



Prevention of prescription errors by computerized, on-line surveillance of drug order entry

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Received 7 August 2004; received in revised form 20 March 2005; accepted 20 March 2005

KEYWORDS

Computerized drug
order entry;
Prescription;
Prescription errors;
Adverse drug events

Summary

Aims: The present study was undertaken to quantify the impact of computerized drug order entry system (CDOE) connected to the patients' database, on the incidence and type of prescription errors (PEs) in the medical service, and to delineate the causes for remaining errors.

Methods: Drug orders were reviewed daily by a physician-reviewer, in a department of internal medicine that used for more than 3 years a CDOE (CDOEdept), and in a similar department in which drug orders were handwritten (HWdept). PEs were divided into those not related to the individual patient (type 1 PEs), and PEs resulting from drug–laboratory, drug–disease, and drug–allergy interactions (type 2 PEs).

Results: Ten thousand and two hospitalization days were evaluated. The incidence of type 1 PEs was 5.21 and 1.36 per 100 hospitalization days in the HWdept and CDOEdept, respectively ($p < 0.0001$). Type 2 PEs were more common, 7.20 and 3.02 per 100 hospitalization days in the HWdept and CDOEdept, respectively ($p < 0.0001$), and about 75% of them were due to few drug–laboratory interactions. Most of the remaining errors in the CDOEdept were due to inadequate adjustment of drugs and doses to renal function, or failure to perform adequate changes when new laboratory results became available.

Conclusions: We conclude that linking the CDOE with few, specific, laboratory results has a large impact on the prevention of PEs. Combining the CDOE with a drug–laboratory alert system is expected to further reduce the incidence of PEs.

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1. Introduction

Adverse drug events (ADEs) have been consistently identified as major causes of morbidity and mortality in hospitalized patients [1–8]. The true incidence of ADEs is controversial, and estimates range between 1.5 and 35%, depending on definition and the rigor with which the events were sought [4]. While most ADEs are minor, it has been estimated that as many as 140,000 deaths may occur each year in the United States as a direct result of ADEs [3,12,13,19–21]. A recent study estimated that 18.2% of the deaths in a department of internal medicine were associated with ADEs [10]. In the Harvard Medical Practice Study, ADEs represented the single most common cause of iatrogenic injury [2]. Although many ADEs are unavoidable, up to half are considered to be preventable [2,3,11–13]. While many mistakes occur during the dispensing of medication, most preventable ADEs are related to the prescribing physician [3,7–16]. Therefore, the prevention of errors during the prescription and transcription process is expected to have a large impact on the incidence of preventable ADEs.

In addition to the inability of the average physician to memorize the ever increasing number of drugs, treatment regimens and side effects, prescribing the old-fashioned way with pen and pad is prone to mistakes caused by slips of attention [17]. Computerized drug order entry (CDOE), including comprehensive, real time surveillance of drug order entry, can substantially reduce medication error rates [3,12,13,19,20], and converting to CDOE was placed as top priority for the prevention of ADEs [19,20]. Recent studies have shown that even with the use of selected alerts and guidelines introduced during the drug ordering process, substantial reduction in ADEs could be achieved [18], and the beneficial effect of CDOE increased with additional refinements [13].

To be practical, a CDOE with real time surveillance (i.e., all corrections are performed during the process of order entry) has to be fast, focused on significant items, and provide important, useful, and short information. From the technical point of view, the CDOE has to interact with two databases: a drug database and a patient database [19]. The drug database should contain all drugs available for use and their acceptable doses. This first level of CDOE ensures complete, unambiguous, and legible orders. It is expected to prevent a wide scale of prescription errors (PE's), including non-existing drug names or doses and erroneous dosing intervals. In addition, it eliminates transcription errors, and can provide alerts in the pres-

ence of drug–drug interactions. The next and more comprehensive level is produced by the connection of the CDOE to the patient's medical database. This connection enables immediate alerts when intercepting drug–laboratory interactions (for example, wrong doses in the presence of elevated creatinine values, abnormal potassium levels, etc.), drug–diagnoses interactions (i.e., drugs that should be avoided in the presence of liver disease, etc.) and drug–allergy interactions (including cross-allergy).

Compared to a simple CDOE, a more comprehensive CDOE that also interacts with the patient's database requires additional investment, but only limited information is available about its relative contribution to the prevention of PEs. Also, the relative contribution of the many laboratory parameters, diagnoses and cross allergies to the occurrence of PEs needs to be evaluated, in order to assess if the linking of these parameters to the CDOE will prove useful. Finally, only limited information is available about the type and causes of PEs remaining despite the use of a comprehensive CDOE.

