

BMJ Open Evaluation of medication risk at the transition of care: a cross-sectional study of patients from the ICU to the non-ICU setting

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ABSTRACT

Objectives To describe the incidence and types of medication errors occurring during the transfer of patients from the intensive care unit (ICU) to the non-ICU setting and explore the key factors affecting medication safety in transfer care.

Design Multicentre, retrospective, epidemiological study.

Participants Patients transferred from the ICU to a non-ICU setting between 1 July 2019 and 30 June 2020.

Main outcome measures Incidence and types of medication errors.

Results Of the 1546 patients transferred during the study period, 899 (58.15%) had at least one medication error. Most errors (83.00%) were National Coordinating Council (NCC) for Medication Error Reporting and Prevention (MERP) category C. A small number of errors (17.00%) were category D. Among patients with medication errors, there was an average of 1.68 (SD, 0.90; range, 1–5) errors per patient. The most common types of errors were route of administration 570 (37.85%), dosage 271 (17.99%) and frequency 139 (9.23%). Eighty-three per cent of medication errors reached patients but did not cause harm. Daytime ICU transfer (07:00–14:59) and an admission diagnosis of severe kidney disease were found to be factors associated with the occurrence of medication errors as compared with the reference category (OR, 1.40; 95% CI 1.01 to 1.95; OR, 6.78; 95% CI 1.46 to 31.60, respectively). Orders for bronchorespiratory (OR, 5.92; 95% CI 4.2 to 8.32), cardiovascular (OR, 1.91; 95% CI 1.34 to 2.73), hepatic (OR, 1.95; 95% CI 1.30 to 2.91), endocrine (OR, 1.99; 95% CI 1.37 to 2.91), haematologic (OR, 2.58; 95% CI 1.84 to 3.64), anti-inflammatory/pain (OR, 2.80; 95% CI 1.90 to 4.12) and vitamin (OR, 1.73; 95% CI 1.26 to 2.37) medications at transition of care were associated with an increased odds of medication error.

Conclusions More than half of ICU patients experienced medication errors during the transition of care. The vast majority of medication errors reached the patient but did not cause harm.

INTRODUCTION

Transfer, or handoff, is not only a critical step in a patient's healing process but also a risk exchange point that often leads to unnecessarily high rates of health services

Strengths and limitations of this study

- Cross-sectional studies can describe the risk of medication for intensive care unit referrals in a short period of time.
- The large sample size ensures sufficient statistical power to account for the importance of the research question.
- All three sample sites are teaching hospitals.
- With only three sample points, the statistical impact of institutional information on the research question cannot be described.
- The heterogeneity of the results may be due to a variety of factors.

use and healthcare spending.¹ Medication error is defined as an error occurring in any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient or consumer.² Unfortunately, medication errors are common in care transfers, according to previous research.^{3–4} A statistical review of regulatory errors received by the United States Pharmacopeia found that 66% of medication errors occurred when patients were transferred to another level of care, such as hospitals to nursing homes and geriatric centres or from the intensive care unit (ICU) to the general ward. Of them, the causes of adverse drug events were mostly improper dose or quantity, followed by omission errors and prescription errors.⁵ Prior studies have found that medication errors affect the safety and efficacy of medications in patients, resulting in potential treatment hazards and even prolonging the treatment time and increasing the cost of treatment.^{6–7} Medication errors are a major factor impacting medication risk in the transfer of care.⁸

The ICU is a dynamic and error-prone medical environment that presents particular challenges with regards to medication errors.⁸ An epidemiological study of adverse drug events occurring during transfer from the ICU to the non-ICU setting by Tully showed that nearly half of patients experienced medication errors, and the most common type of error was continuation of medication.⁹ There are many reasons why medication errors occur frequently in ICU patients during the transfer of care. First, ICU patients are sicker, have more comorbidities and require extensive and complex medical treatment. Because their bodies have a lower tolerance for errors, they may be at greater risk of iatrogenic injury.^{8–10} Second, due to the different treatment environments in different departments during transfer, patients admitted to the ICU may discontinue the use of previously taken chronic medications such as antihypertensive drugs and hypoglycaemic drugs and may forget to restart these medications when they move to a non-ICU setting. Meanwhile, short-term medications that begin in the ICU, such as antipsychotics or narcotics, may continue to be used after leaving the ICU or discharge.^{10–11} Finally, the medications used in the ICU are generally potent, diverse and numerous, involving precise doses, drug interactions and frequent infusions. Errors involving drug order, route of administration, dose change and frequency of administration are likely to occur during the patient transfer process.^{8–12–13}

When patients are transferred from intensive care to less monitored environments, adverse drug events are likely to occur in patients due to discontinuity in medical staff and reduced vigilance for patients.¹⁴ In general, a particularly high-risk time for medication errors is when patients transfer from the ICU to the non-ICU setting. Moreover, ICU patients differ from other patients in that even mild adverse events during transfer can lead to complications, readmission, severe disability and increased mortality.^{13–15}

Different drug policies and clinical referral patterns in different regions have different significant effects on the occurrence of drug risks. For example, Meyer-Massetti studied drug-related issues when patients were transferred from the hospital to another care facility,¹⁶ and Lee described common differences in drug use during intra-hospital transfers.¹⁷ An increasing number of countries and researchers are paying attention to medication risk during transfer of care, but there are few investigations in China, especially given the lack of research and analysis in the field of intensive care. The purpose of this study was to describe the incidence and types of medication errors occurring during patient transfer from ICU to non-ICU locations and to explore the key factors associated with the occurrence of medication errors.

