# Incidence of Adverse Drug Events and Medication Errors in Intensive Care Units: A Prospective Multicenter Study

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**Background:** In recent years, medication error has received considerable attention because it causes substantial mortality, morbidity, and additional health care costs. Collecting information in this field depends on the willingness of health professionals to report their errors. Another important point is to identify patients at high risk for an adverse drug event (ADE) to oversee the quality of the entire drug distribution chain, including prescription, drug choice, dispensing, and preparation to the administration of drugs.

**Objective:** To assess the prevalence rate of ADEs. To ascertain those related to medication errors to develop prevention strategies.

**Design:** Prospective cohort study.

**Setting:** Multicenter study, 7 intensive care unit in academic and military hospital of Rabat.

**Period:** Three months.

**Patients:** Adult and pediatric patients in medical/surgical intensive care units.

**Collection Data:** One coordinator for each participating ward collaborates with a pharmacist investigator from Moroccan pharmacovigilance center in the detection of ADEs.

**Measurements and Main Results:** Of the 696 patients studied, the investigators identified 108 incidents (15.5 %) (95% confidence interval, 14.1–16.9). The reviewers concluded that 56 (70%) of 80 ADEs were nonpreventable, which, by definition, are considered as ADRs. Among the 52 medication errors, 28 (53.8%) led to potential ADEs and 24 (46.2%) led to actual preventable ADEs. There were 7.7 medication errors for 1000 patient-days. We noted that the preventable ADEs occurred in the prescribing (71.1%), administration (21.2%), transcription (5.7%), and dispensing stages. Errors of wrong or improper drug use accounted for the majority of potential and actual preventable ADEs (23%), followed by improper dose (21.1%), wrong duration of treatment (19.2%),wrong rate of administration(13.5), errors due to drug omission (9.6%), wrong administration technique (5.8%), wrong dosage form (3.8%), and wrong administration timing (1.9%).

**Conclusions:** This study argues the need for pharmacovigilance to extend its scope to medication errors to improve the safety of drugs. Our results underlined that medication errors are likely to be more serious than ADRs. Our approach based on the collaboration between the pharmacovigilance center and clinicians can be a powerful tool for incorporating error reporting into the culture of medicine.

**Key Words:** ICU, adverse drug event, medication error, proximal causes, contributing factors

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Because drug use patterns are a major determinant in drug safety, it has been increasingly recognized that the scope of pharmacovigilance needs to be extended beyond the strict confines of detecting new signals of drug safety concerns to safety of practices. Medication errors (MEs) are the most common preventable cause of adverse events. Early detection is important, particularly in hospitals, where systems for detecting adverse drug reactions (ADRs) and MEs can save lives and money. Lessons learned from ME detection may help prevent future errors and protect health professionals and ultimately, their patients. The new challenge for pharmacovigilance centers is to extend the role for National Centre of Pharmacovigilance to include collection of information on adverse incidences related to ME to improve patient safety. In this field, a pilot project built by the World Alliance for Patient Safety in collaboration with the WHO Programme for International Drug Monitoring was initiated in 2007. The Moroccan Pharmacovigilance Centre (MPVC) was assigned as project coordinator. As part of this project, a prospective study in ICU was initiated. The ICU would be an optimal location for developing voluntary reporting incentives based on the frequency of events.[1] In fact, patients in ICU may be at higher risk for adverse drug events (ADEs) because of their higher exposure to medicines and because their health condition is weaker than other patients. Cullen et al[2] observed the combined incidence of preventable and potential ADEs in the ICU to be twice that rate in non-ICU areas. Hence, we performed a prospective cohort study in ICU to assess the prevalence rate of ADEs to determine those related to MEs to develop prevention strategies.

