure*

Unit directors

- Elimination of extended physician work schedules† (resulted in a 17% reduction in serious medication errors)[13]
- Computerized physician order entry (effect on medication error in the ICU unclear [RR 87% to > 450%]; no evidence of improved patient outcomes)[14–16]
- Clinical decision support systems[17] (improved practitioner performance in 19 of 29 drug dosing or prescribing system studies‡)
- Computerized intravenous devices[18,19] (no effect on serious medication errors [RR 1.19] or adverse drug events [RR 1.04])
- Pharmacists' participation in rounds (reduces rate of adverse drug events due to prescription errors by 66%)[20]
- Standardized protocols (protocol-specific errors reduced to 0%–1%)[22,23]
- Screening programs for psychological distress[33]
- Bar code technology[74–76]
- New staff orientation (including residents)[77–85]
- Adequate nurse staffing[86–89]
- Intensivist staffing[90]
- Adequate working conditions and caregiver fidelity*

Organization

- Culture of safety[91–93]

Note: RR = relative risk.
*No clear evidence.
†Prevention methods identified in articles that satisfied our search criteria included a summary of effect estimates.
‡Computerized decision support system effect estimate from Garg et al.[94]

What strategies can be used to prevent medication errors in intensive care units?

From the 31 articles identified in our search, we identified potential strategies to prevent medication errors in the ICU (Box 2). Of these, 11 studies satisfied our inclusion criteria. These studies reported 7 prevention strategies: eliminating extended physician work schedules ($n = 1$), computerizing physician order

entry ($n = 3$), implementing support systems for clinical decisions ($n = 1$), computerizing intravenous devices ($n = 2$), having pharmacists participate in the ICU ($n = 1$), reconciling medications ($n = 1$) and standardizing medications ($n = 2$).

Physician work schedules

A single randomized nonblinded study compared the rates of medication errors made by interns working a traditional clinical schedule with those made when extended work shifts were eliminated and the number of consecutive hours of work was limited to about 16.[13] Interns in the traditional clinical schedule worked a mean 77–81 hours a week compared with 60–63 hours a week for the intervention group. Compared with interns working a traditional clinical schedule, those in the intervention group made 17.3% fewer serious medication errors (82.5 errors v. 99.7 errors per 1000 patient-days, $p = 0.03$). Serious medication errors were similarly reduced unit-wide among all clinicians during the intervention schedule (115.5 errors v. 135.2 errors per 1000 patient-days, $p = 0.03$).

Computerized physician order entry

We found 3 studies on computerized physician order entry and medication error in the ICU. Computerized physician order entry is the main component of a clinical information system that allows physicians to enter orders directly into a computer for electronic processing, potential recommendations about dosing, and checking for duplication and drug–drug interactions.[95] Computerized physician order entry targets the prescription and transcription stages of the medication process.

Shulman and colleagues[14] reported the rate of medication errors before and after institution of computerized physician order entry without decision support in their 22-bed multisystem ICU. A pharmacist prospectively identified medication errors during prescription review over 26 days of data collection. Following the introduction of computerized physician order entry, the proportion of prescriptions with errors decreased from 6.7% to 4.8% ($p < 0.04$). A second study by Colpaert and coworkers[15] prospectively compared prescription errors in 2 surgical ICUs, 1 using paper-based prescriptions and 1 using computerized physician order entry. The number of prescription errors was significantly lower in the ICU that used computerized entry (3.4% v. 27%, $p < 0.001$). Finally, Weant and colleagues[16] identified voluntarily reported medication errors before and after the implementation of computerized physician order entry in a neurosurgical ICU. Following implementation of computerized entry, there was an increase in the number of medication errors but a decrease in the number of errors resulting in patient harm. According to 2 recent systematic reviews[96,97] of studies of predominantly non-ICU inpatients, the weight of evidence is that computerized physician order entry systems decrease medication errors, but they do not improve patient outcomes.