METHODS

Study design and site Selection

This was a 1-year, multicentre, retrospective, non-intervention epidemiological study. The study site was comprised of three large comprehensive teaching

hospitals in Anhui Province. Anhui Province is located in southeastern China, with a population of approximately 61 million. In this study, we selected three large general hospitals that rank at the top in Anhui Province, each of which has an annual average of approximately 5 million patients, approximately 226 700 patients discharged annually, and approximately 140 000 surgeries annually. Prior to the start, all participating sites were approved by the bioethics review committee, and the first Affiliated Hospital of Anhui Medical University was used as the coordinating site. All participants were required to attend a meeting to determine uniform data collection tables and the definition of study variables to reduce errors among investigators.

All data were collected during the same study period at all approved medical facilities. The collected patient case data were reviewed by a professional clinical pharmacist. Prior to the review, all clinical pharmacists were required to discuss and determine a unified standard based on the prescription review criteria (such as requiring that drug instructions, drug-related guidelines, drug compatibility contraindication tables and clinical medications be known; official information published by adverse drug reaction monitoring centres and pharmacovigilance websites; and documents issued by some countries such as prescription regulations and antibacterial drug regulations) to reduce heterogeneity.

Patient Selection

By evaluating the data collected from the previous questionnaire, we included patients who were transferred from the ICU to the non-ICU setting at the same site between 1 July 2019 and 30 June 2020. If the patient had more than one transfer during the study, only that patient's first transfer was included. Patients or members of the public were not involved in the design of this study.

Data Collection

Medical records were collected by two investigators, including patient transfer records, electronic health records, home medication lists and written transfers between medical personnel. On the one hand, information including patient demographic characteristics, comorbid conditions and use of medications (generic name, number, dose, frequency, administration) was extracted from the medical records. On the other hand, we collected correlative information related to the transfer process at medical institutions, such as ICU characteristics, transfer time and medical staff configuration. All problems that arose with statistical data were resolved by consensus of the investigators.

Analysis of the characteristics of medication errors

First, a clinical pharmacist commented on the medication list and medical records of the patients before and after transfer, evaluated whether there were adverse drug events and calculated the incidence of medication errors. Medications prior to transfer were defined as the last

Table 1 Basic information characteristics of ICU patients with transfer

Patient characteristics	n=1546
Age, n (%)	
Under 35 years	174 (11.25)
35–44 years	112 (7.24)
45–54 years	255 (16.49)
55–64 years	251 (16.23)
65–74 years	380 (24.58)
75–84 years	274 (17.72)
≥85 years	100 (6.47)
Sex, n (%)	
Male	944 (61.06)
female	602 (38.94)
Admitting ICU, n (%)	
Mixed	574 (37.13)
Emergency	323 (20.89)
Respiratory	333 (21.54)
Neurosciences/neurosurgical	187 (12.10)
Obstetrics/gynecology	129 (8.34)
Admission diagnosis, n (%)	
Severe liver disease	16 (1.03)
Respiratory	190 (12.29)
Lithiasis	29 (1.87)
Pregnancy	68 (4.40)
Burn	19 (1.23)
Neurosurgery	165 (10.67)
Severe kidney disease	23 (1.49)
Trauma	92 (5.95)
Gastrointestinal surgery	45 (2.91)
Cardiac	157 (10.15)
Transplant surgery	25 (1.62)
Cancer	488 (31.56)
Drug poisoning	118 (7.63)
Other	111 (7.18)
Comorbidities, n (%)	
n=1740	
Chronic kidney disease	120 (6.90)
Anaemia	74 (4.25)
Chronic pulmonary disease	245 (14.08)
Heart failure	155 (8.91)
Chronic hepatopathy	106 (6.09)
Diabetes	185 (10.63)
Thyropathy	24 (1.38)
Cancer	85 (4.88)
Hypertension	415 (23.85)
Psychiatric illness	50 (2.87)
Neurologic disease	102 (5.86)

Continued

Table 1 Continued

Patient characteristics	n=1546
Inflammatory disease	64 (3.68)
Lithiasis	37 (2.13)
Hyperlipaemia	78 (4.48)

ICU, intensive care unit.

effective medication order placed before the next phase of treatment, and post-transfer medications were defined as the first effective medication order placed in the next phase of treatment. The time considered was 24 hours before and after the transfer. Medications discontinued prior to admission and extending beyond this defined time period were not evaluated. The reason we chose to evaluate medication information 24 hours before and after transfer was that a previous investigation found that patients' medication information would be completely updated within a period of time after transfer. Moreover, 24 hours is reasonable for the assessment of chronic drug omission or medication continuation in the ICU.

If any of the following occurred, a medication error was recorded: (1) wrong prescription: inappropriate medication chosen (based on indications, contraindications, known allergic reactions, existing medications, medication interactions, repeat administration and other factors); improper dose, dosage form, frequency, quantity or course of treatment; (2) administration and monitoring: technical error in administration (such as wrong route of administration, incorrect speed of administration, inappropriate solvent), inappropriate time or opportunity of administration, incorrect order of administration, medication omitted on transfer; (3) other (as decided by pharmacist's judgement based on the clinical situation).

