

Butler University
Digital Commons @ Butler University

Scholarship and Professional Work – COPHS

College of Pharmacy & Health Sciences

Spring 3-28-2017

Occurrence of Potential Adverse Drug Events from Prescribing Errors in a Pediatric Intensive and High Dependency Unit in Hong Kong: An Observational Study

Chad A. Knoderer Butler University, cknodere@butler.edu

Celeste L. Ewig

Hon Ming Cheung

Kwok Ho Kam

Hiu Lam Wong

Follow this and additional works at: https://digitalcommons.butler.edu/cophs_papers

Part of the Medical Sciences Commons, and the Other Pharmacy and Pharmaceutical Sciences Commons

Recommended Citation

Knoderer, Chad A.; Ewig, Celeste L.; Cheung, Hon Ming; Kam, Kwok Ho; and Wong, Hiu Lam, "Occurrence of Potential Adverse Drug Events from Prescribing Errors in a Pediatric Intensive and High Dependency Unit in Hong Kong: An Observational Study" (2017). *Scholarship and Professional Work – COPHS*. 242. https://digitalcommons.butler.edu/cophs_papers/242

This Article is brought to you for free and open access by the College of Pharmacy & Health Sciences at Digital Commons @ Butler University. It has been accepted for inclusion in Scholarship and Professional Work – COPHS by an authorized administrator of Digital Commons @ Butler University. For more information, please contact digitalscholarship@butler.edu.

Occurrence of Potential Adverse Drug Events from Prescribing Errors in a Pediatric Intensive and High Dependency Unit in Hong Kong: An Observational Study

Celeste L. Y. Ewig¹, Hon Ming Cheung², Kwok Ho Kam¹, Hiu Lam Wong¹, Chad A. Knoderer³

¹ School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong

² Department of Paediatrics, Faculty of Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong

³ College of Pharmacy and Health Sciences, Butler University, Indianapolis, IN, USA

Abstract

Background Critically ill pediatric patients are considered at high risk for medication errors. Although much research focuses on the actual errors, equally important are medication errors that, although intercepted, carried the potential for an adverse drug event. The aim of this study was to determine the occurrence of prescribing errors and potential adverse drug events (pADEs) in a local pediatric intensive and critical care unit (PICU) in Hong Kong. Our secondary objective was to determine the type of error, nature of medication involved and the time of error occurrence.

Methods We conducted a prospective observational chart review among patients in a pediatric intensive and high dependency unit between January 16, 2015 and April 20, 2015. Medical charts for each patient were reviewed for the occurrence of a prescribing error or pADE. Each pADE was assessed for the type of error, the classification of agent involved, clinical severity of the error, and the time the error occurred.

Results Forty-one patients with a mean age of 3.2 years were included in our study. Of these patients, 19 (46.3%) experienced at least one pADE. We identified 131 pADEs, 129 of which were prescribing errors conferring a rate of 6.8 errors per affected patient or 3.1 errors per patient admitted to the PICU. The most common error found in the study was incorrect dose calculation (48.1%), with intravenous fluids (41.7%), cardiovascular agents (15.0%), and anti-infectives (12.5%) the most common agents involved with an error. The majority of the pADEs in our study were either clinically serious (33.1%) or significant (44.9%) in nature. Nearly one in every four errors required monitoring and/or intervention to prevent harm, and almost all (96.9%) of the prescribing errors were intercepted before reaching the patient.

Conclusion This study highlights incorrect dose calculation as the most common prescribing error in a pediatric critical care setting. Intravenous fluids, cardiovascular agents, and anti-infectives were the classes of medication most commonly involved with a pADE. Due to the highrisk nature of medications used and the critical condition of these patients, more than three-quarters of pADEs were considered to be clinically serious or significant in causing patient harm.

1 Introduction

Medication errors are preventable events 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 [1]. Over the past two decades, preventing medication errors have been a major healthcare priority. These errors pose a threat for serious harm and fatality to patients despite a large number occurring without any harm or physical injury [2, 3]. Despite this, medication- or therapy-related incidences are found to be the most common type of safety incidents reported among pediatric intensive care patients, accounting for up to 40% of all safety incidents reported in this setting [3].

Medication errors may result in either an adverse drug event (ADE) or a potential adverse drug event (pADE). Adverse drug events, as defined by the Institute of Medicine (IOM), refer to injuries or patient harm resulting from the use of a drug [4]. Errors that occurred but were intercepted and did not result in patient harm are referred to as near miss incidents or pADEs [5]. pADEs are medication errors with the potential for injury but in which no injury occurred due to either chance or an intervention [5–8]. Although not all ADEs (such as idiopathic allergic reactions) occur due to a medication error, emphasis is often placed on medication errors due to their preventable nature.

