Prevention of Adverse Drug Events through Computerized Surveillance

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ABSTRACT

Adverse drug events (ADEs) are a serious health problem and are the leading adverse event experienced by hospitalized patients. Numerous hospitals have used different methods to improve the reporting of ADEs but few have undertaken studies aimed at the prevention of ADEs. We found that computerized ADE surveillance identified significantly more ADEs than our previous voluntary reporting method. Moreover, the computerized ADE surveillance system created a database of ADEs which allowed us to analyze the ADEs and design methods for prevention. We found that computer alerts of previously known drug allergies generated when drugs were ordered significantly reduced the number of type B ADEs, 56 vs 8 ($p < 0.001$). In addition, we found that the timely surveillance of ADEs combined with physician notification reduced the number of severe ADEs, 41 vs 12 ($p < 0.001$). Initial analysis of the ADE database has shown that on average patients with type B ADEs are hospitalized longer (17 vs 14 days) and have larger hospitalization costs ($30,617 vs $23,256) than patients with type A ADEs. Patients with severe ADEs also are hospitalized longer (20 vs 13 days) and have larger hospitalization costs ($38,007 vs $22,474) than patients with moderate ADEs. This indicates that the prevention and early treatment of ADEs can reduce the length of hospitalization and result in a considerable cost savings to the hospital.

INTRODUCTION

As many as 140,000 deaths may occur each year in the United States as a direct result of adverse drug events (ADEs) [1]. ADEs are a more serious health problem than most infectious diseases and many degenerative diseases [2]. In addition, ADEs are the most frequent adverse events experienced by hospitalized patients [3]. While 3% to 6% of hospital admissions are due to ADEs, many ADEs result from drugs administered in the hospital [4]. Some studies have found that from 10% to 20% of hospitalized patients experience ADEs [5-10]. ADEs to hospital administered drugs increase the morbidity, length of stay, cost of hospitalization, and mortality of patients. It has been estimated that one seventh of all hospital days is devoted to the care of ADEs, at an yearly cost of three billion dollars" [11].

The World Health Organization defines an adverse drug event as "any response to a drug which is noxious, unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease" [12]. Type B ADEs are allergic or idiosyncratic reactions whereas type A ADEs are the results of known toxicities of drugs and are believed to be preventable. However, some type B ADEs can be prevented by not permitting patients to receive drugs to which they have had a previous reaction.

While most ADEs are rated as mild or moderate, as many as 3 percent of hospitalized patients may experience severe or life-threatening ADEs [13]. Mild ADEs are self eliminating whereas moderate ADEs require a change in therapy or require an increase in the length of hospitalization. Severe ADEs include arrhythmia, bone-marrow depression, central-nervous-system depression, seizures, and bleeding. Up to 10% of severe events result in death [14].

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) now requires hospitals to have established methods for reporting adverse drug events [15]. The JCAHO also advocates that methods to reduce the number of ADEs should be developed within the hospital. The Food and Drug Administration recommends the use of concurrent surveillance systems to document ADEs [16].

Because the voluntary reporting of ADEs by physicians

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and nurses has been unreliable, a number of hospitals have developed methods to determine the ADE rates among their patients [17-19]. Most studies have been designed to determine the rates and types of ADEs. Few studies have been initiated specifically to determine methods to prevent or reduce ADEs in hospitalized patients [20]. We found that our hospital information system could be used to help identify ADEs and to create a database of ADEs [10]. This paper describes the further use of that system to prevent specific types of ADEs in hospitalized patients.

