Medication Errors and Adverse Drug Events in Pediatric Inpatients

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Context  Iatrogenic injuries, including medication errors, are an important problem in all hospitalized populations. However, few epidemiological data are available regarding medication errors in the pediatric inpatient setting.

Objectives  To assess the rates of medication errors, adverse drug events (ADEs), and potential ADEs; to compare pediatric rates with previously reported adult rates; to analyze the major types of errors; and to evaluate the potential impact of prevention strategies.

Design, Setting, and Patients  Prospective cohort study of 1120 patients admitted to 2 academic institutions during 6 weeks in April and May of 1999.

Main Outcome Measures  Medication errors, potential ADEs, and ADEs were identified by clinical staff reports and review of medication order sheets, medication administration records, and patient charts.

Results  We reviewed 10778 medication orders and found 616 medication errors (5.7%), 115 potential ADEs (1.1%), and 26 ADEs (0.24%). Of the 26 ADEs, 5 (19%) were preventable. While the preventable ADE rate was similar to that of a previous adult hospital study, the potential ADE rate was 3 times higher. The rate of potential ADEs was significantly higher in neonates in the neonatal intensive care unit. Most potential ADEs occurred at the stage of drug ordering (79%) and involved incorrect dosing (34%), anti-infective drugs (28%), and intravenous medications (54%). Physician reviewers judged that computerized physician order entry could potentially have prevented 93% and ward-based clinical pharmacists 94% of potential ADEs.

Conclusions  Medication errors are common in pediatric inpatient settings, and further efforts are needed to reduce them.
creased antibiotic-associated medication errors and ADEs, as well as total costs for patients in an ICU.18

Less information is available regarding the epidemiology and prevention of medication errors and ADEs in pediatric inpatient settings.19 Children pose unique challenges to the system for ordering, dispensing, administering, and monitoring medications. For example, since weight-based dosing is needed for virtually all drugs in pediatrics, ordering medications typically involves more calculations than for adults. Dispensing drugs in pediatrics is also error-prone because pharmacists often must dilute stock solutions. Young children do not have the communication skills to warn clinicians about potential mistakes in administering medications, or about adverse effects that they may experience. Finally, all children, especially neonates, may have more limited internal reserves than adults with which to buffer errors. For example, the cardiovascular system of a premature baby may be unable to cope with even a small error in the dosage of an inotropic agent.

To assess the epidemiology of medication errors, potential ADEs, and ADEs in hospitalized children, we performed a prospective cohort study in 2 academic institutions. Our goals were to (1) determine the rates of medication errors, potential ADEs, and ADEs; (2) compare rates in a pediatric hospital setting with previously reported rates in adult hospitals; (3) analyze the major types of errors; and (4) assess the potential impact of prevention strategies.

**METHODS**

**Study Sites**

The study was conducted at 2 urban teaching hospitals with socioeconomically diverse patient populations. One hospital (hospital A) is a freestanding pediatric institution. The other hospital (hospital B) treats both adult and pediatric patients, but has a geographically and administratively distinct pediatric service. Adults comprise less than 5% of patients treated on the pediatric wards. They generally have complex long-term medical and surgical conditions, such as congenital diseases (eg, cystic fibrosis, cardiac anomalies, metabolic diseases, sickle cell disease), multiple disabilities, immunosuppressive conditions, and eating disorders.

At hospital A, we studied 2 randomly selected general medical wards, 1 randomly selected general surgical ward, the short-stay medical ward, and the pediatric medical/surgical ICU (which has few cardiac patients because there is a separate cardiac ICU). The oncology ward and neonatal ICU (NICU) were not studied at this hospital because these units were preparing for possible introduction of computerized order entry. At hospital B, all pediatric wards were studied, including the general medical/surgical wards (including oncology patients), the pediatric medical/surgical ICU, and the NICU. In total, we studied 9 wards.

**Medication Systems**

Physicians at both hospitals currently handwrite orders, copies of which are sent to the pharmacy. At hospital A, nurses transcribe orders into the medication administration record (MAR). Hospital A has satellite-based pharmacists who dispense ready-to-administer doses to the floor, but do not actively participate in other activities, such as ward-based rounds.

At hospital B, clerks transcribe orders into the MAR. A supply of medications is provided to the units, with nurses subsequently performing dose calculations and drug administration. Pediatric clinical pharmacists attend work rounds, monitor transcriptions, and assist nurses with calculations. Since these pharmacists are assigned to multiple units daily, they have limited time to spend on each unit.