Information regarding medication errors among the pediatric population, although limited, points towards a higher occurrence, with pediatric patients exposed to a three-times-higher rate of pADE [8]. Kaushal et al. also reported prescribing errors among pediatric inpatients to be significantly high with 74% of medication errors occurring during the physician ordering process [8]. Within the pediatric intensive care unit, prescribing error rates range from 11.11 to 78.1% depending on the type of critical care unit and whether orders were electronic or handwritten [2, 9–11]. Dosing errors in particular contribute to this increased risk for adverse drug events among the pediatric population [12]. Such errors result due to the individualized weight-based dose calculations necessary in this patient population, thereby resulting in a wide range of acceptable doses prescribed. Other factors precipitating a higher risk for errors include the lack of appropriate formulations and unfamiliarity with caring for pediatric patients [13].

Critically ill pediatric patients/2 years of age are at an even higher risk for adverse events [14]. The complexity of their condition, the likelihood of being on a large number of medications, and the high-risk nature of the medications used in this setting contribute to the higher risk for clinically severe to potentially lethal medication errors [15]. These patients also have limited physiologic reserves to compensate for or accommodate such errors, further increasing their risk for harm [8]. In addition, the majority of the medications used within this subgroup of pediatric patients are used off label with no FDA approval for use or with approval among limited age groups [16]. Many of these medications are on the Institute of Safe Medical Practice's (ISMP's) list of high-risk medications due to their ability to increase risk for patient harm when used in incorrectly [17]. Given the multiple factors involved and the individualized dose calculation made during the prescribing process, prescribing errors are often recognized as a leading cause of medication error among this group of patients [14].

The primary objective of the study is to determine the occurrence and nature of prescribing errors and pADEs among critically ill pediatric patients in a Hong Kong hospital. Although we expect some similarities in our results, some potential differences between our findings and those from other countries might be present due to differences in error reporting culture, use of a paper-based medication ordering system, workflow logistics, and other factors that may translate to differences in the occurrence, type, and nature of prescribing errors in a pediatric intensive care unit (ICU).

2 Methods

2.1 Study Design, Study Site and Patient Population

This is a prospective observational study to identify prescribing errors among patients admitted to the pediatric intensive care and high dependency unit (PICU) of a regional 870-bed acute care public hospital in Hong Kong. The study was conducted from January 16, 2015 to April 20, 2015. Patients \geq 29 days old and on at least one active medication were included in the study for the duration of their PICU stay. The institution is accredited by the Australian Council of Healthcare Standards (ACHS) and serves as the major referral center for hospitals in the New Territories East Cluster. The study unit is a tertiary level pediatric ICU equipped with respiratory support, various modes of ventilation and circulatory support in renal replacement therapy. The unit consists of three pediatric high dependency beds and five acute intensive care beds. Patients admitted to the acute intensive care unit have a patient to nurse ratio of approximately 1:4.6, while those in the high dependency unit have a ratio of approximately 1:2–1:2.5. A two-tier system for physicians is adopted during the daytime ward rounds with one first call physician and a more senior team head. The level of experience for the first call physician varies from a first year medical offer to a specialist with up to 6 years of experience, while physician team heads have more than 10 years of experience. All prescription orders are hand-written on a paper-based medication chart. Orders are then manually transcribed onto a Medication Administration Record (MAR) form, which is sent electronically to the main pharmacy for preparation and dispensing. A clinical pharmacist is available on weekdays and reviews all orders written on the patient's chart for errors and drug-related problems.

2.2 Definition of Potential Adverse Drug Events and Identification of Errors

We defined prescribing errors based on the IOM definition, wherein the error occurred during the order writing or transcribing phase. All orders, pharmacological (such as medications) and non-pharmacological (such as nutritional supplements or milk formulas), written by physicians were included in our review. The research team, consisting of a PICU senior physician team head, a clinical pharmacist, and two pharmacy students, reviewed all written orders for prescribing errors. The team evaluated each error to determine whether the correction or discrepancies from the original order was intentional (i.e., based on the recommendations of a consultant physician or pharmacist) or not. Intentional corrections were not considered to be

errors and were subsequently excluded from further data analysis. Prescribing errors that were true errors were assessed for the type of error, the classification of medication or agent involved, and the time of day the error occurred. Errors were categorized as wrong rate of administration, wrong drug, wrong dose, wrong unit, wrong dosage interval (frequency), wrong dosage form, wrong body weight, wrong diluent, wrong strength (or strength unavailable), and wrong route. A modified version of the World Health's Organization's (WHO's) Anatomical Therapeutic Chemical (ATC) classification was used to categorize the medications involved [18].