The current study was undertaken three years after the implementation of a comprehensive CDOE in a department of internal medicine. We reviewed daily and prospectively all orders written in this department, and compared the incidence of PEs to the incidence found on the second, similar medical department, in which all drug orders were handwritten. As our reviewer was expected to intercept and prevent most, if not all, prescription-related preventable ADEs, we aimed to quantify PEs rather than ADEs, since writing an error-free prescription is both the direct goal of a CDOE and the most important measure for the prevention of ADEs. Our specific goals were: (1) to compare the usefulness of different components of the CDOE in reducing PEs, primarily by assessing the importance of connecting the CDOE to specific patients' data, and (2) to evaluate the causes for remaining PEs in a department that uses CDOE for several years, in order to suggest possible methods to further reduce these PEs.

2. Methods

2.1. Location and patients population

The Bnai-Zion Medical Center is an acute care university hospital, with two 44 beds general medical wards, entitled Departments of Internal Medicine A and B. Both departments are completely

independent, and have their own residents, attending physicians, directors, nurses, and other staff. However, the departments are equal in respect to average patient occupancy, as well as the number of nurses, residents and attending physicians. Sub-specialties are organized in independent units, and the same consultants serve both departments. This, as well as common educational staff-meetings and hospital guidelines, result in practically identical clinical policies, treatment practices and use of medication on both departments. Patients admitted to both departments are almost exclusively acute admissions from the emergency department, distributed equally (24 h shifts) to the two departments. The only difference between the two departments is in the mode physicians write drug orders: In one department drug orders are hand-written and transcribed by nurses (HWdept), while the other uses a comprehensive CDOE (CDOEdept).

2.2. Computerized drug order entry

The CDOE was developed exclusively for the prevention of PEs, and was implemented for routine use in one department three years before the present study, as part of the electronic patient records. It includes a drug database, and a patients' database connected to the hospital's administrative and laboratories database. The drug database is based on a list of all drugs available in the hospital, including all acceptable doses and administration frequencies, and other names or dosing are not permitted. Hours of administration are coupled to all administration frequencies for each individual drug, along with orders to the nurses concerning relationships to food (before or with meal) or mode of administration (with much water, etc.) whenever indicated. Up to two reminders are attached to each drug, usually reminding the physician the availability of a blood-drug-level test or the need for specific monitoring. In addition, abbreviated information about the drug, including major side effects and risks, is available by a mouse click. Treatment guidelines are available, and drugs can be transferred from the guidelines to the prescription. The drug order can be printed only after a drug-drug interaction check is performed.

The patients' individual database provides a real-time drug-allergy (including cross-allergy to similar drug class or compounds), drug-disease and drug-laboratory alerts, which appear immediately after the drug name is typed or chosen. On the first admission to the hospital, order entry can begin only after entering the patients' allergies, as well as a limited number of disease classes in the pres-

ence of which the administration of certain drugs should be discouraged. All patient's blood test results are stored automatically and continuously in the CDOE database. A large number of alerts is associated with abnormal laboratory values, and appear when an interaction is encountered between a prescribed drug and a relevant abnormal laboratory result (including abnormal renal function for all drugs that can affect renal function or their dose needs to be adjusted in the presence of renal failure, liver function tests for all drugs that can cause liver injury, anemia and low mean corpuscular volume (MCV) for all non-steroidal anti-inflammatory drugs and anticoagulants, leucopenia and thrombocytopenia for all drugs that can cause bone marrow suppression and so on). The patients' database was designed, therefore, not just for certain reminders, but to provide a wide scale of information that a physician needs to consider while writing a prescription. Each alert contains a short explanatory note. For all drugs whose dosing requires adjustment to renal function, the alert contained the adjusted doses for the specific drug for all creatinine and creatinine clearance time (CCT) ranges.

2.3. Identification of PEs

The study was conducted in parallel on the two departments over 6 months, and was approved by the institutional review board, with full cooperation and active participation of the directors of the two departments (AO and DY). All patients' charts were reviewed for the presence of new orders, new diagnoses, and new laboratory results by a trained physician-reviewer (DZ, a third-year resident from the CDOEdept, that used the CDOE from the beginning of her entire residency). The chart review was conducted daily, with the exception of Saturdays, that were evaluated retrospectively, and PEs and additional data were registered for each patient on forms designed for this study. The chart review was structured, using a check-list of specific items, constituting usual medical routines based on textbooks, guidelines, etc. Our list of PEs followed the definition of medication errors, PEs, or potential ADEs used in previous publications, i.e., errors in the process of drug ordering, with potential to cause harm. All listed items were accepted as potentially clinically important by the participating clinicians of both departments, and, therefore, were included also in the CDOE. PEs were divided into those related to the drug database (misspelled drug names, wrong or missing doses and dosing intervals, transcription errors, and drug-drug interactions) termed as type 1 PEs,