**Definitions**

**Medication errors** were defined as errors in drug ordering, transcribing, dispensing, administering, or monitoring. An example is an order written for amoxicillin without a route of administration. Some medication errors have significant potential for injuring a patient and are considered potential ADEs. Potential ADEs may be intercepted before reaching the patient. An example of an intercepted potential ADE would be an order written for a 10-fold overdose of morphine that is intercepted and corrected by a pharmacist before reaching the patient. A nonintercepted potential ADE would be an overdose of acetaminophen administered to a patient who does not experience any sequelae. ADEs are injuries that result from the use of a drug. Some ADEs are associated with a medication error and therefore are considered preventable, while some are not associated with a medication error and therefore are considered nonpreventable. An example of a preventable ADE is the development of rash after the administration of ampicillin/sublactam to a patient known to be allergic to penicillin. In contrast, a nonpreventable ADE would be development of *Clostridium difficile* colitis after appropriate antibiotic use.

Final rule violations are faulty medication orders with little potential for harm or extra work because nursing and pharmacy staff typically interpret them correctly without additional clarification. An example is a pain medication ordered on a per need basis for a postoperative patient without an explicit reason for administration stated. Rule violations were not considered medication errors.

**Case Finding**

One physician (R.K.) trained all data collectors, who were nurses, pharmacists, and physicians, in an identical manner. During the 2-week training period, the unique perspectives of these different disciplines were shared to maximize appreciation of potential error types and to develop a comprehensive, uniform approach to error detection. We determined inter-rater reliability by a random sampling of 10% of the data collected at each institution by a data collector from the other institution.

Data collectors identified medication errors, potential ADEs, and ADEs...
by voluntary and verbally solicited reports from house officers, nurses, and pharmacists; and by medication order sheet, MAR, and chart review of all hospitalized patients on study wards. On a given day, 1 data collector was assigned to each study ward based on individual availability. Data collected for each incident included name, dose, route and category of drug, point in the system where the error occurred, and type of error. Data collectors worked 5 days per week, with recording of weekend data on Mondays for patients still hospitalized. At the end of the study, we obtained administrative data for each patient hospitalized on the study wards, including age, sex, and race.

Reliable detection of medication errors requires cooperation and engagement of the staff, which depends in large measure on reducing suspicion and fear of reporting. Before initiating this study, we gained the support of the leadership of nursing, pharmacy, medical staff, and administration at each hospital. House staff, nurses, and pharmacists received informal seminars that emphasized the roles of complex systems and human factors in predisposing to error, as opposed to individual blame. We stressed the importance of understanding the epidemiology and causes of error, and reinforced the multidisciplinary nature of systems improvement. We performed the study over 6 weeks in April and May of 1999, after obtaining institutional review board approval at each institution.

**Review Process**

Two physicians (D.W.B. and D.A.G.) independently reviewed suspected ADEs and potential ADEs and classified them as ADEs, potential ADEs, medication errors, and rule violations. The physician reviewers rated ADEs and potential ADEs according to the severity of injury to the patient using a 4-point Likert scale. They also rated ADEs on preventability using a 5-point Likert scale and attribution (ie, the likelihood that the incident is due to the specific drug) using the Naranjo algorithm. The 2 evaluators resolved all disagreements through discussion and consensus.

**Statistical Methods**

We report rates of errors per 100 orders, 100 admissions, and 1000 patient-days. We did subanalyses of preventable and potential ADEs. We measured age-specific rates per 100 admissions, and analyzed them assuming that the number of errors occurring during an admission followed a Poisson distribution. We measured ward-specific rates per 100 orders and compared them using the chi-squared test for categorical variables since it was extremely rare for more than 1 error to occur during a single order. Similarly, we compared rates per 100 orders between adult and pediatric hospital settings and analyzed them using the chi-squared test. When we assumed that the number of errors per order followed a Poisson distribution, we obtained similar results, so we report only the chi-squared test results. The SAS statistical package (for Windows 6.12) was used (SAS Institute Inc, Cary, NC).

We calculated inter-rater reliabilities using the percentage of agreement and the k statistic. The data collectors and physician reviewers had moderate-to-excellent agreement with 87%-to-100% agreement and k statistics of 0.65 to 1.0.