Each prescribing error was initially considered a potential ADE as the error had the possibility of resulting in a negative outcome [19]. Those corrected before reaching the patient were considered as intercepted pADEs. A non-intercepted pADE referred to a prescribing error that was not corrected, reached the patient, but did not result in patient harm [9]. Intercepted prescribing errors were identified based on the presence of a correction or alteration in the original handwritten order on the patient's medical record or medication administration record. Non-intercepted prescribing errors were identified based on discrepancies between clinical notes and order regimen in the absence of any corrections. All non-intercepted pADEs were evaluated for the occurrence of patient harm. Errors that were not intercepted or corrected, reached the patient, and resulted in patient harm were considered actual ADEs. Drug-related problems identified by clinical pharmacists were also included as pADEs. The National Coordination Council for Medication Error Reporting and Prevention (NCCMERP) index was used to categorize medication errors while the clinical severity of the error was assessed by adopting the rating based on Overhage and Lukes (Table 1) [1, 20].

2.3 Data collection and Data Analysis

Medical charts of all patients eligible for inclusion were reviewed twice weekly for any prescribing errors during their PICU admission. Data collection times were scheduled on Monday and Thursday to consolidate the collection times and minimize interference with workflow. Demographic and clinical data including gender, age, and diagnosis were collected along with details of the prescribing errors such as time the order was written, name of the medication, along with its dose and frequency of administration. The total number of concurrent medications each patient had at the time of the occurrence of the error was also noted. Descriptive statistics were used for baseline characteristics and primary and secondary outcomes, and were analyzed using Microsoft Excel version 2010. Statistical analyses were conducted using Statistical Package for Social Sciences version 23.0 (SPSS, Inc., Chicago, USA). The study obtained approval by the institution's investigational review committee.

3 Results

3.1 Patient Demographics and Characteristics

Forty-two patients were admitted to the PICU during our study. One patient did not meet the minimum age criteria of 29 days and was excluded from the study. The remaining 41 patients

included in our study had a mean age of 3.2 years (interquartile range [IQR] 2.3–5). Admission into the PICU was most frequently due to diseases in the respiratory system. Patients were also noted to have an average of 5.3 concurrent medications during the time of medication chart review. Characteristics of the study population are presented in Table 2.

3.2 Prescribing Errors and Potential Adverse Drug Events

We reviewed 217 medication orders suspected to be prescribing errors, with 86 considered by the investigational team to be error free and excluded from subsequent analysis. The remaining 131 (60.4%) medication orders were determined to be pADEs. Two were the use of an unnecessary drug and were categorized as drug-related problems. The remaining 129 (96.9%) were category B errors or intercepted pADEs. We classified these as prescribing errors. This corresponded to19 (46.3%) patients having a minimum of one pADE. The number of prescribing errors found resulted in a rate of 6.8 errors per patient affected or 3.1 errors per patient admitted to the study unit. Of the 129 prescribing errors, two intercepted errors involved an incorrect body weight documented. We classified both as a wrong dose prescribing error; however, they were excluded from analysis for classification of medication and clinical severity as it was difficult to determine which of the medications could have been involved, if any. This resulted in 127 intercepted prescribing errors included in our medication class and clinical severity analysis (Table 3).

3.3 Clinical Significance of Potential Adverse Events, Type of Error and Nature of Medication Involved

Over three quarters (78%) of the 127 errors were found to be at least clinically significant or clinically serious and 20.5% were found to be of minor clinical severity. Two pADEs (1.6%) were classified by investigators as potentially lethal. The first potentially lethal pADE involved an order for fentanyl while the second involved noradrenaline. Nearly one of every four pADEs required monitoring and/ or intervention to prevent harm (Table 4).

We reviewed all orders prescribed to patients, both pharmacological and non-pharmacological, and found intravenous fluid solutions were involved in 50 (41.7%) of the pADEs, representing the class of medications with the largest number of prescribing errors. Cardiovascular agents, anti-infectives, and analgesics followed with 18 (15.0%), 15 (12.7%), and 12 (10.0%) pADEs associated with each class, respectively. Errors of various clinical severity occurred across all medication classes and non-pharmacological products. Of the 50 pADEs due to intravenous fluid solutions, 14 (28%) and 25 (50%) were potentially severe and significant pADEs. Further subgroup analysis found approximately three quarters of errors from the aforementioned class of medication were either clinically severe or serious (Fig. 1). The most frequent type of error involved a wrong dose, which occurred among 62 (48.1%) of the pADEs noted. A wrong rate of administration, wrong drug, and wrong dosing interval were subsequently the most common prescribing errors with 24 (18.6%), 11 (8.5%), and 10 (7.8%) errors, respectively. Among the

pADEs assessed, a higher number of such prescribing errors occurred in the early morning to noon period.