## PATIENTS AND METHODS

### Study Site

The study was conducted in 7 ICU wards at the Academic Hospital and Military Hospital of Rabat (Morocco). The areas included 2 medical ICU wards for adults, 3 surgical ICU for adults, 1 pediatric ICU, and 1 neonatology ward. Medical treatment of patients in both the medical and surgical services was managed by residents and senior physicians. Daily rounds of all of the patients were completed in the morning; decisions regarding the management of these patients were also taken at the same time. Medication orders were handwritten by physicians. Verbal orders were accepted when the physician was

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unable to immediately write the medication order. Nurses completed the transcription process; as for the actual drug distribution, it was the responsibility of the chief of the nursing staff who is in charge of the stock ward.

## Study Design and Data Collection

It is a prospective cohort study. All consecutive patients admitted to the ICU between April 23 and July 23, 2007, were eligible for the study. Patients were followed until transfer, unit discharge, or death. For 3 months, 1 pharmacist-investigator from MPVC was assigned in a specific ward. Two methods of data collection were combined. Observational study, the pharmacist-investigators participated in daily physician rounds and monitored ordering and transcribing medication. The pharmacist was present in the ward 8 hours a day (8 A.M. to 4:30 P.M.), 5 days a week, with recording of week end data on Mondays. Solicited reports from health professionals were the second method of incident identification. On each participating ward, 1 coordinator (senior physician) collaborated with the investigator. The investigators recorded the following data for all patients, using the patient's medical chart review: patient characteristics (age and sex), diagnoses, daily drug exposure, duration of hospitalization, and outcome. A standardized ADR form was filled in for each patient for whom an ADE was identified. These forms require at least demographic characteristics, risk factors (e.g., renal or hepatic impairment), medical history, treatment, indication of treatment, circumstances of ADE, ADE type, drugs, onset delay, and outcome. In the case of actual or potential ME (see below), an ME form is filled in by the coordinator to report targeted information: descriptive elements, medicines involved (given, intended), stage of the error in the medication use system, delay of ME detection, consequences of the ME, type of error, causes of error, and contributing and environmental factors. The study was performed with the approval of the wards' supervisors. Because this was an observational study, no attempt was made to alter the performance of medication use process. Informed consent was not obtained from patients because this study was part of an ICU quality assurance (Table 1).

## Definitions

An *incident* was defined as any event that the observers thought might be an ME or a potential or actual ADE.[3] An *ADE* is "any injury resulting from medical interventions related to a drug" and includes both ADRs in which no error occurred and complications resulting from MEs.[4] According to the World Health Organization's definition,[5] an ADR is "any response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function." This implies that there was no error in the use of the drug.[6] *Medication error* is "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is under the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use."[7] Medication errors may not systematically result in an adverse outcome. A *potential ADE* was defined as "a medication error with the potential to cause any injury but which does not actually cause any injury, either because of specific circumstances, chance or because the error was intercepted and corrected."[7] Examining potential ADEs helps to identify both where the system is failing (the error) and where it is working (the interception). An *actual ADE* was defined as "an injury or patient harm occurring as the result of a medication intervention."[3] *Seriousness of ADEs* has been defined according to WHO classification as "an ADE, that at any dose, results in death or is life threatening, or requires inpatient hospitalization or prolongation of existing hospitalization or results in persistent or significant disability/incapacity."[5]

## Classification of Incidents and Assessment of ADE

Two reviewers of the MPVC staff independently evaluated all incidents on the basis of data entries to determine whether they represented an ADE or potential ADE and to highlight their