METHODS

The development of our computerized system to identify ADEs is based on monitoring patient "signals" of possible ADEs. Our hospital information system (HELP) constantly monitors patients for clinical manifestations of ADEs entered by routine nurse charting or a computerized ADE reporting program, abnormal results of laboratory tests, drug levels, and pharmacy orders for drugs commonly used to treat ADEs. A knowledge base accesses the patient's computerized medical record and determines if the signal can be explained by the patients underlying condition or other known causes. If not, the system identifies the patient as having a possible ADE. A complete overview of the system is described elsewhere [21]. Since the system was installed in May, 1989, it has constantly monitored patients for evidence of possible ADEs. The computer identifies patients with possible ADEs through a daily list sent to the Department of Clinical Epidemiology (Figure 1). This is an example of a patient who received diphenhydramine, the drug most commonly used to treat an ADE. The ADEs are verified by a clinical pharmacist specialist or study nurse using a computerized ADE verification program. ADEs are verified only if the patient demonstrates an actual clinical manifestation due to the drug, eg. rash, change in heart rate, etc. While the computer monitors patients 24 hours a day, the ADE verification is performed Monday through Friday. ADEs identified by the computer during weekends are verified on Monday mornings. The verification requires one person an average of one to two hours a day.

During the first year of computerized ADE surveillance, pharmacists and physicians were not notified by the hospital information system of patients' previous drug allergies when drugs were ordered. Since the second year of computer ADE surveillance, the hospital information system has alerted pharmacists of previously identified drug allergies when drugs were ordered. The pharmacists then notified the prescribing physicians concerning the problem.

From May, 1989 through December, 1990, physicians were only notified of verified ADEs if they were classified as severe or life-threatening. Starting in January, 1991, physicians were immediately notified of all ADEs when they were verified. Either the clinical pharmacist specialist or ADE study nurse contacted the prescribing physician and recommended a change in drug or dosage.

POSSIBLE ADE REPORT FOR AUGUST 12, 1991
(Past 24 Hours)
PRINT TIME: 08/12/91.08:00

***** 08/11/91.21:50 Pat. Received: DIPHENHYDRAMINE *****
PAT: 11111111 Jones, John P. 76 M E999 MR#: 00001
DOC: 0776 Smith, Ralph P.
ADMITTED: 08/09/91.1915 ADMIT DIAG: Bowel Obstruction
PREV. ADMIT: 06/01/1989 PREV. DSCH: 06/20/1989
PAT. IS ALLERGIC TO: Codeine and Codeine Compounds
CURRENT DRUGS
08/10/91.16:49 Meperidine 75.0mg, Inj, IV q6h prn
08/10/91.17:27 Furosemide 20.0mg, Inj, IV q12h
08/11/91.09:00 Digoxin 0.25mg, Tab, PO qd
DISCONTINUED DRUGS
08/10/91.09:20 Morphine 6.0mg, Inj, IV stat
08/10/91.17:00 Furosemide 80mg, Inj, IV q12h
08/11/91.21:52 Cefotaxime 2000mg, Inj, IV q12h

Figure 1. Example of a computerized alert for a patient with a possible ADE.

A control population of 2,733 patients who received drugs and who were hospitalized for at least three days but did not have ADEs was created from a random sample of patients in the hospital information system database. The control population was used to determine the average cost of hospitalization and length of stay for patients without ADEs. The cost of hospitalization was determined from clinical care data in each patient file. These costs were based on time and motion studies which are updated yearly. Chi-square tests were used to check for significant differences of type B and severe ADEs and 2-sample t-tests were used to compare the difference in length of stay and the cost of hospitalization between patient groups with an alpha of 0.05.

RESULTS

Computerized ADE surveillance has identified significantly more ADEs than our previous method (Table 1). Before the computerized surveillance, ADEs were reported by voluntary use of incidence reports. Since May, 1989, the computerized surveillance has identified 1,528 ADEs from 1,363 different patients. Analysis of this ADE database has enabled us to determine methods to prevent or reduce certain types of ADEs in hospitalized patients.

During the first year of computerized surveillance, 373 of the 401 identified ADEs resulted from drugs administered in the hospital. Of the 373 ADEs to hospital-administered drugs, 56 (15%) were type B ADEs (Table 2). During the second year of computerized surveillance, the hospital information system generated 124 alerts of

drug allergies and the physicians were notified by clinical pharmacists. The physicians changed drugs 99 percent of the time. As a result, there were only eight (1.4%) ADEs identified as type B out of 560 verified ADEs due to hospital administered drugs during the second year ($p < 0.001$). The actual number of verified ADEs increased in the second year because of the addition of patient signals and improvement in the computerized surveillance. The eight type B ADEs were from eight different patients and resulted from first time use of the drug.