4 Discussion

Our study sought to determine the incidence of prescribing errors and corresponding actual or potential ADEs in a pediatric critical care unit. We adopted the term 'pADE' rather than 'near miss', however both terms have been used interchangeably in other clinical risk management studies [9]. We focused on this patient group due to the increased risk for medication errors, up to 60%, among patients <2 years of age in the pediatric ICU [15]. Although patients in our study with at least one pADE were younger (2.1 vs 4.2 years), previous studies indicate no correlation between age and the occurrence of prescribing errors [3, 14, 19].

Prescribing errors have an alarmingly high incidence with up to 79% of pADEs reported during the prescribing process [8]. Our study identified that 46.3% of patients admitted to the PICU experienced at least one pADE. This was similar to results from a cohort of Swiss patients, where 42.48% of patients in the PICU had at least one prescribing error [14]. Other studies show a larger range with one study in New Zealand reporting the frequency of pADEs to be 26.4% among their pediatric surgical wards while investigators in the US found pADEs comprised 83% of all medication errors [7, 21]. Although numerous studies exist regarding the rate of errors, most of the reported pADEs among pediatric patients were based on medication errors rather than prescribing errors specifically [7, 21].

Almost all (96.9%) of the prescribing errors were intercepted before reaching the patient. However, our results should not underestimate the potential risk in patient safety. In a study conducted among pediatric ICU clinicians, the five most commonly acknowledged high-alert medications used among critically ill pediatric patients were also included in the ISMP list [22]. Given the heavy use of such medications in our study population, more than three quarters (77.1%) of all pADEs were clinically significant with most of them being severe or serious pADEs. Potentially lethal errors were also reported most frequently among patients admitted to the pediatric ICU (0.29 vs 0.09; p<0.001), further suggesting the significance of such errors [15]. In our study, two errors were found to be of such grave severity. The first error pertained to the use of fentanyl in a 17-month-old male infant with respiratory failure where the original order was written as per minute rather than per hour. The second error involved noradrenaline in a 5year-old male child with multiple comorbidities. The initial order was written in mg/kg rather than $\mu g/kg$.

Intravenous solutions, anti-infectives, and cardiovascular agents were the medication classes found to have the most pADEs, a finding similarly observed among pediatric inpatients in other countries [21]. Similar studies conducted to determine errors in the pediatric ICU reported that antiinfective agents, intravenous medications, sedatives, cardiovascular agents, and analgesics were the medications most likely to be associated with an error, with one study reporting that up to 50% of prescribing errors were associated with antihypertensives and antimycotics [8, 14, 21].

Incorrect dose calculations was the most common type of error observed, a finding universally consistent across all studies [8, 15, 22–26]. The National Patient Safety Agency in the UK

highlighted the three most common medication incidence types: wrong or unclear dose, strength or frequency; omitted or missed dose; and wrong drug [26]. One study in Hong Kong also reported consistent findings with 39.5% of problems identified to be drug- or dose-related [27]. The multi-step process involved in calculating a dose is one of the vulnerable areas for prescribing errors to occur. Frequent dose adjustments needed to optimize fluids and electrolytes compound this risk, as dose recalculations are required to achieve the delicate balance between sufficient versus over-hydration or over-correction resulting from the frequent fluctuations in their critical state.

We noted two prescribing errors where no interception was indicated. One occurred over a weekend and was corrected on Monday by the clinical pharmacist assigned to the unit. We were unable to determine if either of the patients were administered the erroneous order or whether harm incurred. We speculate that one of the following situations occurred: the patient was administered the drug but did not experience any harm, or the error was identified and corrected before reaching the patient but was not documented in the patient's chart. Considering the potential outcome of such errors, we predict the latter scenario occurred. Our study also noted that prescribing errors occurred in the morning, coinciding with the time for patient care rounds. This was similar to a previous study where 73% of all errors occurred during the daytime (between 07:00 and 19:00) [9].

