Reduction of Adverse Drug Reactions By Computerized Drug Interaction Screening

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Computerized drug-interaction screening systems (CDISS) have been developed as a tool to help decrease the enormous morbidity and expense related to adverse drug interactions. In previous studies the CDISS was used primarily by pharmacists in hospital settings to screen for interactions after the prescription had been written. This study tests the feasibility of family physicians using CDISS before writing the prescription to allow for changes in the prescription while the patient is still in the office. In a 30-day period, 103 patients were screened by family physicians for potential drug-drug, drug-alcohol, and drug-food interactions. Potential drug interactions of varying clinical significance were detected for 71 patients (68.9 percent). The prescription plan was changed for 16 patients (15.5 percent) as a result of using the CDISS. Participating physicians reported that they gained new information in 45.8 percent of the patient encounters, that their awareness of the potential for drug interactions was heightened by participation in this study, and that their exposure to the CDISS was worthwhile as an educational tool. While a few problems, mainly logistic, were noted with the CDISS as used in this study, the authors conclude that with modifications a CDISS can be of great educational and clinical value to the family physician and his or her patients.

Adverse drug reactions are a major concern for health care providers in terms of both morbidity and expense. It has been estimated that up to 18.4 percent of the hospital admissions in this country are the result of drug-related events[1,2]; the financial cost of all types of adverse drug reactions are estimated at up to $4.5 billion in hospital charges each year.[3] A recent review of malpractice claims estimated the incidence of drug-related claims to range from 5.7 to 30.0 percent of all medical malpractice claims.[4] A 1974 study by the Boston Collaborative Drug Surveillance Program (BCDSP) estimated a total annual number of 29,000 deaths in this country that were the result of adverse drug reactions.[5] It has further been estimated that 70 to 80 percent of these adverse drug reactions are potentially preventable.[6]

Among the potentially preventable adverse reactions are drug-drug, drug-food, and drug-alcohol interactions. Various studies have estimated that between 6.5 and 25 percent of all adverse drug reactions fall into the category of drug-drug interactions.[7-9] Assuming that 7 percent of adverse drug reactions are the result of drug-drug interactions, Morrell et al[10] calculated that drug-drug interactions may cost patients, taxpayers, and third-party agents between $70 million and $315 million each year.

In recent years attention has been focused on discovering methods that will allow for the prevention of drug interactions. Because of the extremely large number of potential drug interactions and the rapid development of new and more potent drugs, it is difficult for physicians or pharmacists to remember even the important drug interactions. As a result, computerized drug-interaction screening systems (CDISS) have been developed to allow detection and screening for drug-drug, drug-food, and drug-alcohol interactions. A review of the literature points out that these screening systems have been used primarily by pharmacists to screen for drug interactions among hospitalized patients.[10-12] Community pharmacists are increasingly using computers and some have incorporated a CDISS to detect potential drug interactions before prescribed drugs are dispensed.

A more idealistic possibility for preventing drug interactions may be to intervene at an even earlier stage, ie, before the prescriptions are written. To test this possibility,

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the study described in this paper was designed to assess the impact of a computerized drug-interaction screening system on physician education and prescribing practices in an academic family practice setting. The major objectives of the study were (1) to describe the number, type, severity, and significance of potential drug interactions that would have occurred during routine office practice without the use of CDISS; (2) to describe prescription changes that would occur as a result of using CDISS (changes in drug type, dosage, frequency of administration, patient education, etc); (3) to assess the attitudes of users of the CDISS toward this approach in preventing drug interactions; and (4) to assess the effectiveness of exposure to a CDISS as an educational tool for family physicians.

METHODS

The participants in this study included all seven physician faculty members and six resident physicians from the Department of Family and Community Medicine in Little Rock, Arkansas. Participants were asked to use the CDISS during each half-day clinic session for the 30-day period of the study. For the convenience of the participants, a maximum of three patients per half-day session were assigned randomly rather than including all patient encounters. Participants were asked to exclude those patients who were taking fewer than two prescription drugs.