Clinical decision support systems

Clinical decision support systems can be used with computerized physician order entry; they include any knowledge-based tool integrated into clinician workflow and patient data to improve quality of care.[98] We identified 1 study[17] of clinical decision support systems and medication error in the ICU, which compared the safety of anti-infective prescription before and after implementation of such a system in a 12-bed ICU. The authors reported that physicians prescribed the medication suggested by the computer for 46% of the orders and the dose and interval suggested by the computer for 93%. The clinical decision support system, which was linked with computerized medical records, was able to decrease prescription of medications to which patients had reported allergies from 146 to 35 ($p < 0.01$), excess dose errors from 405 to 87 ($p < 0.01$) and antibiotic-susceptibility mismatches from 206 to 12 ($p < 0.01$). The number of reported adverse drug events following implementation decreased from 28 to 4 ($p < 0.02$). A systematic review of computerized decision support systems in predominantly non-ICU inpatients suggests that, although these systems may reduce error, they may not improve patient outcomes.[94]

Computerized intravenous devices

Computerized intravenous devices, or "smart pumps," incorporate point-of-care decision support into standard intravenous delivery systems. The bedside clinician selects a medication from a predetermined medication library and is guided through the selection of dose units (e.g., μg/kg per minute or units/hour) and dose limits. Device safeguards include alerts for duplicate medication entry (medication already infusing on another channel) and dose safety limits. We identified 2 studies of computerized infusion pumps in the ICU.[18,19] In the first, Rothschild and colleagues[18] performed a nonblinded, prospective time series analysis that compared real-time decision support by smart pumps with no decision support in 2 cardiac surgery ICUs and 2 cardiac surgery intermediate care units. The rates of serious medication error did not differ between the intervention and control periods (2.41 v. 2.03 errors per 100 patient–pump-days, $p = 0.124$). In the second study, Nuckols and coworkers[19] retrospectively reviewed the medical records of ICU patients in 2 hospitals before and after their conventional pumps were replaced with smart pumps. The rate of adverse intravenous drug events was similar for the 2 periods (4.78 v. 4.95 per 1000 patient-days, $p = 0.96$).

Pharmacist participation in the intensive care unit

We identified 1 study[20] that reported the effects of pharmacist participation in the ICU. Adverse drug events in a medical ICU were compared before and after pharmacist participation in rounds. A coronary care unit with no pharmacist was used as a control. The rate of adverse drug events secondary to prescription errors decreased by 66%, from 10.4 adverse drug events per 1000 patient-days before the intervention to 3.5 per 1000 patient-days after ($p < 0.001$). No change in adverse drug events secondary to prescription errors was observed in the control unit (10.9 v. 12.4 errors per 1000 patient-days, $p = 0.76$). During the 9-month study period, 99% of the pharmacists' recommendations were accepted by the attending physicians. Guideline statements from both the Society of Critical Care Medicine and the American College of Clinical

Pharmacy recommend that pharmacists regularly participate in rounds as members of the multidisciplinary critical care team to provide pharmacotherapeutic advice.[99]

Medication reconciliation

We identified 1 study[21] that described the use of a pre–ICU-discharge survey to compare discharge medication orders with the patient's medical record. The aim was to identify whether discharge medications were the same as the patient's regular medications and to verify the accuracy of documented allergies. According to Pronovost and colleagues,[21] the routine use of this discharge survey prevented an average of 10 medication errors per week in the 14-bed surgical ICU.

Medication standardization

We found 2 studies[22,23] of medication standardization in the ICU. Wasserfallen and colleagues[22] compared compliance with American Society of Health-System Pharmacists' criteria[100] for prescription safety in a surgical ICU before and after implementation of a formatted order sheet. A medical ICU served as a control: physicians continued to use the usual medical order sheet but were briefed on the importance of prescribing in a correct format at the beginning of each new rotation period. The proportion of safe orders increased in both the surgical ICU (74% v. 48%, $p < 0.001$) and the medical ICU (74% v. 66%, $p < 0.001$) during the study. In the second study, McMullin and coworkers[23] prospectively examined implementation of a standardized protocol for treatment of venous thromboprophylaxis to decrease errors of omission in a medical–surgical ICU. They used 5 behaviour-change strategies as part of their thromboprophylaxis safety intervention: interactive education, verbal and written prompts, computer prompts, individual performance feedback and public displays of group performance. Heparin prophylaxis increased from 60% in the baseline period, to 90% in the study period and 100% in the follow-up period ($p = 0.01$).