Risk management strategies such as failure mode and effects analysis (FMEA) offer a systematic approach to prevent the occurrence of medication errors [28, 29]. These strategies have proven to be effective in reducing the risk for medication errors among various pediatric patient populations. Lago et al. reported a reduction of 60% among high-risk failure modes in pediatric prescribing and administration errors with the use of FMEA [30]. At our study institution, all medical or medication incidents are reported through the hospital's Acute Incident Reporting System (AIRS) and forwarded to the hospital's Quality and Risk Department for appropriate action. Root cause analyses (RCAs) and FMEAs are both conducted for all incidences. An incident-specific committee discusses the error and interviews medical, nursing and relevant staff. The risk-management committee within the Department of Pediatrics of the study institution also assists in the evaluation and action of all reported incidents among the pediatric wards. This most likely contributed to the high number of intercepted prescribing errors.

Specific interventions recognized to reduce medication errors in the pediatric ICU and pediatric population in general include computerized physician order entry (CPOE) with or without clinical decision support, standardized intravenous systems, educational methods, protocols and guidelines, pharmacist involvement, and clinical decision support systems [2, 8, 10, 31–33]. Active participation and availability of a unit-based clinical pharmacist during and outside of physician rounds have shown to decrease the number of medication errors in the pediatric population [10, 14, 34]. A reduction in prescribing error rates, from 78.1 to 35.2% (p < 0.001), was observed when pharmacists provided interventions such as the provision of drug use assistance during point of care, structured combined order and administration charts, educational talks, and feedback for resident physicians [9, 11]. Given the limited number of clinical pharmacists in our study institution, clinical pharmacy services are only available from 9 a.m. to

5 p.m., Mondays through Fridays excluding public holidays, and the assigned clinical pharmacist is responsible for patients in the PICU, the neonatal ICU (NICU), and the Special Baby Care Unit (SBCU). With the large number of patients under their care, pediatric pharmacists are often absent during patient rounds. This model of service was adopted to accommodate the high patient-to-pharmacist ratio among public hospitals in Hong Kong. As a result, gaps in patient care continue to exist and the burden of correcting errors before they reach the patient may be unequally distributed among the healthcare team. Although our study shows the absence of patients being harmed, solely preventing errors may not necessarily translate to the most effective and ideal care for the patient.

Numerous interventions also exist specific to dosing errors. These include providing dosing assistance, communication or educational interventions, education of physicians, and zero tolerance prescribing [11, 33]. Additional interventions such as having a standardized prescription information source, pocket tables with dosing guidelines, updated prescription protocols, and education programs significantly decreased prescribing error rate in a PICU [2]. The National Health Service (NHS) in the UK has highlighted the incorporation of computerized software to perform calculations, double checking procedures, electronic prescribing systems, clinical pharmacist activity, and utilization of smart pumps [35]. Standardization of continuous infusions or intravenous drips may also simplify the order process of fluids and electrolytes, thereby reducing dosing errors among these agents [36].

Along with the findings presented, our study has some limitations. The absence of a control group and the limited size of the study population prevented us from identifying and assessing risk factors for prescribing errors and pADEs. Secondly, our study was an observational study. These results do not reflect methods to address or minimize prescribing errors. Furthermore, although the researchers adopted the NCCMERP along with a clinical severity assessment tool, the investigators' clinical judgment was taken into consideration when assigning the clinical severity of the errors. The patients' clinical condition and concurrent medications at the time of the errors may have led to a potential bias in severity assessment. We acknowledge the possibility that errors may have been intercepted after the medication had been administered, thereby under-representing the number of actual or potential ADEs. Finally, our results do not translate to errors during drug dispensing, preparation, or administration.

5 Conclusion

This study provides valuable insight into the occurrence and nature of prescribing errors and potential ADEs among critically ill pediatric patients in Hong Kong. Our study shows the consistency of incorrect dose calculations as one of the leading causes of prescribing errors. Our results also highlight specific classes of medications such as intravenous fluids, cardiovascular agents, and anti-infectives most likely associated with an error. Such results may be applicable to other pediatric populations as well, in particular those requiring continuous intravenous infusion, fluids, and electrolyte supplementation, or requiring frequent adjustments and dose recalculations. Although the current system was able to prevent most of the prescribing errors,

the study emphasizes the high risk for harm based on the significant clinical severity in the majority of these errors should they have gone uncorrected. Future considerations such as broadening clinical pharmacist coverage, and the use of other interventions such as computerized physician order entry systems and standardized infusion regimens may contribute to not only ensuring medication safety but also to improving standard of care among critically ill pediatric patients.

Compliance with Ethical Standards

The study was approved by the research institution's Investigational Review Board. The authors declare no financial assistance was received for conducting the study or preparation of the manuscript.

Conflict of interest Authors C. Ewig, H.M. Cheung, K.H. Kam, H.L. Wong, and C. Knoderer declare they have no conflict of interests with the design, implementation and results of this study or with the contents of the manuscript.