**TABLE 1.** Patients Characteristics

| | Adult Medical ICU | Adult Surgical ICU | Pediatric ICU | Neonatology ICU |
|---|---|---|---|---|
| Observed patients, n | 201 | 226 | 155 | 114 |
| Median (±SD) unit length of stay, d | 7.50 ± 1.4 | 6.66 ± 1.2 | 7.81 ± 2.3 | 22.37 ± 2.6 |
| Observed patient-days, n | 1507 | 1506 | 1212 | 2550 |
| Mean (±SD) age, yr | 42.9 ± 2.6 | 48.4 ± 2.4 | 4.8 ± 0.7 | — |
| Male, n (%) | 109 (54.2) | 119 (52.6) | 104 (67) | 48 (42.1) |
| Acute Physiology and Chronic Health Evaluation II score, mean (±SD) | 19.3 (± 0.7) | 15.2 (± 0.6) | — | — |
| Median number of daily medication | 16.22 ± 1.18 | 7.02 ± 0.47 | 7.3 ± 1 | 7.7 ± 0.6 |
| Reason for unit admission, n (%) | | | | |
| Cardiovascular disease | 14 (6.7) | 41 (18.1) | 24 (15.5) | 2 (1.8) |
| Respiratory disease | 54 (27) | 16 (7.1) | 21 (13.5) | 46 (40.4) |
| Digestive disease | 4 (2.2) | 60 (26.5) | 13 (8.4) | 5 (4.4) |
| Neurological disease | 24 (11.8) | 43 (19) | 22 (14.2) | 0 |
| Metabolic disorder | 12 (6.2) | 5 (2.2) | 9 (5.8) | 1 (1) |
| Infection | 40 (19.7) | 10 (4.4) | 9 (5.8) | 27 (23.7) |
| Urogenital disease | 0 | 21 (9.3) | 0 | 0 |
| Poisoning | 41 (20.2) | 0 | 19 (12.3) | 0 |
| Other | 12 (6.2) | 30 (13.3) | 38 (24.5) | 33 (29) |
| Died in unit, n (%) | 55 (28.4) | 25 (11.1) | 33 (21.3) | 12 (10.5) |

seriousness and preventability. Disagreements between reviewers were discussed with the follow-up committee. Adverse drug event causality assessment was estimated using the French method.[8] They classified the ME according to the type of error, the stage of occurrence within the medication process, the severity of the consequences, and the proximal cause using the National Coordinating Council for Medication Error Reporting and Prevention Taxonomy.[9] The fishbonelike diagram was used to explore the contributory factors or latent system failures underlying the most serious errors. The National Patient Safety Agency contributory factors framework were used, taking into consideration, patients factors, individual factors, task factors, communication factors, team and social factors, education and training factors, equipment and resource factors, working conditions, organizational and strategic factors.[10] Every 2 weeks, the follow-up study committee (ward supervisors and MPVC reviewers) discussed and validated the assessment of the collected data, the root cause analysis of serious ME, and proposed action plans to avoid serious ME recurrence.

### Data Analysis

The collected data were computerized using Microsoft Access software. Qualitative variables were described in terms of proportions, with their percentage. Quantitative variables were described in terms of mean and SD. Qualitative data from patients that experienced ADR or ME were compared using $\chi^2$ test or Fischer exact test according to sample size. The statistical significance level was set at $P < 0.05$. Incidence rates of ADE among all patients hospitalized in the participating services during the study period were estimated in proportions with their 95% confidence interval (CI) estimated using the binomial distribution. Incidence rates of ADE were estimated per 100 admissions and per 1000 patient-days.

## RESULTS

### Classification and Rate Evaluation of Incidents

During the study period, 696 patients were monitored, and 108 (15.5 %) (95% CI, 14.1–16.9) incidents were detected. Among them, 80 were categorized as ADE. The reviewers concluded that 56 (70%) of 80 ADE were nonpreventable, which, by definition, are considered as ADRs. Therefore, 52 incidents were deemed as MEs, 28 (53.8%) of which were associated with potential ADEs and 24 (46.2%) with actual preventable ADEs. Among the potential ADEs collected, there was only 1 intercepted ME.

The incidence rate of ADE was 11.5% (95% CI, 9.1–13.9). The ADR and ME incidence rates per 100 admissions were 8 % (95% CI, 6–10) and 7.5 % (95% CI, 5.5–9.5), respectively.