Then, the types of medication errors and the severity of medication errors were assessed according to the prescription data. We recorded the errors as 'A' through 'I' on the basis of the National Coordinating Council (NCC) for Medication Error Reporting and Prevention (MERP) Index for Categorising Medication Errors.¹⁸

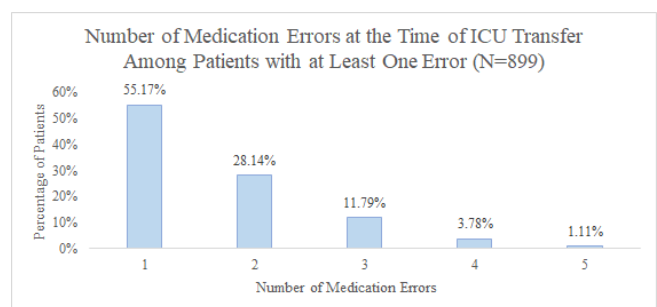


Figure 1 The frequency distribution of errors per patient among patients with at least one error at the time of transition out of the intensive care unit (ICU).

Statistical analysis

The primary outcomes were the incidence of medication errors during ICU transfer at the same institution and the type and severity of adverse drug events. The factors related to medication errors in patients transferred to the ICU were also discussed. Descriptive statistical methods were used to analyse the incidence and characteristics of medication errors. A bivariate analysis was conducted to compare related factors (eg, medication, patient characteristic, institution information) between patients with medication errors found during transfer of care and patients without medication errors. The two-sample t-test was used for continuous normally distributed variables, the Mann-Whitney U test was used for continuous nonnormally distributed variables, and the χ^2 or Fisher's exact test was used for categorical variables.

Variables with a p value less than 0.05 in the bivariate analysis were included in the multivariate logistic regression analysis to identify the factors related to medication errors. All data were analysed with SPSS V.17.0 Statistics.

Patient and public involvement

Patients or members of the public were not involved in the design of this study.

OUTCOMES

Demographics

A total of 1546 patients were included from three tertiary hospitals in Anhui Province (sample point 1=599; sample point 2=524; sample point 3=423). Table 1 shows basic patient information, including age, sex, ICU category, admission diagnosis, and complications. All ICUs had formal policies or guidelines for the transfer of care. There was only one ICU-dedicated clinical pharmacist at sample points 1 and 3, and no ICU-dedicated clinical pharmacist at sample point 2.

Incidence of medication errors and characteristics of errors

Of the 1546 patients from the three sample points transferred from an ICU to a non-ICU setting during the study period, 899 patients (58.15%) had at least one medication error. Among patients with medication errors, there was an average of 1.68 (SD, 0.90; range, 1–5) errors per patient, with most patients (55.17%) experiencing one error (figure 1). The medication classes with an incidence of errors were bronchorespiratory (41.79%), anti-infective (14.84%), cardiovascular (8.18%) and hepatic (6.87%) (table 2). Terbutaline and ambroxol accounted for 59.85% and 33.63%, respectively, of bronchorespiratory medications. Among the anti-infective medications, β -lactams accounted for 37.81% and peptides accounted for 23.67%. Calcium channel blockers accounted for 23.72% and antithrombotic drugs accounted for 16.67% of cardiovascular medications. Adenosine succinate needle injection and thymalfasin accounted for 37.40% and 32.06%, respectively, of hepatic medications.

Table 2 Characteristics of medication errors (n=1546)

Characteristics, n (%)	Errors(n=899)
Medication classes at time of transfer	n=1546*
Bronchorespiratory	797 (41.79)
Anti-infective	283 (14.84)
Cardiovascular	156 (8.18)
Hepatic	131 (6.87)
Endocrine	114 (5.98)
Vitamin	98 (5.14)
Haematologic	91 (4.77)
Anti-inflammatory/pain	75 (3.93)
Antipsychotics	56 (2.94)
Gastrointestinal	37 (1.94)
Immunomodulatory/immunosuppressants	27 (1.42)
Nutritious supplementary	27 (1.42)
Diuretic	11 (0.58)
Other (antiemetic, anticholinesterase, choleric)	4 (0.21)
Type of error	n=1506
Dosage	271 (17.99)
Drug concentration	122 (8.10)
Frequency	139 (9.23)
Omissions	71 (4.71)
Route of administration	570 (37.85)
Drug–drug interaction	84 (5.58)
Duplication	27 (1.79)
Drug monitoring	25 (1.66)
Duration	73 (4.85)
No indication	3 (0.20)
Compatibility taboo	96 (6.74)
Errors related to therapeutic interchange	19 (1.26)
Timing	4 (0.27)
Other	2 (0.13)

*Some medication errors can occur multiple types of medication.

Some medications can cause more than one type of medication error, whereas one error can be caused by more than one medication. The three most common types of medication errors were route of administration (37.85%), dosage (17.99%) and frequency (9.23%) (table 2). Of the 662 errors classified as medication route of administration errors, bronchorespiratory accounted for 570 errors (86.10%) and haematologic accounted for 63 errors (9.52%). Of the 288 errors classified as dosage errors, bronchorespiratory (n=207 (71.88%)) and hepatic (n=50 (17.36%)) medications accounted for the most errors. A total of 142 drugs caused errors in delivery frequency, of which anti-infective drugs accounted for 53 (37.32%) and hepatic drugs accounted for 42 (29.58%).

The survey found that the incidence of drug errors at sample point 3 (21.75%) was the lowest compared with sample point 1 (78.80%) and sample point 2 (63.93%). There was no significant difference in the incidence of medication errors among all sample sites. Most errors

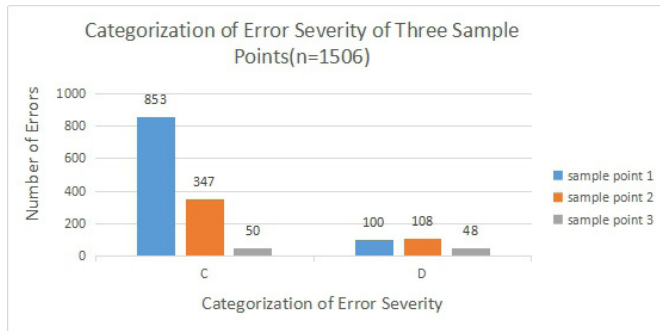


Figure 2 Categorisation and number of severity of medication errors among intensive care unit patients at three sample points.