References

1. National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP). About Medication Errors. [Internet]. [cited July 21 2015]. Available from: http://www.nccmerp. org/aboutMedErrors.html.

2. Martinez-Anton A, Sanchez J, Casanueva L. Impact of an intervention to reduce prescribing errors in a pediatric intensive care unit. Intensive Care Med. 2012;38:1532–8.

3. Skapik J, Pronovost P, Miller M, Thompson D, Wu A. Pediatric safety incidents from an intensive care reporting system. J Patient Saf. 2009;5(2):95–101.

4. Institute of Medicine Committee on Quality Health Care in America. To err is human: building a safer health system. Report of the Institute of Medicine. In: Kohn L, Corrigan J, Donaldson M, editors. National Academy Press; 2000.

5. Bates D, Cullen D, Laird N, Petersen L, et al. Incidence of adverse drug events and potential adverse drug events. JAMA. 1995;274(1):29–34.

6. Bates D, Boyle D, Vander Vliet M, Schenider J, Leape L. Relationship between medication errors and adverse drug events. J Gen Intern Med. 1995;10:199–205.

7. Kunac D, Kennedy J, Austin N, Reith D. Incidence, preventability, and impact of adverse drug events (ADEs) and potential ADEs in hospitalized children in New Zealand. Pediatr Drugs. 2009;11(2):153–60.

8. Kaushal R, Bates D, Landrigan C, McKenna K, Clapp M, Federico F, et al. Medication errors and adverse drug events in pediatric inpatients. JAMA. 2001;285(16):2114–20.

9. Burmester M, Dionne R, Thiagarajan R, Laussen P. Interventions to reduce medication errors in a paediatric cardiac intensive care unit. Intensive Care Med. 2008;34:1083–90.

10. Alagha H, Badary O, Ibrahim H, Sabri N. Reducing prescribing errors in the paediatric intensive care unit: an experience from Egypt. Acta Paediatr. 2011;100:e169–74.

11. Cimino M, Kirsjhbaum M, Brodsky L, Shaha S. Assessing medication prescribing errors in pediatric intensive care units. Pediatr Crit Care Med. 2004;5(2):124–32.

12. Wong I, Ghaleb M, Franklin B, Barber N. Incidence and nature of dosing errors in paediatric medications. Drug Saf. 2004;27(9):661–70.

13. Wong I, Wong L, Cranswick E. Minimising medication errors in children. Arch Dis Child. 2009;94:161-4.

14. Glanzmann C, Frey B, Meier C, Vonbach P. Analysis of medication prescribing errors in critically ill children. Eur J Pediatr. 2015;174:1347–55.

15. Folli H, Poole R, Benitz W, Russo J. Medication error prevention by clinical pharmacists in two children's hospitals. Pediatrics. 1987;79:718–22.

16. Yang C, Veltri M, Anton B, Yaster M, Berkowitz I. Food and Drug Administration approval for medications used in the pediatric intensive care unit: a continuing conundrum. Pediatr Crit Care Med. 2011;12(5):e195–9.

17. ISMP List of High Alert Medications in Acute Care Settings [Internet]. http://www.ismp.org/Tools/institutionalhighAlert.asp: Institute for Safe Medication Practices [cited 2017 Jan 21].

18. WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment 2013. World Health Organization; 2012.

19. Holdsworth M, Fichtl R, Behta M, Raisch D, Mendez-Rico E, Adams A, et al. Incidence and impact of adverse drug events in pediatric inpatients. Arch Pediatr Adolesc Med. 2003;157:60–5.

20. Overhage J, Lukes A. Practical, reliable, comprehensive method for characterizing pharmacists' clinical activities. Am J Health Syst. 1999;56(23):2444–50.

21. Buckley M, Erstad B, Kopp B, Theodorou A, Priestley G. Direct observation approach for detecting medication errors and adverse drug events in a pediatric intensive care unit. Pediatr Crit Care Med. 2007;8(2):145–52.

22. Franke H, Woods D, Holl J. High-alert medications in the pediatric intensive care unit. Pediatr Crit Care Med. 2009;10(1):85–90.

23. Kaushal R, Bates D, Abramson E, Soukup J, Goldmann D. Unitbased clinical pharmacists' prevention of serious medication errors in pediatric inpatients. Am J Health Syst. 2008;65:1254 60.

24. Committe on Drugs and Committee on Hospital Care. Prevention of medication errors in the pediatric inpatient setting. Pediatrics. 2003;112(2):431–6.