**TABLE 2.** Incidence Rate of ME Per 1000 Patient-days by Ward Category

| Setting | ME Detected | Patient-Days Surveyed | Rate 1000 Patient-Days |
|---|---|---|---|
| Adult Medical ICU (2) | 23 | 1507 | 15.3 |
| Adult Surgical ICU (3) | 8 | 1506 | 5.3 |
| Pediatric ICU (1) | 11 | 1212 | 9.1 |
| Neonatology ICU (1) | 10 | 2550 | 4 |
| Total | 52 | 6775 | 7.7 |

**TABLE 3.** Comparison of ME and ADE Incidence Rate in Pediatric and Adult ICU Settings

| | Pediatric (n = 269) | Adult (n = 427) | *P* |
|---|---|---|---|
| MEs | 21 (7.8) | 31 (7.3) | 0.91 |
| Potential ADE | 17 (6.3) | 11 (2.6) | 0.01 |
| Actual preventable ADEs | 4 (1.5) | 20 (4.7) | 0.01 |
| ADRs | 8 (3) | 48 (11.2) | 0.001 |

### Rate Incidence of ME by Ward Category

The overall ME incidence rate was 7.7 per 1000 patient-days. The prevalence rate of ME was estimated at 15.3 per 1000 patient-days in medical ICU, 5.3 per 1000 patient-days in surgical ICU, 9.1 per 1000 patient-days in pediatric ICU, and 4 per 1000 patient-days in neonatology (Table 2).

### Comparison of ME and ADE Incidence Rate in Pediatric and Adult ICU Settings

We compared the results of pediatric and adult wards. Both settings had similar rates of ME. However, the rate of potential errors was about 2.5 times higher in pediatric wards (6.3 versus 2.6; $P = 0.01$). Compared with the incidence rate of ADRs, which was approximately 4 times higher in the adult area (11.2 versus 3; $P = 0.001$) (Table 3).

### Seriousness of ADEs

The seriousness of ADEs is listed in Table 4. The ADRs were classified by the evaluators as serious in 51.8 %, whereas 79.1 % of actual ME were serious. This difference was statistically significant ($P < 0.05$).

### System Organ Class

The systems and organs most frequently affected by actual preventable ME were cardiovascular and metabolic disorders (20.8% each), whereas the most commonly affected organ systems involved in ADRs were skin and appendages (30.4%).

### Categorization of ADEs by Drug Class

The most involved drugs in ME were antidiabetic (insulin), anesthetics (lidocaine and bupivacaine), cardiovascular (diuretics), anti-infectives, and analgesics medications. All the ME cases that involved insulin, anesthetics, and anticoagulant were classified as serious. Fifty-five percent of ADRs involved psycholeptics, anesthetics, and cardiovascular (diuretics) medications (Table 5).

**TABLE 4.** Seriousness of ADEs (Preventable and Nonpreventable)

| | ADR (n = 56), n (%) | Actual Preventable ADE (n = 24), n (%) | *P* |
|---|---|---|---|
| Hospitalization/ prolonged hospitalization | 21 (37.5) | 10 (41.7) | — |
| Life threatening | 7 (12.5) | 8 (33.3) | — |
| Death | 1 (1.8) | 1 (4.2) | — |
| Total actual ADE (n = 80) | 29 (51.8) | 19 (79.1) | <0.05 |

**TABLE 5.** Medication Classes Involved in Preventable and Nonpreventable ADE

| Medication Classes (Total Doses) | ADR, n (%) | ME, n (%) | Serious ME, n (%) |
|---|---|---|---|
| Anesthetics (n = 33) | 4 (12.1) | 2 (6) | 2 (6) |
| Antidiabetic (insulin) (n = 48) | 1 (2.1) | 4 (8.3) | 4 (8.3) |
| Anti-infectives (n = 1165) | 13 (1.2) | 19 (1.5) | 5 (0.4) |
| Sedation/analgesic (n = 529) | 4 (1.87) | 6 (1.1) | 1 (0.2) |
| Psycholeptics (n = 15) | 7 (46.7) | 0 | 0 |
| Cardiovascular (n = 253) | 7 (2.8) | 3 (1.2) | 1 (0.4) |
| Anticoagulant (n = 370) | 4 (1.08) | 1 (0.27) | 1 (0.27) |
| Anti-inflammatory and antirheumatic products (n = 290) | 3 (1.09) | 0 | 0 |
| Others | 13 | 17 | 5 |

Total doses: the overall doses of medication prescribed during the period.