Table 1 Patients information

	HWdept	CDOEdept
Hospitalization days evaluated, <i>n</i>	4969	5033
Number of patients, <i>n</i>	641	709
Mean age (years)	70.7 (68.7–71.9)	70.8 (69.0–72.3)
Mean duration of hospitalization (days)	7.85 (7.34–8.37)	7.01 (6.60–7.42) ^a
Mean number of drugs per patient, <i>n</i>	6.81 (6.63–7.02)	6.69 (6.46–6.94)

Data are mean and in parenthesis 95% confidence interval.

^a Significantly different, $p < 0.01$.

and PEs related to the patients' database (a list of drug–allergy, drug–disease and drug–laboratory interactions), termed type 2 PEs. Any medication change not undertaken up to 24 h from the time a new laboratory result or diagnosis was known, was considered to represent a PE. Following the chart review, the reviewer discussed with the relevant physicians the PEs, and they either agreed that, in the particular circumstance, the order was not a PE, or the PE was corrected. In cases of disagreement, an appropriate consultant or another attending was asked to make the decision. Finally, all forms were reviewed by the senior investigator (AO) to ascertain that all PEs were registered according to the study guidelines.

2.4. Analysis

Background measures of patients in the two departments were compared by one-way ANOVA. Means for types and classes of PEs were calculated both per patient (admission) and per 100 patient hospitalization days. In addition, the presence or absence of PEs, for each patient, was used to cal-

culate the relative risk (odds ratio) of the major PE types in the two departments. Forced steps regression analyses were conducted in order to examine the effects of duration of hospitalization, mean number of drugs administered daily and age, on the incidence of PEs in each department. Data are given as mean and 95% confidence interval (CI). All analyses were performed using SPSS.

3. Results

Information about the patients in the two departments is given in Table 1. Ten thousand and two patient-hospitalization days (4969 and 5033 in HWdept and CDOEdept, respectively), were evaluated. The average age of the patients, as well as the average percentage of patients less than 65 years was similar in both departments. The mean hospitalization duration in HWdept was slightly longer than in CDOEdept. The average daily number of drugs per patient was similar in both departments.

Table 2 Incidence of prescription errors in the two departments

	HWdept	CDOEdept	<i>p</i>
Erroneous dose or interval ^a	0.11 (0.08–0.13)	0.02 (0.01–0.03)	<0.0001
Drug–drug interactions	0.08 (0.06–0.11)	0.04 (0.02–0.05)	<0.01
Transcription errors	0.22 (0.17–0.26)	0.04 (0.02–0.05) ^b	<0.0001
All type 1 PEs	0.41 (0.35–0.47)	0.10 (0.07–0.12)	<0.001
Drug–laboratory interactions	0.50 (0.43–0.57)	0.18 (0.14–0.22)	<0.0001
Drug–disease interactions ^c	0.05 (0.03–0.07)	0.02 (0.01–0.03)	<0.01
Drug–allergy interactions	0.02 (0.01–0.03)	0.02 (0.01–0.02)	NS
All type 2 PEs	0.56 (0.49–0.64)	0.21 (0.17–0.25)	<0.0001

Data are given as mean number of errors per patient (and 95% confidence interval).

^a Wrong dosing due to inadequate adjustment to renal failure not included.

^b Errors resulting from handwriting on the typed prescription.

^c Renal failure not included (counted under drug–laboratory interactions).

The frequency of type 1 PEs is shown in Table 2. Only PEs considered having the potential to cause harm to the patient (unclear and misspelled drug names that caused transcription of a different drug, dosing errors, drug–drug interactions and transcription errors) were considered. We found a mean of 0.41 and 0.10 type 1 PEs per admission (or 5.21 and 1.36 per 100 hospitalization days) in HWdept and CDOEdept respectively, i.e., odds ratio of 4.25 (CI 3.14–5.76, $p < 0.001$). Although misspelling drug names and ordering non-existing doses was prevented by the CDOE, it remained possible to choose inadequately low doses reserved for patients with renal failure (inadequate dose adjustment to patients' diseases were not counted in this category). In the HWdept, transcription errors occurred, on average, in every fifth patient during hospitalization (although all transcriptions are regularly double-checked by the department head-nurse). In the CDOEdept, no transcription was needed. However, some patients brought their own medications that were not available in the hospital (or in the country), and these drugs had to be added by hand writing to the typed prescriptions. These added handwritten orders were prone to errors when a new prescription was printed.