25. Costello J, Torowicz D, Yeh T. Effects of a pharmacist-led pediatric medication safety team on medication error-reporting. Am J Health Syst. 2007;64:1422–6.

26. National Patient Safety Agency. Safety in doses: medication safety incidents in the NHS. London: Patient Safety Observatory report; 2009.

27. Rashed A, Wilton L, Lo C, Kwong B, Leung S, Wong I. Epidemiology and potential risk factors of drug-related problems in Hong Kong paediatric wards. Br J Clin Pharmacol. 2013;77(5):873–9.

28. Agency for Healthcare Research and Quality [Internet].: U.S. Department of Health and Human Services [cited Feb. 7 2007]. Available from: https://healthit.ahrq.gov/health-it-tools-andresources/workflow-assessment-health-it-toolkit/all-workflowtools/ fmea-analysis.

29. Spath P. Using failure mode and effects analysis to improve patient safety. AORN. 2003;78(1):16–37.

30. Lago P, Bizzarri G, Scalzotto F, Parpaiola A, Amigoni A, Putoto G, et al. Use of FMEA analysis to reduce risk of errors in prescribing and administering drugs in paediatric wards: a quality improvement report. BMJ Open. 2012;2(e001249):1–9.

31. Rinke M, Bundy D, Velasquez C, Rao S, Zerhouni Y, Lobner K, et al. Interventions to reduce pediatric medication errors: a systematic review. Pediatrics. 2014;134:338–60.

32. Dickinson C, Wagner D, Shaw B, Owens T, Paslp D, Niedner M. A systematic approach to improving medication safety in a pediatric intensive care unit. Crit Care Nurs Q. 2012;35(1):15–26.

33. Booth R, Sturgess E, Taberner-Stokes A, Peters M. Zero tolerance prescribing: a strategy to reduce prescribing errors on the paediatric intensive care unit. Intensive Care Med. 2012;38:1858–67.

34. Krupicka M, Bratton S, Sonnenthal K, Goldstein B. Impact of a pediatric clinical pharmacist in the pediatric intensive care unit. Crit Care Med. 2002;30(4):919–21.

35. Wong I, Ghaleb M, Franklin B, Barber N. Ways to reduce drug dose calculation errors in children. J Health Serv Res Policy. 2010;15(Suppl 1):68–70.

36. Hilmas E, Sowan A, Gaffoor M, Vaidya V. Implementation and evaluation of a comprehensive system to deliver pediatric continuous infusion medications with standardized concentrations. Am J Health Syst Pharm. 2010;67:58–69.

Category/clinical Definition severity National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) [1] A No error Circumstances or events that have the capacity to cause error в Error, no harm An error occurred but the error did not reach the patient С Error, no harm An error occurred that reached the patient, but did not cause patient harm D Error, no harm An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm Е Error, harm An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention F Error, harm An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization G Error, harm An error occurred that may have contributed to or resulted in permanent patient harm н Error, harm An error occurred that required intervention necessary to sustain life I Error, death An error occurred that may have contributed to or resulted in the patient's death Modified Overhage Clinical Severity Rating [20] No error Clarification or change in recommendation made by physicians or other healthcare professional Minor Incomplete information in medication order Unavailable or inappropriate dosage form Illegible, ambiguous, or nonstandard abbreviation Non-compliance with standard formulations and hospital policies Significant High dosage (1.5-4 times upper limit of normal) of drug with low therapeutic index Drug dosage too low for patient's condition High dosage (1.5-10 times upper limit of normal) of drug without low therapeutic index Errant dual-drug therapy for single condition Inappropriate dosage interval Omission of a medication order Serious Low dosage of drug given for a serious disease in a patient with acute distress High dosage (4-10 times upper limit of normal dosing range) of drug with low therapeutic index High dosage (≥10 times normal) of drug with normal therapeutic index Misspelling or mix-up in medication order could lead to dispensing of wrong drug Involvement of highly potent drugs (e.g., inotropes, paralytics, sedatives) in situations that would lead to serious clinical outcomes Potentially lethal High potential for life-threatening adverse reactions Potentially lifesaving drug at a dosage too low for the condition being treated Very high dosage (such as ≥10 times upper limit of a normal dosing range) of a drug with low therapeutic index

