ORIGINAL ARTICLE

Medication Prescription Errors in the Intensive Care Unit: Prospective Observational Study

Mandeep Kumar[1], Neeru Sahni[2], Nusrat Shafiq[3], Lakshminarayana Yaddanapudi[4]

Abstract

Introduction: The WHO launched a 5-year global initiative to address the problem of medication errors on March 29, 2017, targeting a decrease in severe and avoidable medication-related harm by 50% in all the countries. Since prescription errors are preventable, this study was conducted to determine incidence and severity of medication prescription errors (MPEs).

Settings and design: Intensive care unit of a tertiary care academic hospital, prospective observational study.

Methods and materials: For all patients admitted in a medical ICU, baseline data (demographic, APACHE II, length of ICU stay, and days of mechanical ventilation) were noted. Treatment charts were reviewed daily, and each prescription was compared against a master chart prepared using standardized references to study the incidence of prescription errors. Severity classification was done using National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) classification. Mean and median, along with standard deviation and interquartile range, were calculated for all quantitative variables. Multivariate linear regression analysis model was used.

Results: Out of the total 24,572 medication orders, 2,624 had prescription errors, an error rate of 10.7% (95% CI, 10.3–11.1). When analyzed for severity, 1,757 (7.15%) (95% CI, 6.8–7.5) MPEs did not result in patient harm and 867 (3.52%) (95% CI, 3.3–3.8) MPEs required interventions and/or resulted in patient harm. Patients with deranged creatinine (p <0.001) and INR (p = 0.024) had higher number of severe MPEs.

Conclusion: The incidence of MPEs in the medical ICU at the tertiary care hospital was 10.7%, 3.52% being severe errors.

Keywords: Critically ill, Intensive care unit, Medication errors, Prescription.

Indian Journal of Critical Care Medicine (2022): 10.5005/jp-journals-10071-24148

Highlights

- The World Health Organization (WHO) launched a 5-year global initiative to address the problem of medication errors on March 29, 2017.
- This large observational study with 24,572 medication orders in an adult medical intensive care unit (ICU) showed 10.7% incidence of prescription errors with 3.5% severe errors.
- Patients with abnormal creatinine and international normalized ratio (INR) had higher number of severe errors.

Introduction

Medication errors (MEs) affect an estimated 1.3 million people every year in the United States, and mortality is as high as at least one death every day. The WHO launched a 5-year global initiative to address the problem of MEs on March 29, 2017, targeting a decrease in severe and avoidable medication-related harm by 50% in all countries.[1] Critically ill patients in the ICU are at high risk of experiencing MEs owing to the use of multiple medications, the severity of illness, associated comorbidities, and narrow safety margin of certain drugs.[2,3]

Medication involves selecting and prescribing the drug, documenting the prescription, preparing and dispensing the drug, administering the drug, and monitoring the effects. A prescription error is defined as the failure of the process of prescription writing/documentation that results in wrong instruction about one or more of the normal features of a prescription, like the date of prescription, patient identification, and the correct drug with the complete instruction on its use. Prescription should be correct regarding dose, frequency, route of administration, and duration of the drug to be taken.[4]

[1,2,4]Department of Anaesthesiology and Intensive Care, Postgraduate Institute of Medical Education and Research, Chandigarh, India

[3]Department of Pharmacology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Corresponding Author: Neeru Sahni, Department of Anaesthesiology and Intensive Care, Postgraduate Institute of Medical Education and Research, Chandigarh, India, Phone: +91 9872646106, e-mail: neerunalin@yahoo.com

How to cite this article: Kumar M, Sahni N, Shafiq N, Yaddanapudi L. Medication Prescription Errors in the Intensive Care Unit: Prospective Observational Study. Indian J Crit Care Med 2022;26(5): 553–557.

Source of support: Nil

Conflict of interest: None

Since prescription errors are the most preventable MEs, this study was conducted with the primary aim of determining the incidence of MPEs in ICU patients in a tertiary care teaching hospital. The secondary aim was to ascertain the severity of each ME through a semi-quantitative analysis.