**RESULTS**

The 36-day study period included 1120 admissions and 3932 patient-days, during which 10778 orders were written. The patients included 183 (16%) neonates, 326 (29%) infants, 223 (20%) preschoolers, 161 (14%) school-aged children, 191 (17%) teenagers, and 36 (3%) adults. Of the children, 525 (49%) were female, 731 (65%) were white, 139 (12%) were Hispanic, and 79 (7%) were black.

There were 616 medication errors (5.7%) or 55 medication errors per 100 admissions (Table 1). In total, 320 patients accounted for these medication errors and 64 patients had 3 or more errors. We found 26 ADEs (0.24%), of which 5 (19%) were preventable. In addition, we identified 115 potential ADEs (1.1%), which occurred at a rate of 10 potential ADEs per 100 admissions.

Medication errors occurred more frequently in adults compared with other age groups (86 vs 62 for neonates, 41 for infants, 48 for preschoolers, 58 for school-aged children, and 63 for teenagers per 100 admissions; P = .006). The rate of potential ADEs was considerably higher in neonates than in other age groups (20 vs 5 for infants, 8 for preschoolers, 12 for school-aged children, 11 for teenagers, and 14 for adults per 100 admissions; P < .001).

Given the high rate of neonatal potential ADEs, we performed a subanalysis comparing the 54 neonatal patients in the NICU with the 129 neonatal patients in other wards. The NICU neonates were primarily premature with low birth weights and respiratory and nutritional issues, while non-NICU neonates were primarily admitted for infections or congenital abnormalities. Neonates in the NICU experienced significantly higher medication error and potential ADE rates (91 and 46 per 100 admissions, respectively) than neonates in other wards (50 and 9 per 100 admissions, respectively) (P < .001 for both comparisons).

Error rates were similar across units (5.9 errors per 100 orders for the NICU, 5.7 for pediatric ICUs, 6.0 for medical wards, 6.1 for combined medical/
surgical wards, and 4.7 for the surgical ward; \( P = .31 \). However, the NICU had a significantly higher rate of potential or preventable ADEs compared with other wards (2.8 per 100 orders vs 0.78 for medical wards, 0.44 for surgical wards, 0.77 for combined medical/surgical wards, and 1.3 for pediatric ICUs; \( P < .001 \)).

Most medication errors were dosing errors (28%), followed by route of administration, MAR transcription and documentation, date, and frequency of administration errors (TABLE 2). Similarly, most potential ADEs were due to dosing errors (34%), followed by frequency and route errors. The most common stage for medication errors and potential ADEs was physician ordering (74% and 79%, respectively), followed by transcription and nurse administration. The most common drugs involved in medication errors and potential ADEs were anti-infective agents, analgesics and sedatives, electrolytes and fluids, and bronchodilators. The drug routes of medication errors and potential ADEs were most commonly intravenous followed by oral and inhalation.

In addition, physician reviewers judged that 93% of the potential ADEs were potentially preventable by physician computer order entry with clinical decision support, 94% by ward-based clinical pharmacists, and none by computerized MAR. Finally, they judged that computerized physician order entry could have prevented 4 of the 5 preventable ADEs and that ward-based clinical pharmacists could have prevented 4 of the 5 preventable ADEs. For these judgments, the role of the clinical pharmacist included full-time participation in work rounds, monitoring the MAR transcription process, communicating with satellite pharmacies, and assisting nurses with medication dose calculation and administration.

During the study period, 26 ADEs were identified, 5 of which resulted from medication errors and thus were judged to be preventable (TABLE 3). The preventable ADEs included excessive sedation, hypothermia, worsening pain, a rash, and stool impaction. Errors associated with these 5 incidents included 2 overdoses, a missing dose, a drug administration error, and administration of a medication to a patient with a known allergy. Two events involved narcotics, 1 an analgesic, 1 an antibiotic, and 1 a laxative. The route of 2 medications