TABLE 1
DIFFERENCE BETWEEN VOLUNTARY AND COMPUTERIZED IDENTIFICATION OF ADEs*

PERIOD	ADEs	PATIENTS
May 88 - April 89	9 (0.04%)	25,142
May 89 - April 90	401 (1.7%)**	23,297
May 90 - April 91	598 (2.7%)	22,247
May 91 - April 92	529 (2.4%)	21,963

* From May 88 - April 89 voluntary reporting of ADEs was used. Since May 89, computerized surveillance has been used.
** $p < 0.001$, difference between voluntary and computerized surveillance.

TABLE 2
REDUCTION OF TYPE "B" ADEs WITH COMPUTER ALERTS*

PERIOD	VERIFIED ADEs	TYPE "B" ADEs
May 89 - April 90	373	56 (15%)
May 90 - April 91	560	8 (1.4%)**

* From May 90 - April 91, computer alerts of known drug allergies were generated when drugs were ordered.
** $p < 0.001$, difference in type B ADEs.

During 1990, there were 41 (7.6%) out of 542 ADEs from drugs administered during hospitalization rated as severe. During 1991, the computerized surveillance methods were the same as during 1990 except that physicians were notified of all ADEs when they were verified. The total number of verified ADEs were very similar during the two years, however, there were only 12 (2.2%) severe out of 545 ADEs during 1991 ($p < 0.001$) (Table 3). The physicians were generally very cordial and grateful when they were notified of the verified ADEs. The patients with severe ADEs displayed from one to five different clinical manifestations with some being life-threatening (Table 4).

The average length of stay for patients with type B ADEs to hospital-administered drugs was 17 days compared to 14 days ($p < 0.013$) for patients with type A ADEs and only five days for the control patients that did not have ADEs (Table 5). The average cost of hospitalization for patients with type B ADEs was $30,617 compared to $23,256 ($p < 0.001$) for patients with type A ADES and $6,320 for patients without ADEs.

TABLE 3
REDUCTION OF SEVERE ADEs WITH EARLY PHYSICIAN NOTIFICATION*

YEAR	VERIFIED ADEs	SEVERE ADEs
1990	542	41 (7.6%)
1991	545	12 (2.2%)**

* During 1991, physicians were notified of all ADEs as soon as they were verified.
** $p < 0.001$, difference in severe ADEs.

TABLE 4
TYPES OF CLINICAL MANIFESTATIONS DISPLAYED BY PATIENTS WITH SEVERE ADEs

SYMPTOM	NUMBER OF PATIENTS
Agitation	2
Anaphylaxis	3
Anemia	1
Arrhythmia	9
Bleeding	2
Bradycardia	16
Bradypnea	4
Cardiac arrest	2
Confusion/lethargy	10
Diarrhea	1
Dizziness/vertigo	5
Fever	7
Headache	4
Hypotension	22
Hypoprothrombinemia	2
Itching	4
Leukopenia	6
Nausea/vomiting	9
Nephropathy	7
Nervousness	1
Neutropenia	2
Oliguria	2
Rash/hives	6
Renal failure	7
Respiratory failure	12
Seizure	7
Stomatitis	1
Tachycardia	7
Tachypnea	4
Thrombocytopenia	3
Ulcers	2

TABLE 5
AVERAGE LENGTH AND COST OF HOSPITALIZATION FOR PATIENTS WITH ADES

PATIENTS WITH	LOS*	COST**
Type B ADEs	17	$30,617
Type A ADEs	14	$23,256
Severe ADEs	20	$38,007
Moderate ADEs	13	$22,474
No ADEs	5	$ 6,320

* Length of stay in days.
** Average cost of hospitalization.

The average length of hospitalization for patients with severe ADEs was 20 days compared to 13 days ($p < 0.024$) for patients with moderate. The average cost of hospitalization was $38,007 for patients with severe ADEs compared to $22,474 ($p < 0.002$) for patients with moderate.