Methods

This is a study of the rate of errors during the prescribing phase of the medication process conducted from January 1 to June 30, 2018, in the ICU of an academic tertiary care hospital in North India. After obtaining approval from the Institute's Ethics Committee (NK/3820/MD/349) and registration of the study protocol (CTRI/2017/11/015951), all patients admitted to the ICU for more

than 24 hours were included in the study, after obtaining consent from their attendant.

Baseline characteristics of all the included patients were recorded, including demographic data (name, gender, age, weight, height, and admission number), diagnosis, and Acute Physiological and Chronic Health Evaluation (APACHE) II score at 24 hours of admission. Further data, such as total number of days of mechanical ventilation, number of days of ICU stay, outcome, and mortality in ICU, were also acquired.

As per the practice of our unit, a senior resident (registrar level) writes paper prescriptions and these treatment charts are renewed every day for every patient. Prescription errors were identified if the treatment chart mentioned wrong spelling, wrong dose, wrong route of administration, or wrong frequency of administration of any drug. For this, a dedicated team consisting of a resident and two consultants from the specialty of anesthesia and one from pharmacology reviewed the treatment charts of all patients daily. The daily treatment chart of each patient was considered a separate entity. Each drug in the chart was evaluated against standard prescriptions regarding dose, frequency, and route.

In the unit, the dose of antimicrobials for patients with raised creatinine was prescribed based on the calculated creatinine clearance, which is calculated using the Cockcroft–Gault formula. Antimicrobials were evaluated using Sanford Anti-Microbial Guide 2017. All other drugs were compared against the master chart prepared by the study team using standardized references from pharmacology, prior to the start of data collection. Dose modification of each drug was considered in relation to the renal and liver function tests of each patient. Intravenous fluids, drugs in continuous infusion, blood products, and feeds (enteral or parenteral) were not included. Medications in continuous infusion, e.g., insulin, inotropes, vasopressors, etc., requiring continuous titration according to their effects, were not included. Also, in the best interest of patient care, the ICU team was informed of the recognized MPE daily.

Data were entered into a custom database application using the database engine MySQL, version 5.7.19, and the scripting language PHP, version 5.6.31. Drugs were grouped into 11 classes, i.e., antibiotics, antivirals, antifungals, antihypertensive, nutrition and general care, cardiovascular, steroid and immunosuppressants, antiepileptics, decongestants, sedatives, and miscellaneous drugs. MPEs were classified for severity using the NCCMERP classification into eight classes from A to H.[5] MPEs of A, B, and C categories were not considered harmful for the patient. Category D to H drug errors were considered potentially harmful[6] (Table 1). Data were described in frequencies, percentages, and rates. Statistical analysis was carried out using Jamovi (version 0.9.5.14, www.jamovi. org). As the distribution of demographic parameters was skewed, the data were presented in violin plots. Mean and median, along with standard deviation and interquartile range, were calculated for all quantitative variables as measures of central tendency and of dispersion. A multivariate linear regression analysis model was developed to describe the association between the number of severe MPEs and patients' characteristics.

Results

In total, 146 out of 186 patients admitted during the study period were eligible for inclusion and 138 were included in the final analysis (Flowchart 1). Demographic characteristics of the patients and overall distribution are depicted in Figure 1.

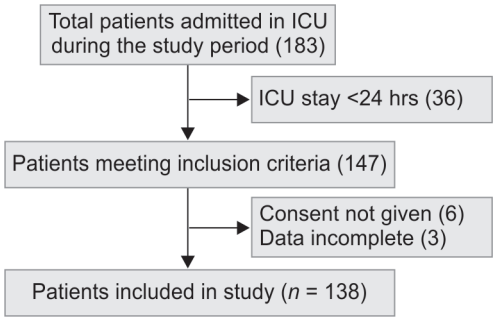
The primary diagnosis of the patients was categorized by the organ system involvement on admission to the ICU. Most patients had respiratory involvement (37), followed by central nervous system (27), poisoning (15), infections (12), renal (12), gastrointestinal (10), cardiovascular (9), musculoskeletal (9), and endocrinological involvement (4). Ten patients were grouped in the miscellaneous category.