Type 1 PEs did not include common faults that characterize hand written orders, like unclear or misspelled drug names that required clarification with the physicians but were transcribed correctly, unidentifiable identity of the ordering physician, and lack of instructions regarding relationship of drug administration to meal, considered to be known to the nurses. These inadequacies, very common in the HWdept (19.6 per 100 hospitalization days) were almost completely eliminated by the CDOE (0.6 per 100 hospitalization days).

The incidence of all type 2 PEs (i.e., drug–laboratory, drug–disease and drug–allergy interactions) was 0.56 and 0.21 per admission (or 7.20 and 3.02 per 100 hospitalization days) in HWdept and CDOEdept, respectively (odds ratio 2.70, CI 2.08–3.49, $p < 0.0001$) (Table 2). In both departments, most PEs were caused by the lack or insufficient consideration of abnormal laboratory results. The CDOE-associated decrease in drug–laboratory interactions reached almost 60% (from 6.32 to 2.56 PEs per 100 hospitalization days, $p < 0.0001$). Drug–disease interaction-related PEs (inappropriate drugs or doses in the presence of liver, heart, or prostate diseases) were far less common (errors related to renal failure were counted as drug–laboratory interactions only, i.e., related to abnormal creatinine or CCT values). Prescrib-

Table 3 Drug–laboratory interactions in the two departments

	HWdept	CDOEdept
Elevated creatinine level	139 (44.3)	57 (44.2)
Hypokalemia	80 (25.5)	16 (12.4)
Hyperkalemia	17 (5.4)	26 (20.1)
Anemia or low MCV ^a	39 (12.4)	19 (14.7)
Others ^b	39 (12.4)	11 (8.5)
Total	314	129

Numbers indicate drug–laboratory interactions related to the specific laboratory abnormality. In parenthesis percentage of the total number of drug–laboratory interactions in this department. Only interactions that led to changes of drugs or doses after the intervention of the physician-reviewer were counted.

^a Mean corpuscular volume.

^b Elevated transaminases, uric-acid or creatinine-phosphokinase, leucopenia, thrombocytopenia, and prolonged partial thromboplastin time, in the presence of which discontinuing certain medications was indicated.

ing inappropriate drugs to patients who reported allergies was relatively uncommon, although cross-allergy was also evaluated, and similar on both departments. In CDOEdept, both drug–disease and drug–allergy interactions occurred when physicians failed to enter the specific disease or allergy into the digital diagnoses list, or ignored the CDOE warning.

Table 3 depicts the specific causes of drug–laboratory interaction-related PEs. Lack or insufficient consideration of three abnormal laboratory tests accounted for 87.6 and 91.5% of the PEs in this category in HWdept and CDOEdept, respectively: creatinine (elevated, or reduced CCT), potassium (hypo- or hyperkalemia), and hemoglobin/MCV (anemia in association with the administration of aspirin, or occasionally other non-steroidal anti-inflammatory drugs, as well as anticoagulants). With the exception of hyperkalemia-related interactions, marked reduction in all interactions was noted in CDOEdept. However, the relative frequency of the drug–laboratory interactions groups in the two departments (including the total number of interactions related to abnormal potassium levels) remained surprisingly similar.

Forced steps regression analysis, performed in order to evaluate the effects of several variables expected to affect the frequency of PE, showed a positive correlation between the length of hospitalization and the incidence of PEs ($p < 0.01$ for both departments). After controlling for average number of drugs, patient age had no effect on the incidence of PEs. However, the

incidence of PEs increased significantly with increasing average number of drugs in HWdept ($p < 0.003$), but not in CDOEdept ($p = 0.512$). The difference between HWdept and CDOEdept in the incidence of both types of PEs remained highly significant ($p < 0.0001$) also after controlling for length of hospitalization and average number of drugs.

4. Discussion

Computerized order entry is becoming increasingly available, preventing typographical and transcription errors, and often enabling drug–drug interaction control. However, very few hospitals are already using CDOE connected to the patients' database and capable of providing on-line surveillance of drug–laboratory, drug–disease and drug–allergy interactions related to the individual patient [18]. Therefore, only limited information is available about the impact of individual components of the CDOE on the quality of prescriptions, i.e., prevention of PEs. The results of the present study provide new information, obtained in a department in which all residents use CDOE routinely from the beginning of their training, on two major aspects related to the effects of the CDOE on PEs on the medical service: First, quantification of the effect of a comprehensive CDOE on specific types and categories of PEs, enabling evaluation of the relative impact of individual components of the CDOE. And second, quantification and categorization of PEs that remained despite the use of CDOE, providing specific recommendations expected to further reduce these PEs.