### Delay of ME Detection

Two thirds of the ME were detected within 24 hours. One ME was intercepted.

### Errors by Type of ADE and Stage of the Process

Approximately 71.1% of ME were attributed to the medication-prescribing stage of the process, 21.2 % to the administration stage, and 5.7% to the transcription stage. One dispensing error was reported. The majority of potential ADEs were noted in the prescribing stage. Approximately two-thirds of the actual preventable ADEs were attributable to the prescribing stage of the medication use process (Table 6).

### Types of Errors by Stage of Process

Errors of wrong or improper drug and improper dose accounted for most potential and actual preventable ADEs (44.2%), followed by wrong duration of treatment (19.2%), wrong rate of administration (13.5%), and drug omission and wrong administration technique (9.6% and 5.8%, respectively). The most likely error during prescription stage was represented by wrong duration of treatment, followed by improper dose and inappropriateness of medication for the patient conditions. Wrong rate of administration represented two-thirds of the errors arising during the administration stage (Table 6).

### Severity of the ME Consequences by Stage

One fatal ME was observed, resulting from a severe hypokalemia developed by a young man with diabetes undergoing insulin therapy for acidosis. Eight observations (15.4%) were associated with an error that resulted in a near-death event. Four of these instances involved the prescription of excessive dose of different medications (lidocaine, fluids, insulin, and vecuronium). Two were attributed to the prescription of a wrong or improper drug (enoxaparin and salbutamol), and two resulted from drug omission (sodium valproate and insulin) (Table 6).

### Proximal Causes

Rule violation, lack of drug knowledge, and poor communication at the prescribing stage were the most common proximal causes of errors (n = 34). On the other hand, insufficient infusion pump and inappropriate administration technique contributed to errors during the administration stage of the process (n = 4 each) (Table 6).

### Identification of System Failures

The primary systems failures were lack of written procedure for managing ICU patients and drug knowledge dissemination (Table 7).

## DISCUSSION

Our evaluation of ADE in ICU is derived from a prospective cohort study that involved pharmacists-investigators from MPVC and clinicians-coordinators from each participating ward. During the 3-month period of the study, efforts were made by both investigators and coordinators to monitor patients and prescription orders to pick up any ADE.

This study confirms that ADEs represent a real disease burden in ICU patients. Our data show that the incidence rate of ADE was 11.5 per 100 admissions, of which, 65 % were preventable. It seems difficult to compare the obtained rates to the literature data because ADE/ADR operational definitions and methodologies are manifold, and many have different scopes. However, prospective studies conducted in hospitals reported ADE incidence rates ranging from 2.4 to 6.5 ADEs per 100 admissions in the United States.[11] An estimated proportion of 44.3% to 60.9% of all ADEs in intensive care patients result from MEs and would be preventable.[12]