Out of a total of 24,572 medication orders, 2,624 had prescription errors (error rate 10.7%; 95% CI 10.3–11.1). A total of 867 MPEs (3.5%; 95% CI 3.3–3.8) required interventions or resulted in patient harm (severity categories D to H) and 1,757 MPEs (7.2%; 95% CI 6.8–7.5)

Table 1: Severity of MPEs—classification according to the NCCMERP[5]

Errors with no harm	Category A	Circumstances that have the capacity to cause error
	Category B	Error did not reach the patient because it was intercepted before or during the administration process
	Category C	Error reached the patient but did not cause patient harm
Errors, potential preventable MPEs	Category D	Error reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm
Errors with preventable MPEs	Category E	Error may have contributed to or result in temporary harm to the patient and required intervention
	Category F	Error may have contributed to or result in temporary harm to the patient and required initial or prolonged hospitalization

Flowchart 1: Study flowchart



did not result in patient harm (severity categories A, B, and C) (Table 2, Fig. 2). Out of 138 patients, 129 (92.8%; 95% CI 89.3–97.5) had one or more MEs. Among these, 62 (44.9%; 95% CI 36.6–53.2) required intervention or resulted in patient harm. The remaining 67 patients (48.6%; 95% CI 40.2–56.9) had non-harmful MPEs.

Approximately 70% of the severe MPEs occurred in the antibiotics group alone, constituting 2.8% (95% CI 2.1–3.6) of the total MPEs. Non-severe MPEs occurred in medications of the following groups with decreasing frequency: general care and nutrition 1,367 (5.6%; 95% CI 5.3–5.8), antibiotics 89 (0.4%; 95% CI 0.3–0.4), cardiovascular 82 (0.3%; 95% CI 0.3–0.4), and