The results of the present study need to be viewed in the context of its design. The study evaluated PEs rather than ADEs, and the true clinical benefit of the reduction in PEs achieved in the CDOEdept is unknown. However, it is probably safe to assume that the administration of wrong drugs due to transcription errors, inappropriate dosing in patients with renal failure, and many similar PEs, should be prevented, even if the accurate harm done to patients by these errors is difficult to quantify. We choose to identify PEs rather than ADEs (or even potential ADEs), because any study designed to prospectively evaluate all prescriptions by an experienced physician-reviewer precludes the occurrence of most prescription-related preventable ADEs. Therefore, the effect of CDOE on preventable ADEs can be evaluated only by a retrospective chart review, a method with substantial limitations. In addition, the definition of ADEs and PE's is com-

plex, and we found it difficult to distinguish PEs from "potential ADEs" or to define the potential risk of many PEs. For example, defining the level of drug-induced hypokalemia that should be considered as potentially life threatening is arbitrary, and depends often on the patient's medical condition. On the other hand, administration of an insufficient dose of antibiotics due to exaggerated dose-reduction in the presence of renal failure is an error that may have grave consequences, but such consequences are not defined as ADEs. In addition, many pathological processes, like deterioration in renal function, are multi-factorial, and it is often unclear whether they represent an ADE, even when a potentially causative drug is involved. We believe, therefore, that despite the relatively low incidence of ADEs that actually occur in the presence of PEs [15], good clinical practice should be to prevent errant order entries with the potential to cause harm, and the primary role of CDOE is to help the physician with this task.

A large number of studies have assessed the incidence and type of ADEs and PEs in hospitalized patients [1–3,7–17,22–26], and PEs have been found to be caused by a wide spectrum of mistakes. Obviously, the incidence and type of errors depend on many factors, including the definition of PEs, how the PEs were evaluated (retrospective chart review, prescription-check in the pharmacy, prospective surveillance, etc.) and by whom (nurses, pharmacists, physicians, etc.), the prescribing service (i.e., medical, surgical, etc.) and many others. The wide disparity in the estimates of ADEs and PEs between studies is probably a direct result of the diversity in methodology. We believe that the methodology used in the present study, i.e. prospective daily examination of all drug orders by an experienced and trained physician-reviewer, using all information available in the patients' charts, is expected to provide the best surveillance results. An additional advantage of the present study was the availability of unique local conditions (two "twin" ward-departments, with only one using CDOE), enabling us to conduct a simultaneous, parallel, prospective comparison, rather than use an historic control. Although the medical personnel on the two departments was not the same, this difference was probably not larger than the one occurring in studies that conducted comparisons before and after implementation of CDOE. On the other hand, our study design prevented the bias of technical difficulties and learning process associated with the introduction of a new CDOE. Finally, the fact that the chart reviewer was a resident of the CDOEdept could produce a

bias. However, as the primary goals of the study were to evaluate the relative importance of different components of the CDOE and the causes for remaining PEs in the CDOEdept, such a bias was unlikely.

4.1. Specific effects of CDOE

CDOE has the potential to almost completely eliminate most type 1 PEs, as evident from the findings in CDOEdept. Interestingly, although the CDOE significantly reduced the incidence of potential drug–drug interactions, the reduction of this interaction reached only about 50%. Although drug–drug interactions constitute only a small proportion of adverse drug reactions, they are important, because they are often predictable and therefore avoidable or manageable. Also, in the hospitalized elderly, concomitant use of many drugs is very common, and the risk for drug interactions is likely to be increased. Although only about 10% of potential interactions result in clinically significant events, and death or serious clinical consequences are rare, low-grade morbidity may be much more common. However, the bulk of the clinical literature that has been published about drug interactions has focused either on the mechanisms, pharmacokinetic studies, or cases observed by clinicians. When it comes to the true risk of a drug–drug interaction, or the probability of such an interaction occurring in a given population, a dearth of information is available. Therefore, primary care physicians ignore most alerts related to drug–drug interactions, including almost 90% of those considered as high severity interactions [27], and residents may judge the risk of many drug–drug interaction to be relatively low in the hospitalized patient under close surveillance. Interestingly, the association between the number of drugs prescribed to a patient and the incidence of PEs, was eliminated by the CDOE.