(83.00%) were NCC MERP category C (reached the patient, no harm;) (figure 2). A small number of errors (17.00%) were category D (required monitoring and/or intervention to preclude harm). The most common types of errors associated with category D were drug–drug interactions (n=74/256 (28.91%)), duration (n=47/256 (18.36%)) and omissions (n=45/256 (17.58%)). The medication classes most commonly represented in category D errors were cardiovascular (n=102/369 (27.64%)), anti-infective (n=79/369 (21.41%)) and anti-inflammatory/pain (n=54/369 (14.63%)).

Risk factors for medication errors

The results of the multivariate logistic regression of risk factors for medication errors are presented in table 3. In the multivariate logistic regression model, daytime ICU transfer (07:00–14:59) and an admission diagnosis of severe kidney disease were found to be factors associated with the occurrence of medication errors as compared with the reference category (OR, 1.40; 95% CI 1.01 to 1.95; OR 6.78; 95% CI 1.46 to 31.60, respectively). Orders for bronchorespiratory (OR, 5.92; 95% CI 4.21 to 8.32), cardiovascular (OR, 1.91; 95% CI 1.34 to 2.73), hepatic (OR, 1.95; 95% CI 1.30 to 2.91), endocrine (OR, 1.99; 95% CI 1.37 to 2.91), haematologic (OR, 2.58; 95% CI 1.84 to 3.64), anti-inflammatory/pain (OR, 2.80; 95% CI 1.90 to 4.12) and vitamin (OR, 1.73; 95% CI 1.26 to 2.37) medications at the transition of care were associated with increased odds of a medication error. Other factors, such as age, sex, comorbidities, mechanical ventilation, vasopressin use, surgery in the ICU and the number of medications before and after transfer, were not associated with error risk. Specific univariate analysis results are shown in tables 4–6.

DISCUSSION

The transfer of care plays an important role in patient recovery, especially for ICU patients. During transfer, medication safety is the priority. Previous studies have found that more than half of general medical patients and those receiving emergency treatment had ≥ 1 medication discrepancy at admission.^{19 20} A retrospective

cohort study on the coordination of inpatient admission and discharge medications reported that 23% of patients had medication discrepancies, with 19% of them potentially at high risk.¹⁰ According to Unroe *et al*,¹⁰ 6 out of 10 patients exhibited medication transfer errors during the process of moving from one ward to another.

Most of the current studies have focused on transfer errors, such as medication errors, patient education and information gaps, occurring between medical institutions or during admission and discharge. However, medication use during the transfer of ICU patients to the next phase of treatment is not well described.^{21 22} The purpose of this study was to evaluate medication use in ICU patients during internal transfer within the same medical institution. Our results indicated that more than half of ICU patients experienced medication errors during this transfer. As patients transfer, their medication regimens need to move with them in an organised, reliable and accurate way. Therefore, it is not only the sender who is responsible for ensuring the completeness and timeliness of the key information delivered but also the receiver who is responsible for providing feedback. It is particularly important to implement medication reconciliation to reduce preventable medication errors during the transfer of ICU patients.

Almost 38% of errors identified were related to an inappropriate route of medication administration, and of these, 86% were due to injection route of administration, such as aerosolized ambroxol and gentamicin injections. On the one hand, there are potential safety hazards of atomised injections; on the other hand, the stability and effectiveness of atomised drug injections are still uncertain.²³ At present, serious adverse reactions have been reported with drug injection atomisation.^{24 25} Given that there has been no formal safety assessment of atomised injections and that this method of administration is off-label, clinical use of injections should be strictly in accordance with the correct route of administration. A national study of medication errors found that 44% of medication errors occurred during the administration phase of drugs in both the ICU and non-ICU settings and that ICU patients experienced more errors and more serious injuries due to incorrect administration methods than non-ICU patients.²⁶ In addition, route error occurs during the last step in the medication process before the patient receives the drug, and errors are less likely to be detected and intercepted by other medical personnel. Viscusi and Eugene also showed in a literature review that in anaesthesiology, emergency medicine, obstetrics and oncology, incorrect route of administration has been reported to have serious consequences.²⁷ In particular, inappropriate intravenous or intravascular delivery errors impose a high burden of patient morbidity, mortality, patient suffering and cost.^{28 29}

In addition to incorrect route of administration, approximately 18% of errors were related to improper dosage. In a study on adverse drug events in ICUs, Kopp and Benkirane found that drug dosage errors accounted