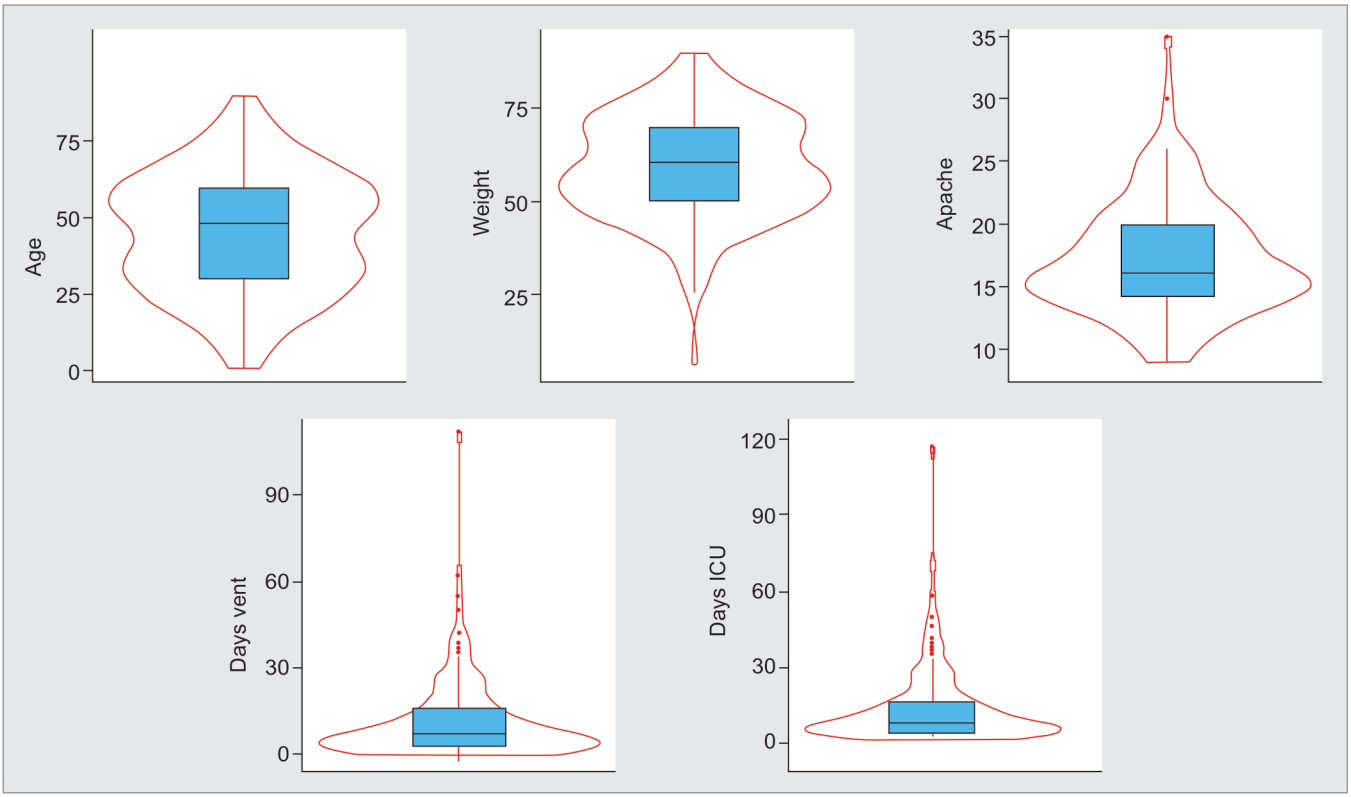


Fig. 1: Violin plots for demographic parameters

Table 2: MPEs and their severity (numbers and percentages)

Medication group	*Drugs*	*MPEs*	*MPEs %*	*Non-severe MPEs*	*Severe MPEs*	*Non-severe MPE rate (%)*	*Severe MPEs rate (%)*
Antibiotics	3,210	698	26.6	89	609	0.4	2.5
Antiviral	75	0	0	0	0	0	0
Antifungal	410	138	5.2	52	86	0.2	0.4
Antihypertensive	527	55	2.1	55	0	0.2	0
Cardiovascular	699	91	3.4	82	9	0.3	0
Nutrition and general care	16,353	1,510	57.6	1,367	143	5.6	0.6
Miscellaneous	1,630	60	2.2	52	8	0.2	0
Steroids and immunosuppressants	413	42	1.6	35	7	0.1	0
Antiepileptics	919	16	0.6	13	3	0.1	0
Decongestants	265	10	0.3	8	2	0	0
Sedatives	71	4	0.1	4	0	0	0
Total	24,572	2,624	100	1,757	867	7.2	3.5

antihypertensives 55 (0.2%; 95% CI 0.2–0.3). Although general care and nutrition constituted the highest number of MPEs, nearly 91% of these were non-severe.

We developed a multivariate linear regression model (adjusted $R^2 = 0.479$) which showed that increased creatinine and INR were predictive of severe MPEs (Table 3).

Discussion

Medication errors are classified as prescribing, prescription, transcription, dispensing, and administration errors, based on the process of medication. About 70% of the MEs leading to adverse effects are prescription errors, which are also the most preventable.[7]

Many authors have collected data retrospectively or used representative sampling to study the incidence of MEs.[6,8–10] We have studied the incidence of MPEs prospectively in a single center, using total sampling for 6 months. We analyzed 24,572 medication orders and found that nearly 11% had prescription errors. About one-third (3.5/10.7) of the prescription errors were severe enough to require intervention or resulted in patient harm. Prescription errors for antibiotics contributed to a large proportion (70%) of severe MPEs.