In the medical departments, with many old patients suffering from heart and renal failure, treated with high-dose diuretics, ACE inhibitors, potassium and anticoagulants, we found that type 2, patients-related PEs were more frequent than type 1 PEs, emphasizing the importance of connecting the CDOE to the patients' database. About 90% of all type 2 PEs were associated with drug–laboratory interactions, and the bulk of these PEs was caused by insufficient consideration of few laboratory results, namely indices of renal failure, hypo- and hyperkalemia, and anemia. The total number of PEs associated with liver, heart and prostate diseases collectively were less than a quar-

ter of the number of PEs associated with renal failure. Similarly, prescribing inadequate drugs to allergic patients was relatively rare, probably due to the high awareness of both medical personnel and patients to this problem. These findings indicate, therefore, that a major effort should focus on the prevention of PEs associated with a limited number of abnormal laboratory test results. Before expanding the computerized surveillance over a large number of rare drug–disease and additional drug–laboratory interactions with the potential to cause harm, the side effects of overwhelming the drug ordering physician with numerous alerts and advises of marginal or seldom value should be considered [18].

4.2. PEs remaining after CDOE — lessons from the findings in CDOEdept

Most of the remaining type 1 PEs were due to handwriting on the typed prescription, and ignoring (or disagreement with) the CDOE recommendations concerning drug–drug interactions. Therefore, even the introduction of this relatively simple level of CDOE, that does not require connection to the patients' records, prevents many errors and misunderstandings. Because hand written supplements and corrections on the typed order are often lost when new orders are issued, they should be prevented by the institutional handling of CDOE, and other local solutions for unavailable drugs should be provided when necessary. Some disagreements between physicians and the recommendations of the CDOE are likely to remain, and further experience is needed to assess their clinical significance.

Unlike type 1 PEs, most of which can be fully prevented by the CDOE, interception of type 2 PEs evokes alerts that the prescribing physician can disregard, thereby leaving orders considered to represent PEs. In addition, failure to enter relevant allergies and diseases into a diagnoses list accessible to the CDOE precludes their interception. However, the bulk of the remaining PEs in CDOEdept was associated with abnormal laboratory results. It should be noted that tests most relevant for PEs (creatinine, potassium and hemoglobin) were performed every 1–3 days in almost all patients and with equal frequency in the two departments. Most drug–laboratory interactions were corrected shortly after the new laboratory test results became available, and, therefore, were not considered to represent PEs according to the study definitions. This was particularly the case with severe laboratory abnormalities, due to the

independent laboratory “panic-alert” available in the hospital. The remaining PEs in the CDOEdept were caused primarily by two causes: First, assuming they knew the right doses, physicians sometimes failed to read the instructions for the adjustment of drug doses to the severity of renal failure. Second and more important, the CDOE alerted the physician only during the drug ordering process. On days when no change in prescription was performed, physicians sometimes failed to recognize the need for prescription changes indicated by the arrival of new test results. These findings drove us to implement (after the conclusion of this study) two refinements to reduce these errors. First, the adjustment of drug doses for patients with renal failure has been fully automated, and the CDOE now presents the appropriate dose calculated automatically using the patient’s weight, age, sex, and most recent creatinine level. The second improvement was the integration of the CDOE with an automated daily drug–laboratory interaction check for all patients. A checkmark appears on the main screen near the name of each patient for whom a drug–laboratory interaction was found. Examining the causes for the alert has become part of the evening rounds routine. It remains, however, to evaluate the impact of these improvements on remaining PEs. Also, CDOE can be easily linked to decision support systems, but the effects of such systems, and the importance of specific items, remain to be evaluated. In addition, one should keep in mind that the CDOE provides support mainly to the process of drug prescription, with little effect on drug delivery and administration by the nurses (automated, drug-specific, instructions regarding relationships to food, as well as required precautions in the presence of high or low pulse rate and/or blood pressure are provided). The extent of errors during drug distribution is difficult to assess, but is considered to be substantial [28]. Both clinical pharmacists, that can also provide independent prescription control, and linking the CDOE to a semi-automated drug distribution system, are likely to reduce the incidence of these errors.