The CDISS program used for this study was version 85-2 of *The Drug Master,*[13] developed by the Medical Software Consortium. This program includes a database of over 1,200 medications and allows the user to enter from one to ten drugs or drug classes at each session. When more than one drug or drug class is entered, the program is designed to determine all possible drug-drug interactions as well as drug-food and drug-alcohol interactions. The program is menu-driven, provides screen viewing, and allows for hard copy printout after each entry (Figure 1). All participants were trained to use the program and were monitored by a research assistant until satisfactory competence was achieved.

For each selected patient, the participants were asked to adhere to the following protocol: (1) Proceed as usual with the patient encounter up to the point at which the "prescription plan" is provided to the patient. (For the purpose of this study "prescription plan" included the name of the drug, dosage, frequency or time of administration, and any other patient instructions related to the proper use of the drug.) (2) Before using *The Drug Master* program, dictate the complete prescription plan, any information that you previously provided to the patient regarding potential drug interactions, and any other information of which the physician is aware regarding drug interactions related to the patient's drug regimen. (3) Enter the proposed drug regimen into *The Drug Master* program and review the description of interactions provided by the program. (4) Following review of the drug interaction data, dictate changes to be made in the prescription plan and new information gained as a result of using *The Drug Master* program.

The printouts and dictations were collected on a daily basis for later analysis. At the end of the study, a survey, which included both open-ended questions and responses on a Likert-type scale, was administered to each physician participant to test participant attitudes in five areas: (1) the importance of drug interaction screening, (2) the impact of the use of a CDISS on prescribing practices, (3) the educational value of using a CDISS for the 30-day period of the study, (4) the advantages and disadvantages of having a CDISS in clinical practice, and (5) problems with the use of *The Drug Master* program during the 30-day study. The data were analyzed as to frequency and percentage to meet the objectives of this descriptive study.

RESULTS

During the study period, 13 physician participants used *The Drug Master* program to screen 103 patients for whom a total of 297 drugs had been prescribed. *The Drug Master* program detected 152 potential drug interactions for 71 patients and classified each interaction according to its potential clinical significance. Information pertaining to the types of potential interactions and the clinical significance of these interactions is summarized in Table 1.

The physician participants reported that the use of *The Drug Master* program resulted in a change in prescription plan with 16 (15.5 percent) of the 103 patients and no change in the prescription plan with 87 (84.5 percent) of the patients. Only one of the 16 changes in prescription plan actually involved eliminating a specified drug. All other changes were in patient education as to the proper use of the drugs, eg, taking nitrofurantoin with food to minimize gastric irritation, avoiding alcohol while taking metronidazole (Flagyl), separating hydralazine from propranolol (Inderal) doses to avoid large variations in beta-blocker serum levels. The participating physicians further reported that they gained new information as a result of using the CDISS with 47 (45.6 percent) of the 103 patient encounters; no new information was gained in 56 (54.4 percent) of the encounters.

In the attitude survey administered at the end of the study, all 13 physician participants indicated that they have legal responsibility for knowing about previously described drug interactions. Nine of the participants felt that the use of the CDISS could help reduce physician liability, while four were undecided on this issue.

Ten of the 13 physicians agreed that their awareness of the potential for drug interactions was heightened by par-

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DRUG INTERACTION TESTING PROGRAM

Data for the following drug(s) - FOOD and ALCOHOL included

1 FOOD
2 ALCOHOL
3 DIGOXIN
4 QUINIDINE

DRUG INTERACTION #1

FOOD and QUINIDINE

CLINICAL SIGNIFICANCE: MODERATE

ACTION: Foods that alkalinize the urine may increase the quinidine reabsorption and blood serum levels, possibly leading to quinidine toxicity. Signs of toxicity include tinnitus, headache, blurred vision, nausea, vomiting, diarrhea. In extreme cases quinidine toxicity can precipitate other arrhythmias.

RECOMMENDATIONS: Patients should avoid the excessive intake of foods that can increase urinary pH. Alkalinizers include milk and other dairy products, citrus juices, almonds, coconuts, and others.