### Table 2. Types of Medication Errors and Potential Prevention Strategies*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Medication Errors (n = 616)</th>
<th>Potential Adverse Drug Events (n = 115)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Error type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>175 (28)</td>
<td>44 (34)</td>
</tr>
<tr>
<td>Frequency</td>
<td>58 (9.4)</td>
<td>23 (20)</td>
</tr>
<tr>
<td>Route</td>
<td>109 (18)</td>
<td>16 (14)</td>
</tr>
<tr>
<td>Medication administration record transcription or documentation</td>
<td>85 (14)</td>
<td>9 (7.8)</td>
</tr>
<tr>
<td>Wrong drug</td>
<td>8 (1.3)</td>
<td>6 (5.2)</td>
</tr>
<tr>
<td>Wrong patient</td>
<td>1 (0.16)</td>
<td>1 (0.86)</td>
</tr>
<tr>
<td>Known allergy</td>
<td>8 (1.3)</td>
<td>5 (4.3)</td>
</tr>
<tr>
<td>Illegible order</td>
<td>14 (2.3)</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Missing or wrong weight</td>
<td>23 (3.7)</td>
<td>1 (0.86)</td>
</tr>
<tr>
<td>No or wrong date</td>
<td>74 (12)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other</td>
<td>61 (9.9)</td>
<td>8 (7)</td>
</tr>
</tbody>
</table>

| Stage of error |                            |                                        |
| Physician ordering | 454 (74)               | 91 (79)                                |
| Transcribing    | 62 (10)                   | 13 (11)                                |
| Nurse administering | 78 (13)               | 5 (4.3)                                |
| Pharmacy dispensing | 6 (0.97)               | 4 (3.5)                                |
| Patient monitoring | 4 (0.65)               | 0 (0)                                  |
| Missing        | 12 (1.9)                  | 3 (2.6)                                |

| Drug category |                            |                                        |
| Anti-infective drugs | 120 (20)              | 32 (28)                                |
| Analgesics and sedatives | 101 (16)            | 19 (17)                                |
| Electrolytes and fluids | 162 (26)             | 17 (15)                                |
| Bronchodilators | 44 (7.1)                  | 11 (9.6)                               |
| Other            | 166 (27)                  | 36 (31)                                |
| Missing          | 23 (3.7)                  | 0 (0)                                  |

| Drug route |                            |                                        |
| Intravenous | 337 (55)                  | 62 (54)                                |
| Oral        | 126 (21)                   | 25 (22)                                |
| Inhalation  | 46 (7.5)                   | 14 (12)                                |
| Other       | 82 (13)                    | 14 (12)                                |
| Missing     | 25 (4.1)                   | 0 (0)                                  |

| Potential prevention strategy |                            |                                        |
| Ward-based clinical pharmacist | 587 (95)             | 108 (94)                               |
| Computerized physician order entry with decision support | 479 (88)             | 107 (93)                               |
| Computerized medication administration record | 110 (18)             | 0 (0)                                  |

*Values are expressed as number (percentage).
was intravenous, 1 oral, 1 epidural, and 1 via suppository. Physician reviewers classified 4 of the preventable ADEs as serious and 1 as significant. Of the 21 nonpreventable ADEs, 14 were related to antibiotic use, including *C difficile* infections, rashes, allergic reactions, gastrointestinal tract distress, and a yeast infection. The remaining 7 were narcotic-related, including respiratory depression, sedation, and gastrointestinal tract and allergic reactions. Fifteen of the medications were administered intravenously, 5 orally, and 1 via epidural.

Of the 115 potential ADEs, 68 (59%) were intercepted while 47 (41%) were not (Table 3). The physician reviewers determined that 18 (16%) of the potential ADEs were potentially fatal or life-threatening, 52 (45%) were serious, and 45 (39%) were significant. Examples of potentially fatal or life-threatening intercepted potential ADEs included physician orders for a heparin overdose, a digoxin overdose, and amoxicillin for a patient with a previous anaphylactic reaction to penicillin. Among the most common errors associated with potential ADEs were physicians ordering inappropriately high or low doses of medications, ordering medications despite known allergies, ordering medications without routes, and the pharmacy dispensing incorrect medications.

**COMMENT**

We found that medication errors were common in the inpatient pediatric setting. Potential ADEs occurred more frequently in neonates, particularly in the NICU. The rate of medication errors was higher in adults cared for in the pediatric hospital setting. Errors occurred most commonly at the stage of drug ordering. Dosing errors and errors involving the intravenous route were most frequent. The drug classes associated most frequently with errors were antibiotics, electrolytes and fluids, and anesthetics and sedatives. Most errors appeared to be preventable by pharmacist computer order entry with clinical decision support or full-time, ward-based clinical pharmacists.