Focusing on ME, we evaluated the overall ME rate at 7.7 per 1000 patient-days. When assessing the rate incidence by ward, we found that the highest rate was recorded in medical ICU. The incidence rates of ME were 15.3 per 1000 patient-days in medical ICU and 5.3 per 1000 patient-days in surgical ICU. By using daily prospective chart reviews and voluntary incident reports, the ADE Prevention Study Group evaluated the rate of preventable ADE and potential ADE at 19.4 per 1000 patient-days[2]; with a significantly higher rate in the medical ICU (25 per 1000 patient-days) than in the surgical ICU (14 per 1000 patient-days). Thus, our data are consistent with the findings of ADE Prevention Study Group, with some important differences. The high ADE rate in medical ICU is commonly reported and could be explained by impaired renal function as part of the patient's multiorgan dysfunction, polymedication, the median number of daily medication in medical ICU being 16.22 (95% CI, 15.04–17.54) versus 7.02 (95% CI, 6.55–7.49) in surgical ICU. The length of hospitalization period remains another predisposing factor; in our study, the median duration of stay in medical ICU was 7.5 days and that in surgical ICU was 6.6 days. Our estimates of ME rates are lower than those of ADE Prevention Study Group research, but a direct comparison is limited by temporal changes in data collection methods and local differences in drug use and patient populations. When using a solicited incident reporting system, only a fraction of incidents may be detected. In the ADE Prevention Study Group research, the authors highlighted that solicited reporting by health workers was inferior to chart review for identifying ADEs but was effective for identifying potential ADEs. By using a direct observation in a mixed medical/surgical ICU, Kopp et al[3] found a higher incidence of potential and actual ADEs and an increased ratio of potential to actual preventable ADEs (5:1 ratio) compared with information reported by chart reviews and solicited incident reporting. In 1962, Barker and McConnell[13] compared incident report review and voluntary report review with direct observation and projected that the errors observed represented 1422 times the number identified by incident report review.

In our study, the identification of ADE involved 2 methods: solicited reporting by health workers; and monitoring, ordering, and transcribing medication. We found that, among the 52

**TABLE 6.** Types of MEs

| Description of ME (n = 52) | Prescribing (%) | Administration (%) | Transcription (%) | Dispensing (%) | All (%) |
|---|---|---|---|---|---|
| Type of ADE | | | | | |
| Actual preventable ADE | 15 (62.5) | 8 (33.3) | 1 (4.1) | 0 (0) | 24 (46.2) |
| Potential ADE | 22 (78.6) | 3 (10.7) | 2 (7.1) | 1 (3.6) | 28 (53.8) |
| Total | 37 (71.1) | 11 (21.2) | 3 (5.7) | 1 (1.9) | 52 |
| Error type | | | | | |
| Wrong/improper drug | 12 | 0 | 0 | 0 | 12 (23) |
| Medication not indicated/inappropriate for the condition being treated (n = 7) | | | | | |
| Inappropriate medication (n = 1) | | | | | |
| Medication contraindicated (n = 2) | | | | | |
| Therapeutic duplicity (n = 2) | | | | | |
| Drug omission | 4 | 1 | 0 | 0 | 5 (9.6) |
| Improper dose (n = 11) | 9 | 1 | 1 | 0 | 11 (21.2) |
| Wrong duration of treatment (n = 10) | 10 | 0 | 0 | 0 | 10 (19.2) |
| Wrong administration timing (n = 1) | 0 | 1 | 0 | 0 | 1 (1.9) |
| Wrong dosage form | 2 | 0 | 0 | 0 | 2 (3.8) |
| Wrong administration technique | 0 | 3 | 0 | 0 | 3 (5.8) |
| Wrong rate of administration | 0 | 5 | 2 | 0 | 7 (13.5) |
| Wrong preparation, manipulation, and/or mixing | 0 | 0 | 0 | 1 | 1 (1.9) |
| Severity of the consequences of ME | | | | | |
| Category A | 0 | 0 | 0 | 0 | 0 (0) |
| Category B | 1 | 0 | 0 | 0 | 1 (1.9) |
| Category C | 4 | 2 | 0 | 0 | 6 (11.5) |
| Category D | 17 | 1 | 2 | 1 | 21 (40.4) |
| Category E | 0 | 5 | 0 | 0 | 5 (9.6) |
| Category F | 6 | 3 | 1 | 0 | 10 (19.2) |
| Category H | 8 | 0 | 0 | 0 | 8 (15.4) |
| Category I | 1 | 0 | 0 | 0 | 1 (1.9) |
| Proximal causes | | | | | |
| Inadequate monitoring | 1 | 0 | 0 | 0 | 1 (1.9) |
| Lack of drug knowledge | 13 | 1 | 0 | 1 | 15 (28.8) |
| Rule violation | 9 | 0 | 0 | 0 | 9 (17.3) |
| Memory lapses | 3 | 1 | 0 | 0 | 4 (7.7) |
| Inappropriate administration technique | 0 | 4 | 0 | 0 | 4 (7.7) |
| Fatigue | 0 | 1 | 0 | 0 | 1 (1.9) |
| Transcription error | 0 | 0 | 2 | 0 | 2 (3.8) |
| Communication | 11 | 0 | 1 | 0 | 12 (23.1) |
| Lack of infusion pump | 0 | 4 | 0 | 0 | 4 (7.7) |