Although many CDOE systems are commercially available, their potential impact remains somewhat speculative, as only one was evaluated for effectiveness, and the evaluation was conducted before implementation of some of its most important components [13,14]. The currently available knowledge on the effects of CDOE on medication safety has been recently reviewed [18]. In an extensive medline search, the authors found only five adequate publications, four of which were studies related to the CDOE at Brigham and Women’s Hospital (published by the same authors), and the

fifth evaluated a limited, specific effect of the CDOE (the utility of CPOE in improving prescribing for corollary orders). Therefore, the conclusions of this review were based primarily on two publications describing the study conducted by Bates et al. shortly after implementation of a comprehensive CDOE [13,14]. At the time of the study, the CDOE modules designed to prevent the major type 2 errors (drug–disease and drug–laboratory interactions, including suggested doses in the presence of renal failure) were not yet implemented. Therefore, this study evaluated primarily the effect of CDOE on type 1 errors. The authors found an 86% reduction in non-intercepted serious medication errors (compared to historic control), associated with a borderline-significant ($p=0.05$) decrease in the number of preventable adverse drug events [13,14]. The authors emphasized the limitations of their review, which was based primarily on their CDOE system, which was still under development. They concluded that the study provided evidence that the use of CDOE can substantially reduce medication error rates, but further studies are required, targeted at critical questions, including the effectiveness of specific applications of the CDOE.

The results of our study not only support previous conclusions (regarding type 1 PEs), but also provide new information regarding specific applications of the CDOE not previously evaluated (mostly related to type 2 PEs). We have already shown that with the availability of increasingly faster computers, a fast and user-friendly CDOE system that requires no “computer literacy” can be implemented and used easily, in conjunction with available electronic patient chart, on a busy small-town medical service [29]. Although our results derive from the department of internal medicine, a similar [3] or higher [8] incidence of ADEs was found in surgical units. While moving toward CDOE is an accepted goal [18], physicians need convincing evidence that proposed means for reducing errors are effective [30]. Our results demonstrate not only that a comprehensive CDOE is most effective, but also point to the specific components most useful for the prevention of PEs. Our findings indicate that connection to the laboratory database is most important, and only a small number of laboratory tests are actually relevant for the prevention of most PEs. Providing explanations and instructions (originally used for drugs requiring dose adjustment to renal failure) is insufficient, and automated solutions should be used whenever possible. Finally, drug orders often become erroneous when new laboratory results become available, and combining the CDOE with an alert system may be useful to optimize its potential.

Specific summary points

What is already known on this topic

Computerized drug order entry (CDOE) is believed to reduce medication errors and adverse drug events.

Only one limited CDOE has been previously evaluated.

Information on the impact of specific components of such a system, as well as causes for remaining errors, is scarce.

Our study points to specific components of CDOE most useful for the prevention of prescription errors

Connecting the CDOE to the individual database of the patient is at least as important as the other components of the CDOE.

Connection to the laboratory database is by far the most important.

However, only a small number of laboratory test is actually relevant for the prevention of most prescription errors.

Automated adjustment of doses of relevant drugs to renal function is required.

Combining the CDOE with an alert system may be useful to optimize its potential.

Acknowledgement

The statistical evaluation was performed by M. Sarid, Ph.D., Statistical and Research Consultation.