The 11% prescription error rate in our study is slightly better than in the study conducted in adult ICUs in the United Kingdom[11] (15%) and in a European pediatric ICU (5) (14%). The latter could be due to strict weight-based dose calculation in the pediatric population leading to more errors.[6]

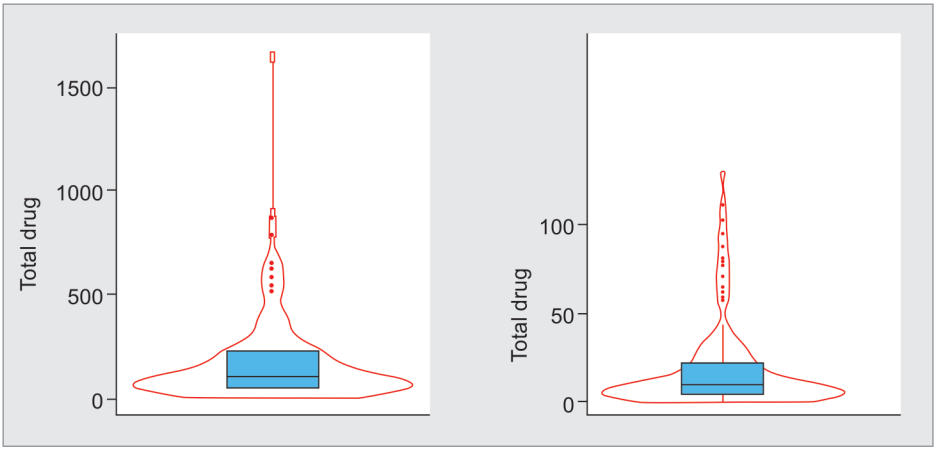


Fig. 2: Violin plots for total drugs and total MPEs

Table 3: Results of linear regression model for MPEs (independent variable) and patients' characteristics (dependent variables)

Predictor	*Estimate*	*SE*	*t*	*p*
Intercept	−5.070	6.227	−0.814	0.417
Age	−0.015	0.049	−0.299	0.766
Gender: Male–Female	2.304	1.890	1.219	0.225
Weight	−0.045	0.077	−0.584	0.560
Weekend: 1–0	−0.907	1.715	−0.529	0.598
ICU days	0.451	0.329	1.373	0.172
Ventilation days	0.039	0.346	0.112	0.911
Comorbidity: 1–0	−1.153	1.746	−0.661	0.510
Outcome: Death–discharge	3.667	2.105	1.742	0.084
Creatinine	2.082	0.576	3.612	<0.001
Hemoglobin	0.236	0.343	0.687	0.493
INR	3.799	1.664	2.282	0.024
PaO_2/FiO_2 ratio	0.004	0.006	0.632	0.528

SE, standard error

While we reported prescription errors exclusively, others have reported MEs occurring at all stages, ranging from errors in prescribing, transcribing, to dispensing till administration, e.g., Jennane et al. (about 10%),[7] Jain et al. (9.6%),[8] and the studies included in the systematic review by Wilmer et al.[10]

The incidence of MPEs varies in various studies, being higher in process-oriented studies than in the ones targeting outcomes, such as adverse events.[7] For example, though Benkirane et al.[2] (109 adverse events), Merino et al.[3] (350 MEs in 1,424 incidents), and Morimoto et al.[12] (1,010 adverse drug events and 524 MEs) reported adverse events, the absence of a denominator does not allow calculation of the incidence of MPEs.

The method of data collection for MEs also varies widely, direct observation, internal or external reviews by physicians or pharmacists, interviews, or verbal self-reporting.[2,3,5,7–10] Due to fear of punitive action, self-reporting is considered ineffective.[13] A direct review of treatment charts involving a pharmacist is considered beneficial.[14] We adopted direct daily chart review to minimize undetected data.

The method of drug prescription, paper-based or computer-based, also affects the error rates. Colpaert et al. found a 27% MPE rate in a paper-based unit compared to just 3.4% in a computerized unit.[15] Even after implementation of computer-based prescription, errors persist, and it requires repeated training of physicians or a support system for clinical decision to sustain a low error rate.[16] However, the MPE rate in our study was low (10.7%) despite our drug prescription practice being paper-based. This may be due to prescription writing by a registrar and review by ICU consultants on daily rounds.