Table 1 Index for categorizing prescribing errors and adverse drug events

| Table 2 | Study-site | patient d | lemographics |
|---------|------------|-----------|--------------|
|---------|------------|-----------|--------------|

| Variable | All patients | Patients with no pADE | Patients with ≥ 1 pADE |
|--|--------------|-----------------------|-----------------------------|
| No. of patients, n (%) | 41 (100) | 22 (53.7) | 19 (46.3) |
| Age group, n | | | |
| 28 days to <6 months | 9 | 4 | 5 |
| 6 months to <2 years | 9 | 5 | 4 |
| 2–6 years | 17 | 7 | 10 |
| 7–12 years | 6 | 6 | 0 |
| Mean age, years (SD) | 3.2 (3.2) | 4.2 (3.8) | 2.1 (1.6) |
| Gender, <i>n</i> (%) | | | |
| Male | 32 | 17 (77.3) | 15 (78.9) |
| Female | 9 | 5 (22.7) | 4 (21.1) |
| Diagnosis upon admission to PICU | | | |
| Diseases of the respiratory system | 12 | 6 | 6 |
| Post-operative \pm complications | 5 | 4 | 1 |
| Neoplasms | 4 | 3 | 1 |
| Sepsis \pm shock | 4 | 1 | 3 |
| Gastroenteritis | 3 | 2 | 1 |
| Diseases of the digestive system | 3 | 2 | 1 |
| Endocrine, nutritional, and metabolic diseases | 2 | 2 | 0 |
| Neurotransmitter disease | 1 | 0 | 1 |
| Acute disseminated encephalomyelitis | 1 | 0 | 1 |
| Neuromuscular disorder | 1 | 1 | 0 |
| Undefined/multiple co-morbidities | 5 | 1 | 4 |
| Number of concurrent medications, mean (SD) | 5.3 (2.8) | 5.5 (3.5) | 5.2 (1.9) |

pADE potential adverse drug event, PICU pediatric intensive and critical care unit, SD standard deviation

| Characteristic | Ν |
|---|------------------|
| Number of prescribing orders suspected to be errors | 217 |
| NCCMERP category, n (%) | |
| Α | 86 (39.6) |
| В | 131 (60.4) |
| С | 0 |
| D | 0 |
| Е | 0 |
| pADEs | 131 |
| Prescribing errors, n (%) | 129 |
| Intercepted orders | 125 (96.9) |
| Non-intercepted/unknown orders | 2 (1.5) |
| Incorrect body weight | 2 (1.5) |
| Clinical severity of prescribing errors, n (%) | 127 ^a |
| Potentially lethal | 2 (1.6) |
| Serious | 42 (33.1) |
| Significant | 57 (44.9) |
| Minor | 26 (20.5) |
| | |

Table 3 Characteristics of potential adverse drug events

pADE potential adverse drug event

^a Excluding two errors involving incorrectly documented body weight

| adverse drug events | |
|---|------------|
| Potential adverse drug events, n (%) | 131 |
| Pharmacologic/medications | 120 (91.6) |
| Drug-related problem (unnecessary drug) | 2 |
| Non-pharmacologic | 9 (6.9) |
| Milk/nutrition formulas | 8 (6.10) |
| Topical agent | 1 (0.7) |
| Non-product related (incorrect body weight) | 2 |
| Medications involved in a pADE, n (%) | 120 |
| Intravenous fluids | 50 (41.7) |
| Cardiovascular agents | 18 (15.0) |
| Anti-infectives | 15 (12.5) |
| Analgesics | 12 (10.0) |
| Blood products/perfusion solutions | 8 (6.7) |
| Antiepileptics | 4 (3.3) |
| Anesthetics | 3 (2.5) |
| Muscle relaxants | 3 (2.5) |
| Antithrombotic agents | 2 (1.7) |
| Antihistamines | 2 (1.7) |
| Gastrointestinal agents | 2 (1.7) |
| Anti-inflammatory agents | 1 (0.8) |
| Type of prescribing error, n (%) | 129 |
| Wrong dose | 62 (48.1) |
| Wrong rate of administration | 24 (18.6) |
| Wrong dosing interval (frequency) | 11 (8.5) |
| Wrong drug | 10 (7.8) |
| Illegible hand-writing | 9 (7.0) |
| Wrong route | 6 (4.6) |
| Wrong unit | 4 (3.1) |
| Wrong IV diluent | 2 (1.5) |
| Wrong strength (strength unavailable) | 1 (0.8) |
| Time of pADE occurrence, n (%) | 129 |
| AM (00:00-12:00) | 63 (48.8) |
| 00:00-06:00 | 12 |
| 06:00-12:00 | 34 |
| Unknown | 17 |
| PM (12:00-24:00) | 44 (34.1) |
| 12:00-18:00 | 28 |
| 18:00-24:00 | 14 |
| Unknown | 2 |
| AM or PM (not specified) | 22 (17.1) |

Table 4 Characteristics of prescribing errors resulting in potential adverse drug events

pADE potential adverse drug event