References

- [1] T.A. Brennan, L.L. Leape, N.M. Laird, et al., Incidence of adverse events and negligence in hospitalized patients, *N. Engl. J. Med.* 324 (1991) 370–376.
- [2] L.L. Leape, T.A. Brennan, N. Laird, et al., The nature of adverse events in hospitalized patients, *N. Engl. J. Med.* 324 (1991) 377–384.
- [3] D.W. Bates, D.J. Cullen, N. Laird, et al., Incidence of adverse drug events and potential adverse drug events, *JAMA* 274 (1995) 29–34.
- [4] F.E. Karch, L. Lasagna, Adverse drug reactions: a critical review, *JAMA* 234 (1975) 1236–1241.
- [5] D.C. Classen, S.L. Pestotnik, R.S. Evans, J.F. Lloyd, J.P. Burke, Computerized surveillance of adverse drug events in hospital patients, *JAMA* 266 (1991) 2847–2851.
- [6] L.L. Leape, Patient safety: reporting of adverse events, *N. Engl. J. Med.* 347 (2002) 1633–1638.
- [7] T.S. Lesar, L.L. Briceland, D.S. Stein, Factors related to errors in medication prescribing, *JAMA* 277 (1997) 312–317.
- [8] T.S. Lesar, L.L. Briceland, K. Delcours, J. Crilly Parmalee, V. Masta-Gornic, H. Pohl, Medication prescribing errors in a teaching hospital, *JAMA* 263 (1990) 2329–2334.
- [9] R.S. Evans, S.L. Pestotnik, D.C. Classen, S.D. Horn, S.B. Bass, J.P. Burke, Preventing adverse drug events in hospitalized patients, *Ann. Pharmacother.* 28 (1994) 523–527.
- [10] J. Ebbesen, I. Buajordet, J. Erikssen, et al., Drug-related deaths in a department of internal medicine, *Arch. Intern. Med.* 161 (2001) 2317–2323.
- [11] D.C. Classen, S.L. Pestotnik, R.S. Evans, J.F. Lloyd, J.P. Burke, Adverse drug events in hospitalized patients: excess length of stay, extra costs, and attributable mortality, *JAMA* 277 (1997) 301–306.
- [12] D.W. Bates, A.C. O'Neal, D. Boyle, J. Teich, G.N. Chertow, A.L. Komaroff, et al., Potential identifiability and preventability of adverse events using information systems, *J. Am. Med. Assoc.* 271 (1994) 404–411.
- [13] D.W. Bates, L.L. Leape, D.J. Cullen, N. Laird, L.A. Petersen, J.M. Teich, et al., Effect of computerized physician order entry and a team intervention on prevention of serious medication errors, *JAMA* 280 (1998) 1311–1316.
- [14] D.W. Bates, J.M. Teich, J. Lee, D. Seger, G.J. Kupermann, N. Ma'Luf, et al., The impact of computerized physician order entry on medication error prevention, *J. Am. Med. Assoc.* 281 (1999) 313–321.
- [15] D.W. Bates, D.L. Boyle, M.B. Vander Vliet, J. Schneider, L.L. Leape, Relationship between medication errors and adverse drug events, *J. Gen. Intern. Med.* 10 (1995) 199–205.
- [16] R.S. Evans, S.L. Pestotnik, D.C. Classen, T.P. Clemmer, L.K. Weaver, J.F. Orme, et al., A computer assisted management program for antibiotics and other anti-infective agents, *N. Engl. J. Med.* 338 (1998) 232–238.
- [17] B. Dean, M. Schachter, C. Vincent, N. Barber, Causes of prescribing errors in hospital inpatients: a prospective study, *Lancet* 359 (2002) 1373–1378.
- [18] R. Kaushal, K.G. Shojania, D.W. Bates, Effects of computerized physician order entry and clinical decision support systems on medication safety, *Arch. Intern. Med.* 163 (2003) 1409–1416.
- [19] G.D. Schiff, T.D. Rucker, Computerized prescribing. Building the electronic infrastructure for better medication usage, *JAMA* 279 (1998) 1024–1029.
- [20] D.W. Bates, A.M. Burrows, D.G. Grossman, P.J. Schneider, B.L. Strom, Top-priority actions for preventing adverse drug events in hospitals: recommendations of an expert panel, *Am. J. Health Syst. Pharm.* 53 (1996) 747–751.
- [21] D.F. Doolan, D.W. Bates, Computerized physician order entry systems in hospitals: mandates and incentives, *Health Aff. (Millwood)* 21 (2002) 180–188.
- [22] L.L. Leape, Preventing adverse drug events, *Am. J. Health Syst. Pharm.* 52 (1995) 379–382.
- [23] S. Rolfe, N.J.N. Harper, Ability of hospital doctors to calculate drug doses, *BMJ* 310 (1995) 1173–1174.
- [24] T.S. Lesar, Common prescribing errors, *Ann. Intern. Med.* 117 (1992) 537.
- [25] D.J. Cullen, B.J. Sweitzer, D.W. Bates, E. Burdick, A. Edmondson, L.L. Leape, Preventable adverse drug events in hospitalized patients: a comparative study of intensive care and general care units, *Crit. Care Med.* 25 (1997) 1289–1297.
- [26] D.W. Bates, E.B. Miller, D.J. Cullen, L. Burdick, L. Williams, N. Laird, et al., Patient risk factors for adverse drug events in hospitalized patients. ADE Prevention Study Group, *Arch. Intern. Med.* 159 (1999) 2553–2560.

- [27] S.N. Weingart, M. Toth, D.Z. Sands, M.D. Aronson, R.B. Davis, R.S. Phillips, Physicians' decision to override computerized drug alerts in primary care, *Arch. Intern. Med.* 163 (2003) 2625–2631.
- [28] K.N. Barker, E.A. Flynn, G.A. Pepper, D.W. Bates, R.L. Mikeal, Medication errors observed in 36 health care facilities, *Arch. Intern. Med.* 162 (2002) 1897–1903.
- [29] D. Zalman, M. Odeh, A. Oliven, Physician assessment of computerized prescribing, *Harefuah* 138 (2000) 434–440.
- [30] R.J. Blendon, C.M. DesRoches, M. Brodie, J.M. Benson, A.B. Rosen, et al., Patient safety: view of practicing physicians and the public on medical errors, *New Engl. J. Med.* 347 (2002) 1933–1940.

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