Antibiotics are a commonly prescribed drug class, and their prescription is dynamic as modification is required based on organ dysfunction as well as pharmacokinetic and pharmacodynamic properties of the drug. We recorded 26% of total MPEs to be related to antibiotic prescription, which is intermediate between those reported in a pediatric ICU (Glanzmann et al., 15%) and an adult ICU (Jennane et al., 33%).[6,8] This can certainly be improved by sensitizing and training the personnel. Romero et al. reported almost 50% reduction in MEs related to antibiotics (from 65.9 to 32.4%) in a pre- and post-intervention study.[17]

Nutrition and general care drugs, like multivitamin and mineral supplements, recommended for overall well-being in the ICU,[18] contributed to more than half of the errors. Despite daily feedback as per our protocol, the errors of prescription of these drugs (especially missing dose/route of administration) persisted.

An important finding of our study is that patients with raised creatinine had twice the chance of having severe MPEs. Once the need for renal replacement therapy arises, the dose of antibiotics needs further modification, sometimes on a daily basis depending upon the method of renal replacement therapy.[19] Antibiotics also need to be prescribed as per their pharmacokinetic and pharmacodynamic properties to prevent low serum concentration. Chertow et al. proposed incorporating a real-time dose-guiding algorithm in units using computer-based prescription, to reduce MPEs in patients with renal insufficiency.[20]

Patients with extended ICU stay had more MPEs, which we believe merely represents the fact that a longer ICU stay leads to more drug prescription and more errors, as shown earlier by Glanzmann et al., who found that days of hospital stay and mechanical ventilation, and the number of prescribed drugs positively correlate with the number of MEs.[5]

As our study was a single-center study in a tertiary care academic hospital, the results may not be generalizable. Also, Hawthorne effect could have resulted in fewer errors, as the same dedicated team visited the ICU for direct chart review daily. After the identification of errors, feedback was given to treating doctors on a daily basis. This might have reduced the probability

of similar errors till the time the same team of doctors was posted in the ICU. Another limitation of the study is that MPEs for drugs administered as continuous infusions were not analyzed. Due to dynamic titration of drugs in infusion, we decided to omit these drugs for detecting MPEs.

Detecting MPEs with direct chart review and total sampling is an important strength of our study. Also, as the same team recorded all observations, interobserver variability and undetected errors are expected to be minimal. Focusing only on numbers and severity of prescription errors provides an opportunity to adopt practices targeting the reduction in these errors in critically ill patients.

The availability of incidence of MPEs in our unit and the high risk of MPEs in patients with multiorgan dysfunction (acute kidney injury and deranged coagulation profile) will help improve the quality of care and reduce MPEs to a minimum. A larger study to analyze all forms of drug errors occurring during the medication process may be planned in future.

This observational study demonstrated the incidence of prescription errors in a medical ICU at a tertiary care hospital to be 10.7%. However, only 3.5% were severe errors that required interventions or resulted in patient harm. This incidence can be reduced further with sensitization, training, monitoring, and reinforcement.

Orcid

Mandeep Kumar https://orcid.org/0000-0003-3816-7845
Neeru Sahni https://orcid.org/0000-0002-8506-8076
Nusrat Shafiq https://orcid.org/0000-0001-7053-003X
Lakshminarayana Yaddanapudi https://orcid.org/0000-0002-9822-0217