DRUG INTERACTION #2

DIGOXIN and QUINIDINE

CLINICAL SIGNIFICANCE: HIGH

ACTION: Studies have shown that quinidine can produce a significant increase in serum digoxin levels. There is a decreased distribution as well as decreased renal clearance of this digitalis glycoside. The toxic effects of digoxin may be increased while the therapeutic effectiveness may be decreased. This interaction is dose dependent.

RECOMMENDATIONS: When a patient is stabilized on digoxin and quinidine therapy is started, the digoxin dose should be reduced. Serum digoxin levels should be monitored and the dosage adjusted accordingly. If a patient is receiving quinidine therapy and digoxin is started, a smaller than expected dose of digoxin may be required.

Figure 1. Sample of computerized drug-interaction screening system printout. From *The Drug Master*[13]

TABLE 1. CLINICAL SIGNIFICANCE AND TYPE OF POTENTIAL DRUG INTERACTIONS

Type of Interaction	Clinical Significance					Total No (%)
	Low No (%)	Low to Moderate No (%)	Moderate No (%)	Moderate to High No (%)	High No (%)	
Drug-drug	11 (7.3)	0 (0)	16 (10.5)	0 (0)	5 (3.4)	32 (21.2)
Drug-alcohol	11 (7.3)	2 (1.4)	27 (17.5)	11 (7.1)	13 (8.6)	64 (41.9)
Drug-food	41 (26.9)	0 (0)	14 (9.0)	0 (0)	1 (1.0)	56 (36.9)
Total	63 (41.5)	2 (1.4)	57 (37)	11 (7.1)	19 (13)	152 (100)

ticipation in this project, whereas 3 disagreed or were undecided. Nine participants agreed that exposure to the CDISS was worthwhile as an educational tool; 2 disagreed and 2 were undecided on this issue.

Seven of the 13 participants indicated that they would continue to use a CDISS if it were available, 2 participants were undecided on this issue, and 4 participants indicated that they would not continue to use a CDISS. Only 4 participants indicated that they would incorporate a CDISS into their practice; 2 indicated that they would not, and 6 participants were undecided. Four participants indicated that the CDISS was a time-efficient procedure, 1 was undecided on this issue, and 8 indicated that use of the CDISS was not a time-efficient procedure.

In response to questions regarding modifications that would improve the utility of the CDISS for medical practice, participants suggested: (1) increase the speed of the program, (2) expand the program to include important drugs and drug interactions that were omitted from the program used in the study, (3) make access to the computer terminals more convenient, (4) change from a menu-driven program to one in which the user could type in the drug names and have the computer access the interactions, (5) have all patients and their current drug regimens in a computer program so that new prescriptions can be checked against patient databases, and (6) link this program to the transcription process so that interactions are provided automatically at the end of the clinic transcriptions.

DISCUSSION

Numerous previous studies have clearly demonstrated the importance of adverse drug reactions as a public health concern. In the early 1970s, Congressional hearings were held on how to cope with the billions of wasted dollars, hundreds of thousands of unnecessary hospitalizations, and thousands of lives needlessly lost as a result of adverse drug reactions. Nevertheless, little has been done since that time in the way of a systematic approach to the reduction of adverse drug reactions. As previously described, drug interactions are likely to be among the most preventable of these adverse reactions, any system that encourages the prevention of adverse drug interactions should be examined as to its utility in patient care. While there are no definitive studies concerning the cost effectiveness of drug-interaction screening of any type, computerized screening would appear to be more practical than manual screening and therefore have greater acceptance as a means of preventing the adverse consequences of drug interactions.

Computerized drug-interaction screening could take place before or after the prescription has been written. The primary advantage of applying the CDISS before writing the prescription is that it allows the physician to modify the plan at the time the patient is still in the office. Although the prescription plan is most commonly modified by patient education rather than by substituting or eliminating drugs, the decision of how to modify the plan must often be made by the physician. If the CDISS were used after the prescription had been written, changes would require (1) additional conversation between whoever did the screening and the physician to determine the proper remedy for the problem, and (2) contacting the patient a second time to remedy the situation.