detected MEs, 53.8% were associated with potential ADEs and 46.2% with actual preventable ADEs (ratio, 1.17:1).

## Comparison of ME and ADE Rates in Pediatric and Adult ICU Settings

Unexpectedly, the rate of ADRs was significantly lower in pediatric wards. Nevertheless, the ME incidence rate in the pediatric ICU is consistent with some studies.[14] As has been reported by Kaushal et al,[14] we found that the rates of ME in adult and pediatric populations were similar, whereas potential ADE rate was significantly higher in pediatric wards. The relatively higher rates of potentially harmful errors in hospitalized children compared with adults probably occur primarily because dosing is more complex and often lacks a clinical trial evidence base across the pediatric age range. This underscores the need for safer systems in this setting and the need to investigate drugs that will be used in children more fully for safety, if not efficacy.[14]

## Seriousness of ADE

In our study, actual preventable ADE were more likely to be serious than ADRs, further justifying ME detection to improve patient safety.

## Type of Adverse Outcome and Drugs Involved

While examining system-organ classes affected, we found that, in concordance with literature information, cutaneous effects represented one-third of ADRs. This could be explained by the fact that anti-infectives were the most prescribed drugs. The cardiovascular and metabolic systems were predominantly affected by ME attributable to cardiovascular drugs, anesthetics, and insulin.

**TABLE 7.** Contributory Factors Identified Relevant to Systems Failures

| Contributory Factors | No. | Description |
|---|---|---|
| Communication | 12 | Poor communication among staff members |
| Education and training | 24 | Insufficient training of junior physician, unfamiliar with the medicine used in ICU |
| | | Lack of drug knowledge |
| | | The change over of junior medical staff increase ME risk |
| | | Lack of identification of patient at risks |
| Individual | 4 | Mistakes resulting from fatigue |
| | | Insufficient nursing personnel |
| Equipment and resource | 6 | Insufficient infusion pump |
| Organizational and strategic | 37 | No policy for checking junior's prescriptions |
| | | Lack of written procedure for managing ICU patients |

We found that anti-infectives were the most common drug class to cause ME as has been reported in several studies.[1] However, when we adjusted the number of observed ME by drug class to the overall medication use belonging to the corresponding class prescribed during this period of study, we found that insulin was the major drug involved in ME. Two hypoglycemic episodes were recorded. The first one was relevant to a patient's omission of food intake, and the second was associated with the "sliding scale" approach. The remaining errors involving insulin were in relation with insufficient potassium supplementation. Literature emphasizes that insulin is one of the top five "high-risk medications in the inpatient setting." A report from the United States Pharmacopoeia, based on Med MARX 2001 data, also indicated that insulin remains the most commonly involved drug in harmful MEs.[15] Our study identified that insulin was mostly involved in serious ME. This drug should be emphasized in the ongoing education of juniors' residents (Table 8).