We compared the results of this study to a 1992 study using similar methods in an adult patient population (TABLE 4). In 1992, physicians at the adult hospital hand-wrote orders, clerks primarily transcribed orders to the MAR, and pharmacists were primarily satellite-based, with some ward-based involvement in the medical ICU. Both studies had similar rates of medication errors, ADEs, and preventable ADEs; however, the rate of potential ADEs was about 3 times higher in this pediatric study (1.1% vs 0.35%; *P* < .001). Interinstitutional comparisons can be difficult to standardize, although in this case 1 physician (D.W.B.) was involved in both studies.

Relatively little research has addressed the problem of medication errors and ADEs in pediatric inpatient settings. Reliable error detection requires intensive, comprehensive, and active ward-based data collection. We used a multidisciplinary approach that examined all aspects of the medication system, from the physician’s order through administration of the drug to the patient. Moreover, we encouraged voluntary reporting by emphasizing the role of systems problems in the origin of errors and by nurturing a blame-free environment. In a previous pediatric study by Folli et al, errors were detected solely by pharmacist review of physician orders, and lower error rates of 0.45 to 0.49 per 100 orders were found. Although 74% of errors in our study occurred in drug orders, many of these errors were detected and corrected prior to the order reaching the pharmacy.

As expected, we found that the errors with potential for harm occurred most often in the youngest, most vulnerable patients cared for in the NICU. Neonatal weights change rapidly, making appropriate dosing particularly difficult. Moreover, medication errors in critically ill neonates may have more serious consequences compared with relatively healthy neonates or older children because they have limited ability to buffer errors. Pharmacists also face special challenges with neonatal drugs because medications generally are not supplied in dosages suitable for neonates and must be diluted.

The relatively small number of adult patients also had significantly higher medication error rates. This may be due to the typically high medical complexity of adult patients cared for in pediatric settings, or the lack of familiarity of pediatric house staff with adult dosing.

The high risk of medication errors highlights the importance of developing, testing, and implementing effective error-prevention strategies in pediatrics. Cogent theories regarding the origin of errors (often categorized as human factor research) have been developed. Most investigators have focused on problems in health care delivery systems that predispose to error, rather than emphasizing the role of individuals. Human fallibility is magnified substantially by complex and poorly designed systems, poor teamwork, and psychological and environmental stressors such as fatigue, anxiety, poor lighting, and noise. The safest work environments address these issues by designing systems to prevent errors, make errors visible, and mitigate the effects of errors.

Ongoing multidisciplinary analysis of incidents, also
MEDICATION ERRORS IN PEDIATRICS


Conclusion: There is a need for further development and testing of interventions to reduce medication errors in pediatrics. The development of computerized physician order entry systems and other interventions, such as those involving ward-based clinical pharmacists, may be effective in reducing medication errors.


This study found that medication errors in pediatrics are common and often preventable. The development and testing of interventions to reduce these errors is important in pediatrics, especially in the NICU, to improve patient safety and outcomes.


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Financial Disclosure: Dr Bates has received honorary for speaking from Eczips Corp, which has licensed the rights for possible commercial development to Brigham and Women’s Hospital Clinical Information System. Dr Bates is coinventor on patent No. 6029318 held by Brigham and Women’s Hospital on the use of decision support software for medical management, licensed to Medicaids Corp. He holds a minority equity position in Medicaids, a privately held company that develops Web-based decision support for radiology test ordering. He also serves as a consultant to Medicaids. Dr Bates is also a consultant and serves on the advisory board for McKesson MedMa- nagement, a company that assists hospitals in preventing adverse drug events. He has received honorary for speaking from Automated Healthcare, which makes robots that dispense medications. He is also on the clinical advisory boards for Becton Dickinson, which develops drug delivery systems; Zynx Inc, which develops evidence-based algorithms; and SoCurious Inc, which compiles information on compliance for drug companies; and he is a consultant for Alaris, which makes intravenous drug delivery systems.

Funding/Support: This work was supported by a grant from the Risk Management Foundation. Dr Kaushal was partially supported by grant T32 HS00063 from the Agency for Healthcare Research and Quality.

Acknowledgment: We would like to thank John Orav, PhD, for his statistical assistance, and Erin Hart- man, MS, for her review of the manuscript. In addition, we would like to thank Priscilla Dasse, RN, MPH, Alan Ezekowitz, MD, PhD, Constance Crowley Ganzer, MS, RN, and Ronald Kleinman, MD, for their support.

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