Compatible with previous studies, the results of this study indicate that potential drug-drug interactions are quite common. Twenty-five (24.3 percent) of the 103 patients screened in this study had one or more potential drug-drug interactions. The current study differs from previously reported CDISS studies in that it also includes consideration of drug-alcohol and drug-food interactions. When these interactions are included, *The Drug Master* program detected one or more interactions in 71 (68.9 percent) of the 103 patients. It seems appropriate that these interactions be included, considering how frequently alcohol is consumed either socially or habitually (and considering that food consumption is universal!). That there were twice as many potential drug-alcohol as drug-drug interactions in this study is somewhat misleading, as potential drug-alcohol interactions were listed for all patients without regard to individual drinking patterns. All of the drug-food interactions, on the other hand, can be assumed to have at least potential significance.

With regard to clinical significance of the different types

of potential drug interactions, it appears from these data that potential drug-food interactions, while common, were rarely of great clinical significance (74 percent of the drug-food interactions were in the category of low clinical significance, 25 percent in the moderate, and only 1 percent in the high category). Potential drug-alcohol interactions, however, tended to be highly significant with nearly 80 percent of this type of interaction falling in the categories of moderate or higher clinical significance. Approximately two thirds of the potential drug-drug interactions detected were in the categories of moderate or high clinical significance.

As indicated in the results, the prescription plan was changed as a result of using the CDISS in 16 of the 71 patients for whom *The Drug Master* program detected one or more interactions. That there was no change in the prescription plan for the other 55 patients for whom potential interactions were noted is not surprising; in a previous hospital study of 1,219 potential interactions initially felt to be clinically significant (and therefore monitored), only 116 (9.5 percent) were actually deemed to be of potential clinical significance.[12] The reason that there are few prescription changes relative to the large number of potential drug interactions described is that many of the interactions are not significant in every clinical situation (eg, an interaction between an oral hypoglycemic and a thiazide diuretic in a diabetic patient whose blood glucose has been well controlled on a regimen including both drugs).

Participants were generally positive as to the value of exposure to the one-month CDISS project as an educational tool, and many indicated that they would use a CDISS in some way if it were available in their practice. Several participants were less than certain that they would incorporate a CDISS into their practice, however. Most of their concerns seemed to be related to this particular CDISS program or with the ease and speed of access to the computer rather than with the CDISS concept itself.

It should be noted that the study required an extensive time commitment from physician participants in addition to the time required for use of the CDISS. It is likely that attitudes would have been significantly different in favor of a CDISS as a time-efficient tool if there were no other study requirements, if the program had been faster, if the database had been more complete, if there had been easier access to the computer, or if the participants had greater familiarity with the system. The study design also dictated which patients were to be screened. It is possible that allowing participants to choose which patients to screen would more closely approximate the use of a CDISS in a practice setting and would possibly have influenced participants' attitudes.

The results indicate that there is considerable educational value in even a brief exposure to a CDISS. Residency programs may find it useful to expose residents to a CDISS for either a brief period of time to raise awareness or for the duration of the residency to reduce problems related to patient morbidity and physician liability, which may be of more direct concern with the physician in training.

Computerized drug-interaction software is available from a variety of sources for most models and configurations of microcomputers and larger systems. Cost of software ranges from less than $100 to several thousand dollars, depending on software sophistication or type of computer. The software used in this study cost $295, with updates available twice yearly for $55 each. To use a CDISS a physician must dedicate a microcomputer to this task at a minimal cost of approximately $1,000, or integrate a CDISS program with an existing multiuser system. Physicians considering incorporating a CDISS into their practice would be well advised to request a trial period with a number of different available programs to find one that is most compatible with the individual practice.

As computer-assisted patient care becomes less expensive and more available, it can be anticipated that a CDISS would be worthwhile if only a few patients were helped significantly or if only a few legal claims were prevented by the intervention. If future studies prove the cost effectiveness of computerized drug-interaction screening by physicians, it is likely that CDISS will become the standard of care in medical practice.

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