References

1. WHO. World Health Organization. WHO launches global effort to halve medication-related errors in 5 years [Internet]. Available from: http://www.who.int/mediacentre/news/releases/2017/medication-related-errors/en/ [Accessed June 10, 2017].
2. Benkirane RR, Abouqal R, Haimeur CC, S Ech Cherif El Kettani SS, Azzouzi AA, Mdaghri Alaoui AA, et al. Incidence of adverse drug events and medication errors in intensive care units: a prospective multicenter study. J Patient Saf 2009;5(1):16–22. DOI: 10.1097/PTS.0b013e3181990d51.
3. Merino P, Martín MC, Alonso A, Gutiérrez I, Alvarez J, Becerril F, et al. Medication errors in Spanish intensive care units. Med Intensiva 2013;37(6):391–399. DOI: 10.1016/j.medin.2012.11.002.
4. Aronson JK. Medication errors: definitions and classification. Br J Clin Pharmacol 2009;67(6):599–604. DOI: 10.1111/j.1365-2125.2009.03415.x.
5. NCCMERP. National coordinating council for medication error reporting and prevention. 2014. Available from: http://www.nccmerp.org/about-medication-errors [Accessed July 16, 2021].
6. Glanzmann C, Frey B, Meier CR, Vonbach P. Analysis of medication prescribing errors in critically ill children. Eur J Pediatr 2015;174(10):1347–1355. DOI: 10.1007/s00431-015-2542-4.
7. Velo GP, Minuz P. Medication errors: prescribing faults and prescription errors. Br J Clin Pharmacol 2009;67(6):624–628. DOI: 10.1111/j.1365-2125.2009.03425.x.
8. Jennane N, Madani N, OuldErrkhis R, Abidi K, Khoudri I, Belayachi J, et al. Incidence of medication errors in a Moroccan medical intensive care unit. Int Arch Med 2011;4:32. DOI: 10.1186/1755-7682-4-32.
9. Jain S, Basu S, Parmar VR. Medication errors in neonates admitted in intensive care unit and emergency department. Indian J Med Sci 2009;63(4):145–151. DOI: 10.4103/0019-5359.50763.
10. Wilmer A, Louie K, Dodek P, Wong H, Ayas N. Incidence of medication errors and adverse drug events in the ICU: a systematic review. Qual Saf Health Care 2010;19:e7. DOI: 10.1136/qshc.2008.030783.
11. Ridley SA, Booth SA, Thompson CM. Prescription errors in UK critical care units. Anaesthesia 2004;59(12):1193–200. DOI: 10.1111/j.1365-2044.2004.03969.x.
12. Morimoto T, Sakuma M, Matsui K, Kuramoto N, Toshiro J, Murakami J, et al. Incidence of adverse drug events and medication errors in Japan: the JADE study. J Gen Intern Med 2011;26(2):148–153. DOI: 10.1007/s11606-010-1518-3.
13. Jha AK, Kuperman GJ, Teich JM, Leape L, Shea B, Rittenberg E, et al. Identifying adverse drug events: development of a computer-based monitor and comparison with chart review and stimulated voluntary report. Am J Med Inform Assoc 1998;5(3):305–314. DOI: 10.1136/jamia.1998.0050305.
14. Leape LL, Cullen DJ, Clapp MD, Burdick E, Demonaco HJ, Erickson JI, et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. Journal of the American Medical Association 1999;282(3):267–270. DOI: 10.1001/jama.282.3.267.
15. Colpaert K, Claus B, Somers A, Vandewoude K, Robays H, Decruyenaere J. Impact of computerized physician order entry on medication prescription errors in the intensive care unit: a controlled cross-sectional trial. Crit Care 2006;10(1):R21. DOI: 10.1186/cc3983.
16. Kadmon G, Pinchover M, Weissbach A, Hazan SK, Nahum E. Case not closed: prescription errors 12 years after computerized physician order entry implementation. J Pediatr 2017;190:236–240.e2. DOI: 10.1016/j.jpeds.2017.08.013.
17. Romero CM, Salazar N, Rojas L, Escobar L, Griñén H, Berasaín MA, et al. Effects of the implementation of a preventive interventions program on the reduction of medication errors in critically ill adult patients. J Crit Care 2013;28(4):451–460. DOI: 10.1016/j.jcrc.2012.11.011.
18. Shenkin A. The key role of micronutrients. Clin Nutr 2006;25(1):1–13. DOI: 10.1016/j.clnu.2005.11.006.
19. Hartmann B, Czock D, Keller F. Drug therapy in patients with chronic renal failure. Dtsch Ärztebl Int 2010;107(37):647–656. DOI: 10.3238/arztebl.2010.0647.
20. Chertow GM, Lee J, Kuperman GJ, Burdick E, Horsky J, Seger DL, et al. Guided medication dosing for inpatients with renal insufficiency. Journal of the American Medical Association 2001;286(22):2839–2844. DOI: 10.1001/jama.286.22.2839.