**Table 3** Risk factors associated with a medication error during transfer: multivariate logistic regression

Characteristic	OR (95% CI)	P value
Age		
35–44 years	1.01 (0.53 to 1.96)	0.967
45–54 years	0.95 (0.53 to 1.70)	0.87
55–64 years	0.97 (0.55 to 1.74)	0.926
65–74 years	0.94 (0.54 to 1.62)	0.81
75–84 years	0.75 (0.42 to 1.35)	0.339
≥85 years	0.74 (0.37 to 1.48)	0.393
Sex		
Male	0.80 (0.59 to 1.09)	0.162
Mechanical ventilation during ICU stay	0.70 (0.40 to 1.23)	0.215
Vasopressor use during ICU stay	1.24 (0.90 to 1.71)	0.195
Surgery is performed during ICU stay	0.65 (0.41 to 1.05)	0.077
ICU length of stay	1.01 (0.99 to 1.04)	0.281
All hospital length of stay	0.99 (0.97 to 1.00)	0.121
Number of medications prior to transfer	1.00 (0.98 to 1.03)	0.775
Number of medications after transfer	1.02 (1.00 to 1.05)	0.087
Time of transfer		
Day (07:00–14:59)	1.40 (1.01 to 1.95)	0.043
Day of transfer		
Weekend	1.28 (0.90 to 1.81)	0.169
Admitting ICU		
Obstetrics/gynecology	0.37 (0.19 to 0.72)	0.004
Emergency	0.62 (0.33 to 1.19)	0.151
Respiratory	1.00 (0.62 to 1.63)	0.991
Neurosciences/neurosurgical	0.89 (0.23 to 3.43)	0.862
Admission diagnosis		
Severe liver disease	0.81 (0.46 to 1.95)	0.99
Respiratory	0.28 (0.15 to 0.55)	<0.001
Neurosurgery	0.84 (0.22 to 3.27)	0.801
Severe kidney disease	6.78 (1.46 to 31.60)	0.015
Trauma	0.63 (0.31 to 1.27)	0.194
Gastrointestinal surgery	0.90 (0.37 to 2.19)	0.815
Cardiac	0.28 (0.13 to 0.62)	0.002
Transplant surgery	9.13 (0.70 to 11.90)	0.091
Cancer	0.76 (0.47 to 1.23)	0.262
Drug poisoning	0.36 (0.15 to 0.86)	0.022
Comorbidities		
Chronic kidney disease	1.29 (0.76 to 2.20)	0.347
Heart failure	1.09 (0.69 to 1.73)	0.713
Chronic hepatopathy	0.97 (0.56 to 1.69)	0.931
Psychiatric illness	0.75 (0.33 to 1.68)	0.481
Hyperlipaemia	0.98 (0.49 to 1.96)	0.957
Medication class at time of transfer		
Anti-infective	1.27 (0.79 to 2.06)	0.326
Bronchorespiratory	5.92 (4.21 to 8.32)	<0.001

Continued

Table 3 Continued

Characteristic	OR (95% CI)	P value
Cardiovascular	1.91 (1.34 to 2.73)	<0.001
Hepatic	1.95 (1.30 to 2.91)	0.001
Endocrine	1.99 (1.37 to 2.91)	<0.001
Gastrointestinal	1.06 (0.75 to 1.51)	0.734
Haematologic	2.58 (1.84 to 3.64)	<0.001
Immunomodulatory/immunosuppressants	1.04 (0.20 to 5.48)	0.968
Nutritious supplementary	1.43 (0.93 to 2.19)	0.107
Anti-inflammatory/pain	2.80 (1.90 to 4.12)	<0.001
Neurologic	1.66 (0.86 to 3.20)	0.132
Diuretic	0.50 (0.30 to 0.84)	0.009
Vitamin	1.73 (1.26 to 2.37)	0.001
Other	1.56 (0.81 to 3.01)	0.185

ICU, intensive care unit.

for 23% and 21.1%, respectively.^{30 31} The high frequency of dosage errors may be related to the use of multiple medications in ICU patients and the need to calculate dosages for most intravenous medications. Moreover, a review of the literature on pharmaceutical events in paediatric and neonatal ICUs showed that dosage errors were the most frequently reported error subtype.³² For children, drug doses often require frequent adjustments (such as dose-weight calculations), which can easily lead to errors.³²

In this study, an admission diagnosis of severe renal disease was found to be a risk factor associated with medication errors. Martin's study also showed that the primary risk factor the occurrence of ICU drug-related problems was a diagnosis of kidney injury (OR=8.38).³³ These data are similar to those presented by Kane-Gill *et al*,³⁴ who concluded that critically ill patients with acute kidney failure are 16 times more likely to experience adverse drug events. This may be related to the frequent need to adjust the medication regimen and dosage based on renal function in patients with renal disease.

In this study, drug overdose, which is higher than normal doses, was the main problem, of which bronchorespiratory medications accounted for 71.88% and hepatic medications accounted for 17.36%. There is insufficient evidence for the clinical application of high-dose medications, which is an off-label use. Although it is generally considered that some drugs are clinically safe to use in overdose, the side effects of these drugs are often concealed by the symptoms and signs of the underlying disease in critically ill patients, especially in patients with impaired consciousness. Therefore, caution should be exercised when considering the use of such an overdose.

In our study, we found that medication errors occurred both in the ICU and from the ICU to the non-ICU. We believe that the reason for this problem may be the lack of evidence-based empirical usage by doctors, followed by

the failure of drug restructuring by the receiving party. The problem of drug overdose with an incorrect route of administration reminds us not only that we should pay more attention to the problem of irrational drug use but also that we should re-examine the responsibility of transferring parties and accepting release from the perspective of working mechanisms. Although no harm reach the patient, it also highlights the risk of medication errors during metastasis.

Due to the severity of their disease, organ dysfunction and polypharmacy, critical patients constitute a group vulnerable to medication errors.^{35 36} One way to improve medication safety is to include clinical pharmacists in the care team.^{37 38} The daily inspection of laboratory data and evaluation of patients' symptoms can not only reduce unnecessary medications, medication errors and potential side effects that lead to complicated drug treatment risks but can also identify potentially harmful medication errors and intercept them to prevent the occurrence of adverse drug events.^{39 40}

In our study, we found that there was one ICU clinical pharmacist at sample points 1 and 3, while there was no ICU clinical pharmacist at sample point 2, however, only the clinical pharmacist at sample point 3 intervened in ICU medications. According to the research, compared with samples 1 and 2, sample 3 had the lowest incidence of drug errors, which may be related to pharmacist intervention.