Other prevention strategies

We found no studies of the prevention of medication errors in critical care with various models of intensivist staffing, nurse staffing, bar code technologies, simulation, cultures of patient safety or medication reporting that satisfied our inclusion criteria. Although these strategies may be intuitive, supported by evidence in other settings or industries and even conceptually simple, further study is warranted to determine whether they prevent medication errors among critically ill patients.

What can clinicians do right now to prevent medication errors?

The quality of most studies that met our inclusion criteria was low, highlighting the fact that most interventions to prevent medication errors are not supported by high-quality evidence and that important gaps exist in the literature. Thus, a practical approach is to recognize that errors are a reality of medicine and that all health care providers have a responsibility to ensure patient safety and to use caution in promoting what are seemingly intuitive interventions. Improved medication safety may be accomplished by optimizing the safety of the medication process, eliminating situational risk factors and adopting strategies to intercept errors and mitigate their consequences. Among the 7 prevention strategies identified in articles that met our inclusion criteria, 3 can be immediately implemented by clinicians.

Medication reconciliation

As many as 50% of all medication errors occur on admission to or discharge from the ICU, and about 60% of regularly scheduled medications are stopped on ICU admission.[21,101,102] Maintaining an up-to-date patient-medication list that includes long-standing medications, reasons why new medications were initiated and planned stop dates, and reasons why old medications were stopped or held may improve patient safety.

Pharmacist participation

Engaging the resources and skills of pharmacists, particularly with regard to patients with multiple risk factors or altered pharmacokinetics, is likely to improve the quality of care delivered.

Medication standardization

Many ICUs have developed protocols to facilitate the management of common important issues (e.g., prophylaxis for venous thromboembolism). Ensuring adherence to protocol for appropriate patients should improve safety.

What should the approach be once an error has occurred?

No studies about the disclosure of medication errors in critically ill patients met our inclusion criteria. However, our literature search identified articles which suggested that patients want full disclosure of harmful errors and that disclosure of medical errors is increasingly recognized as an ethical imperative.[103] Nonetheless, surveys show that only 17%–30% of physicians inform their patients when they experience a medical error.[103–105] Disclosure should take place whenever a patient has suffered an iatrogenic injury and should be guided by the following principles:

- Perform in a timely fashion — as soon as possible after the injury, while ensuring the patient's well-being.
- Perform in a quiet room free of interruptions.
- Disclose facts without speculation, opinion or blame.
- Use simple, unambiguous lay words.
- Include an expression of sympathy.
- Allow time for questions.
- Document disclosure in the medical record.

Resolution of the case

Our case highlights the risks of medication error and the potentially serious consequences in critical care. First, our patient was prescribed heparin, a medication reported to be

associated with increased risk of medication error.[3] Second, medication reconciliation was not carried out when the patient's proton pump inhibitor was discontinued on admission. Third, transition of the patient's care from the ICU to the medical teaching unit provided an opportunity for the temporary administration of heparin to continue unnecessarily. Finally, either the dose of heparin or failure to monitor the patient's condition resulted in a supratherapeutic level, shown by a partial thromboplastin time of greater than 150 seconds. The medication error was disclosed to the patient's family. There was no further evidence of bleeding, and the patient was moved back to the medical teaching unit after 48 hours.

In this case, potential prevention strategies could have included the following. First, educating physicians about the risk factors for medication errors might have prevented prescription of heparin in a questionable risk–benefit scenario. Second, a structured medication reconciliation process on ICU discharge (e.g., re-prescribe all regular medications), such as the strategy proposed by Pronovost and colleagues,[21] might have resulted in restarting the proton-pump inhibitor. Third, a standardized process for transition of care (e.g., verbal communication, written communication, dictated transfer note) that ensures that important information on active diagnoses and important investigations and interventions are transmitted and recorded may have resulted in evaluation of the computed tomography scan result and discontinuation of heparin.

Recommended reading

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Conclusion

Given the large body of literature about patient safety,[106] the limited evidence available to guide clinicians in selecting strategies to prevent and disclose medication errors in critically ill patients is surprising. Nevertheless, patient safety is a first step in providing high-quality health care, and ensuring the safety of patients is everyone's responsibility and challenge.

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