DISCUSSION

Before we developed the computerized ADE surveillance system, all ADEs were reported through voluntary submissions of incidence reports by nurses. The incidence reports required the nurses to report the clinical manifestations presented by the patient, describe what actions were taken to correct the problem, identify which drug caused the event, and have the nursing supervisor and attending physician sign the report. Because of the extra time and inconvenience to submit an incidence report, it was rarely done. Moreover, only 12 percent of the ADEs identified by computerized surveillance are initiated through nursing use of the computerized ADE reporting program [21]. Most verified ADEs are identified by monitoring patient drug levels and the use of drugs to treat ADEs.

Numerous hospital pharmacies have developed computerized methods to identify drug-drug, drug-lab, drug-food, and drug-patient incompatibilities. Stand alone pharmacy systems can generate alerts for drug-drug incompatibilities, but drug-lab and drug-food alerts requires the integration of pharmacy, laboratory, and dietary information. Some hospitals use integrated mainframe computers to capture needed patient information whereas others rely on a network of microcomputers. The generation of drug-patient alerts requires someone to enter information about known drug allergies into the system. Knowledge of previous drug allergies usually must be provided by the patient or a close acquaintance. The creation of an ADE database allows us to automatically identify patients with known drug allergies when they are readmitted to the hospital.

This study demonstrates that the use of pharmacy alerts for known patient allergies can reduce the number of preventable allergic drug events. Although alerts of patient allergies had been part of the hospital information system for almost 15 years, a pharmacy software change eliminated the ability to provide these alerts during the first year of computerized ADE surveillance [22,23]. The hospital information system's ability to automatically generate alerts of drug allergies was restored in May, 1990. Prior to the computerized ADE surveillance we had almost no information about the rates and types of ADEs at our hospital and thus it was impossible to measure the benefits of the allergy alerts. Computerized ADE surveillance during periods with and without drug allergy alerts enabled us to measure the benefit of the alerts.

Once we had used the hospital information system to develop an ADE database, we were able to analyze the types of ADEs and design methods of prevention. During the first 18 months of computer surveillance we only notified physicians about severe ADEs. Starting in January, 1991, physicians were notified of all ADEs as soon as they were verified. Our results indicate that the timely identification of ADEs combined with physician notification provided physicians the opportunity to correct some moderate ADEs before they became severe.

We found that there was a significant difference in the length and cost of hospitalization between patients with type A and type B ADEs and also between patients with severe and moderate ADEs. This suggests that the prevention and reduction of ADEs can reduce the length and cost of hospitalization for certain patients. However, the calculation of the exact cost of a severe or type B ADE will require a matched population study controlling for the number of different drugs and severity of illness. Severely ill patients usually receive a greater number of drugs per hospitalization and the number of drugs received is a known risk factor associated with ADEs [21].

Computerized surveillance has allowed us to design methods to reduce the number of type B and severe ADEs. However, further analysis of the ADE database shows that 1,213 (84%) of the 1,442 ADEs identified from hospital-administered drugs were type A and rated as moderate. We have also found that many of these ADEs were caused by drug doses that were too high based on patients' renal function, age, weight, or underlying disease. Over 60 percent of the verified ADEs at LDS Hospital during the first three years of computerized ADE monitoring were caused by drugs that require dosage adjustments. Almost 50 percent of the ADEs caused by those drugs were due to excessive dosages for the patients' corresponding renal function. Many ADEs that are caused by improper dosages of drugs should also be preventable.

The use of computerized protocols to monitor the dosage of drugs is another function that can be performed by a hospital information system. In addition, the databases from hospital information systems can be valuable tools

in the development of the protocols. These systems can then monitor every hospitalized patient each day and identify patients with drug dosages that do not meet the protocols. This seems to be an achievable method to prevent moderate, type A ADEs. Computerized ADE surveillance can help improve patient care by preventing the inappropriate application and dosing of drugs and by early identification of moderate ADEs. This study indicates that the prevention and early treatment of ADEs to drugs administered in the hospital can reduce the length of hospitalization, result in a considerable cost savings to the hospital, and reduce the morbidity and mortality of hospitalized patients.

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