Pharmacist intervention during hospitalisation and discharge is often studied with positive impacts.⁴¹ A 2019 prospective study showed that pharmacists participating in drug-led transfer care programmes reduced postdischarge drug-related problems.⁴² A prospective intervention study of medication regulation in the ICU also found that patients with ≥ 1 medication error after pharmacist intervention were 30.5% less likely to be hospitalised and 32.7% more likely to be discharged from the hospital.¹¹ In

**Table 4** Comparison of patient characteristics between those with and without medication errors

Patient characteristics	Error (n=899)	No error (n=647)	P value
Age, n (%)			0.007
Under 35 years	84 (9.36)	90 (13.91)	
35–44 years	71 (7.92)	41 (6.34)	
45–54 years	155 (17.28)	100 (15.46)	
55–64 years	161 (17.95)	90 (13.91)	
65–74 years	230 (25.64)	150 (23.18)	
75–84 years	146 (16.28)	128 (19.78)	
≥85 years	52 (5.80)	48 (7.42)	
Sex, n (%)			0.015
Male	572 (63.63)	372 (57.50)	
Female	327 (36.37)	275 (42.50)	
Admitting ICU, n (%)			
Mixed	417 (46.38)	157 (24.27)	<0.001
Emergency	86 (9.57)	237 (36.63)	<0.001
Respiratory	181 (20.13)	152 (23.49)	0.113
Neurosciences/neurosurgical	166 (18.46)	21 (3.25)	<0.001
Obstetrics/gynecology	49 (5.45)	80 (12.36)	<0.001
Admission diagnosis, n (%)			
Severe liver disease	16 (1.78)	0	0.001
Respiratory	68 (7.56)	122 (18.86)	<0.001
Lithiasis	18 (2.00)	11 (1.70)	0.666
Pregnancy	33 (3.67)	35 (5.41)	0.1
Burn	12 (1.33)	7 (1.08)	0.656
Neurosurgery	145 (16.13)	20 (3.09)	<0.001
Severe kidney disease	20 (2.22)	3 (0.46)	0.005
Trauma	66 (7.34)	26 (4.02)	0.006
Gastrointestinal surgery	34 (3.78)	11 (1.70)	0.016
Cardiac	44 (4.89)	133 (20.56)	<0.001
Transplant surgery	24 (2.67)	1 (0.15)	<0.001
Cancer	328 (36.48)	160 (24.73)	<0.001
Drug poisoning	18 (2.00)	100 (15.46)	<0.001
Other	73 (8.12)	38 (5.87)	0.091
Comorbidities, n (%)			
Chronic kidney disease	57 (6.34)	63 (9.74)	0.014
Anaemia	45 (5.01)	29 (4.48)	0.634
Chronic pulmonary disease	155 (17.24)	90 (13.91)	0.077
Heart failure	78 (8.68)	77 (11.90)	0.037
Chronic hepatopathy	47 (5.23)	59 (9.12)	0.003
Diabetes	103 (11.46)	82 (12.67)	0.467
Thyropathy	16 (1.78)	8 (1.24)	0.394
Cancer	43 (4.78)	42 (6.49)	0.146
Hypertension	231 (25.70)	184 (28.44)	0.23
Psychiatric illness	20 (2.22)	30 (4.64)	0.008
Neurologic disease	55 (6.12)	47 (7.26)	0.37
Inflammatory disease	32 (3.56)	32 (4.95)	0.177

Continued

Table 4 Continued

Patient characteristics	Error (n=899)	No error (n=647)	P value
Lithiasis	17 (1.89)	20 (3.09)	0.128
Hyperlipaemia	19 (2.11)	59 (9.12)	<0.001

ICU, intensive care unit.

an intensive care setting, the work of clinical pharmacists is also recognised as an important factor in improving the quality of care provided, with positive results in terms of cost, mortality and length of hospital stay.

This study has several limitations. First, we cannot avoid researcher variability in the collection of medication data and evaluation of medication errors, although we had a consistent discussion of the variables that might be encountered prior to starting. Second, we only collected medication orders within 24 hours before and after ICU transfer; hence, medication errors occurring outside of the prescribed time period cannot be detected. Moreover, the actual error rate may be higher than reported, as the study was unable to assess errors in dispensing and administration by caregivers. A third limitation is that we only collected data from three sample points. The study was unable to examine the impact of the type of institution and its basic ICU characteristics on the risk of medication errors, nor could it clarify the role of ICU clinical

pharmacists in preventing medication errors, since the number of sample points included in the study could not be statistically calculated. Finally, medication errors are determined by retrospective review of medical records, so data loss or record errors may lead to incorrect results.