## Errors by Type of ADE and Stage

The methodological approach we used detected more ME in the prescribing process. The participation of pharmacist-investigators in rounds as members of the patient care team was a good opportunity for them to easily identify ADE and potential ADE by reviewing daily prescriptions and by interviewing staff members. It is shown that pharmacists are more efficient and accurate data collectors regarding MEs. Indeed, numerous studies demonstrate that hospital pharmacists play a large part in monitoring and improving the use of medicines and that they have a role in medical audit—working with clinicians, identifying problems with medicines, setting standards, and monitoring practice.[16–18]

The literature proves that direct observation is more efficient and accurate method than reviewing charts and incident reports in detecting MEs. Direct observation is the most effective method to detect and quantify administration, dispensing and transcribing errors but is not useful for detecting prescribing errors. Patient chart review identifies mainly errors generated in prescription and monitoring processes. Although the solicited incident approach is limited by underreporting, it could be used as indicator of the safety culture. The ideal detection method would be a combination of the above-mentioned methods to estimate the system performance over time.[19]

## ME Analyses

Review of potential ME and actual preventable ADE by the evaluators in this study suggested that the majority were associated with junior physicians' ordering. Wrong duration of treatment, inappropriate drug for the patient conditions, and the prescription of an improper dose were predominantly represented. Lack of drug knowledge by the prescriber and poor communication among staff were the most proximal causes leading to these errors. One important point is that an error may result from more than one system flaw. Some system failures identified as contributing to these ME were also identified as system problems by Leape et al[6]: lack of protocol standardization and poor communication. In this field, root cause analyses of adverse events in the ICUs in the United States underlined the importance of the nontechnical skill category of team work and specifically communication processes that support good team work in the prevention of incidents.[20,21]

During the investigation, the absence of a policy for checking junior's prescriptions represented another contributing factor pointed out by some coordinators. Fatigue, stress, and workload in ICU were met in our study as commonly claimed factors.

## Recommendations

Because of these identified causes of ME, the follow-up committee has proposed some recommendations to reduce their

**TABLE 8.** Examples of Serious MEs

| Error Type | Description | Consequences |
|---|---|---|
| Inappropriate medication for the condition being treated | Prescription of enoxaparin to a patient with renal failure | Gastrointestinal bleeding |
| Omission | A patient was admitted to the ICU for an acido-cetosic coma, junior resident prescribed insulin without potassium supplementation. Furthermore, the junior resident misinterpreted the electrocardiograph that showed signs of hypokalemia. The junior resident missed to pick up the laboratory test that was received later and indicated a severe hypokalemia (1.7 mEq/L) | Death |
| Therapeutic duplicity | Concomitant prescription of terbutaline and salbutamol to an asthmatic patient | Dyspnea and cardiac failure |
| Medication contra indicated | Prescription of mannitol to a dehydrated patient for intracranial hypertension | Severe hypotension |
| Improper dose | Administration of lidocaine 10 mg/kg instead of 4 mg/kg | Cardiac arrest |

occurrence: standardization of therapeutic protocols, systematic checking of the junior's prescriptions, reducing medical junior's work hours, and assigning a dedicated pharmacist to ICU areas. Furthermore, the implementation of a computerization of medication ordering could be a powerful intervention for improving drug safety because most errors occurred at the prescribing stage.

### Limits of Our Study

Our study has some limitations. The first one is that our investigation was conducted in the teaching hospitals, where ADEs may be more common than in community hospitals and occur more frequently in ICUs. Thus, these findings cannot be applied to all types of units or all types of hospitals. The second is that physicians and nurses on the study wards were aware of the study; the Hawthorne effect is suspected to have affected both the occurrence and the detection of ME.

## CONCLUSIONS

This investigation represents a big challenge in the concept of patient safety in our institutions; it breaks up the barriers to reporting ME. The partnership between the pharmacovigilance center and clinicians was effective, and the data obtained were consistent with existing literature. Moreover, the ADE analyses reinforced our knowledge of patient safety tools and enabled us to propose some consistent safety practices. The next step is to initiate a follow-up investigation in the units to evaluate the effectiveness of the proposed improvements.

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