CONCLUSION

More than half of ICU patients experienced medication errors during the transition of care. The vast majority of medication errors reached the patient but did not cause harm. The study also identified risk factors associated with medication errors. In the process of transferring care, the main responsibilities of each party should be clarified, as well as the risk characteristics affecting drug safety, which deserve further study. Especially in the context of major public health emergencies, it is important to reduce the risk of drug use in the care transfer process because the dynamic and rapid transfer situation between the

Table 5 Comparison of medication order characteristics between patients with and without medication errors

Medication order characteristics	Error (n=899)	No error (n=647)	P value
Number of home medications, mean±SD	11.88±13.29	10.38±12.11	0.069
Number of medications prior to transfer, mean±SD*	23.90±16.29	18.98±17.211	<0.001
Number of medications after transfer, mean±SD†	21.86±11.34	14.57±9.99	<0.001
Medication classes at time of transfer, n (%)‡			
Bronchorespiratory	679 (75.53)	241 (37.25)	<0.001
Anti-infective	825 (91.77)	439 (67.85)	<0.001
Cardiovascular	320 (35.60)	222 (34.31)	0.602
Hepatic	319 (35.48)	86 (13.29)	<0.001
Endocrine	295 (32.81)	86 (13.29)	<0.001
Vitamin	527 (58.62)	428 (66.15)	<0.001
Haematologic	327 (36.37)	217 (33.54)	0.250
Anti-inflammatory/pain	256 (28.48)	150 (23.18)	0.020
Antipsychotics	182 (20.24)	29 (4.48)	<0.001
Gastrointestinal	622 (69.19)	425 (65.69)	0.146
Immunomodulatory/immunosuppressants	50 (5.56)	6 (0.93)	<0.001
Nutritious supplementary	188 (20.91)	48 (7.42)	<0.001
Diuretic	86 (9.57)	75 (11.59)	0.198
Other(antiemetic, anticholinesterase, choleric)	133 (14.79)	20 (3.09)	<0.001

*Active medication orders in the ICU within 24 hours prior to transfer to a lower level of care.

†Active medication orders in the lower level of care within 24 hours after transfer from the ICU.

‡All active medication orders within 24 hours pretransfer and post-transfer.

ICU, intensive care unit.

**Table 6** Comparison of transfer characteristics information between patients with and without medication errors

Transfer characteristics	Error (n=899)	No error (n=647)	P value
Mechanical ventilation during ICU stay, n (%)	853 (94.88)	490 (75.73)	<0.001
Vasopressor use during ICU stay, n (%)	556 (61.85)	196 (30.29)	<0.001
Renal replacement therapy during ICU stay, n (%)	32 (3.56)	13 (2.01)	0.074
The time of the operation, n (%)			
Surgery is performed before ICU	691 (85.63)	280 (88.61)	0.189
Surgery is performed during ICU stay	97 (10.79)	227 (35.09)	<0.001
Surgery is performed after ICU	13 (14.13)	42 (16.73)	0.561
Time of transfer, n (%)			<0.001
Day (07:00–14:59)	568 (63.18)	266 (41.11)	
Evening (15:00–22:59)	331 (36.82)	380 (58.73)	
Night (23:00–06:59)	0	1 (0.15)	
Day of transfer, n (%)			0.012
Weekday	755 (83.98)	511 (56.84)	
Weekend	144 (16.02)	136 (21.02)	
ICU length of stay, median (IQR)	3 (5)	2 (2)	<0.001
All hospital length of stay, median (IQR)	23 (17)	15(14)	<0.001

ICU, intensive care unit.

diagnostic and treatment environments is unforeseeable by both patients and medical staff.

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REFERENCES

- Naylor MD, Aiken LH, Kurtzman ET, *et al*. The care span: the importance of transitional care in achieving health reform. *Health Aff* 2011;30:746–54.
- Elliott RA, Camacho E, Jankovic D, *et al*. Economic analysis of the prevalence and clinical and economic burden of medication error in England. *BMJ Qual Saf* 2021;30:96–105.
- Naylor MD, Shaid EC, Carpenter D, *et al*. Components of comprehensive and effective transitional care. *J Am Geriatr Soc* 2017;65:1119–25.
- Janković SM, Pejčić AV, Milosavljević MN, *et al*. Risk factors for potential drug-drug interactions in intensive care unit patients. *J Crit Care* 2018;43:1–6.
- Using medication reconciliation to prevent errors. *Jt Comm J Qual Patient Saf* 2006;32:230–2.
- Pourrat X, Corneau H, Floch S, *et al*. Communication between community and hospital pharmacists: impact on medication reconciliation at admission. *Int J Clin Pharm* 2013;35:656–63.
- Huynh C, Wong ICK, Tomlin S, *et al*. Medication discrepancies at transitions in pediatrics: a review of the literature. *Pediatric Drugs* 2013;15:203–15.
- Kruer RM, Jarrell AS, Latif A. Reducing medication errors in critical care: a multimodal approach. *Clin Pharmacol* 2014;6:117–26.
- Tully AP, Hammond DA, Li C, *et al*. Evaluation of medication errors at the transition of care from an ICU to Non-ICU location. *Crit Care Med* 2019;47:543–9.
- Unroe KT, Pfeiffenberger T, Riegelhaupt S, *et al*. Inpatient medication reconciliation at admission and discharge: a retrospective cohort study of age and other risk factors for medication discrepancies. *Am J Geriatr Pharmacother* 2010;8:115–26.
- Bosma LBE, Hunfeld NGM, Quax RAM, *et al*. The effect of a medication reconciliation program in two intensive care units in the Netherlands: a prospective intervention study with a before and after design. *Ann Intensive Care* 2018;8:19.
- Kwan JL, Lo L, Sampson M, *et al*. Medication reconciliation during transitions of care as a patient safety strategy: a systematic review. *Ann Intern Med* 2013;158:397–403.
- Camiré E, Moyen E, Stelfox HT. Medication errors in critical care: risk factors, prevention and disclosure. *CMAJ* 2009;180:936–43.
- Janković SM, Pejčić AV, Milosavljević MN, *et al*. Risk factors for potential drug-drug interactions in intensive care unit patients. *J Crit Care* 2018;43:1–6.
- Chaboyer W, James H, Kendall M. Transitional care after the intensive care unit: current trends and future directions. *Crit Care Nurse* 2005;25:16–29.

- 16 Meyer-Masseti C, Hofstetter V, Hedinger-Grogg B, *et al.* Medication-Related problems during transfer from hospital to home care: baseline data from Switzerland. *Int J Clin Pharm* 2018;40:1614–20.
- 17 Lee JY, Leblanc K, Fernandes OA, *et al.* Medication reconciliation during internal Hospital transfer and impact of computerized prescriber order entry. *Ann Pharmacother* 2010;44:1887–95.
- 18 National Coordinating Council for Medication Error Reporting and Prevention: Types of Medication Errors, 2018. Available: <http://www.nccmerp.org/types-medication-errors> [Accessed 10 Feb 2018].
- 19 Cornish PL, Knowles SR, Marchesano R, *et al.* Unintended medication discrepancies at the time of hospital admission. *Arch Intern Med* 2005;165:424–9.
- 20 Vira T, Colquhoun M, Etohells E. Reconcilable differences: correcting medication errors at hospital admission and discharge. *Qual Saf Health Care* 2006;15:122–6.
- 21 Bell CM, Brener SS, Gunraj N, *et al.* Association of ICU or hospital admission with unintentional discontinuation of medications for chronic diseases. *JAMA* 2011;306:840–7.
- 22 Tong EY, Roman CP, Mitra B, *et al.* Reducing medication errors in hospital discharge summaries: a randomised controlled trial. *Med J Aust* 2017;206:36–9.
- 23 Lei TT, Zhao RS. Clinical application and research progress of atomization inhalation therapy. *Clinical Medication Journal* 2016;14:1–5.
- 24 Wang ML, Xie TY, *et al.* Reason analysis of 1 case of dyspnea induced by aerosol inhalation of ambroxol. *China Pharmacy* 2011;22:3791–2.
- 25 Nie ZF, SL L. Analysis of atomization status and adverse reactions of gentamycin injection in a hospita. *Modern medicine and health* 2019;35:1852–4.
- 26 Latif A, Rawat N, Pustavoitau A, *et al.* National study on the distribution, causes, and consequences of voluntarily reported medication errors between the ICU and non-ICU settings. *Crit Care Med* 2013;41:389–98.
- 27 Viscusi ER, Hugo V, Hoerauf K, *et al.* Neuraxial and peripheral misconnection events leading to wrong-route medication errors: a comprehensive literature review. *Reg Anesth Pain Med* 2021;46:176–81.
- 28 Patel S, Loveridge R. Obstetric neuraxial drug administration errors: a quantitative and qualitative analytical review. *Anesth Analg* 2015;121:1570–7.
- 29 Paparella SF, Wollitz A. Mix-ups and misconnections: avoiding intravenous line errors. *J Emerg Nurs* 2014;40:382–4.
- 30 Kopp BJ, Erstad BL, Allen ME, *et al.* Medication errors and adverse drug events in an intensive care unit: direct observation approach for detection. *Crit Care Med* 2006;34:415–25.
- 31 Benkirane RR, Abouqal R, R-Abouqal R, *et al.* Incidence of adverse drug events and medication errors in intensive care units: a prospective multicenter study. *J Patient Saf* 2009;5:16–22.
- 32 Alghamdi AA, Keers RN, Sutherland A, *et al.* Prevalence and nature of medication errors and preventable adverse drug events in paediatric and neonatal intensive care settings: a systematic review. *Drug Saf* 2019;42:1423–36.
- 33 Martins RR, Silva LT, Lopes FM. Impact of medication therapy management on pharmacotherapy safety in an intensive care unit. *Int J Clin Pharm* 2019;41:179–88.
- 34 Kane-Gill SL, Kirisci L, Verrico MM, *et al.* Analysis of risk factors for adverse drug events in critically ill patients*. *Crit Care Med* 2012;40:823–8.
- 35 Cullen DJ, Sweitzer BJ, Bates DW, *et al.* Preventable adverse drug events in hospitalized patients: a comparative study of intensive care and general care units. *Crit Care Med* 1997;25:1289–97.
- 36 Rothschild JM, Landrigan CP, Cronin JW, *et al.* The critical care safety study: the incidence and nature of adverse events and serious medical errors in intensive care. *Crit Care Med* 2005;33:1694–700.
- 37 Abdelaziz K, Abdelrahim ME. Identification and categorisation of drug-related problems on admission to an adult intensive care unit. *Eur J Hosp Pharm* 2015;22:138–41.
- 38 Guignard B, Bonnabry P, Perrier A, *et al.* Drug-Related problems identification in general internal medicine: the impact and role of the clinical pharmacist and pharmacologist. *Eur J Intern Med* 2015;26:399–406.
- 39 Ravn-Nielsen LV, Duckert M-L, Lund ML, *et al.* Effect of an in-hospital multifaceted clinical pharmacist intervention on the risk of readmission: a randomized clinical trial. *JAMA Intern Med* 2018;178:375–82.
- 40 Balling L, Erstad BL, Weibel K. Impact of a transition-of-care pharmacist during hospital discharge. *J Am Pharm Assoc* 2015;55:443–8.
- 41 Ensing HT, Stuijt CCM, van den Bemt BJB, *et al.* Identifying the optimal role for pharmacists in care transitions: a systematic review. *J Manag Care Spec Pharm* 2015;21:614–36.
- 42 Daliri S, Hugtenburg JG, Ter Riet G, *et al.* The effect of a pharmacy-led transitional care program on medication-related problems post-discharge: a before-after prospective study. *PLoS One* 2019;14:e0213593.