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Adverse Drug Event Detection in a Community Hospital Utilising Computerised Medication and Laboratory Data

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Abstract

Objective: Computerised monitors can detect and, with clinical intervention, often prevent or ameliorate adverse drug events (ADEs). We evaluated whether a computer-based alerting system was useful in a community hospital setting.

Methods: We evaluated 6 months of retrospectively collected medication and laboratory data from a 140-bed community hospital, and applied the rules from a computerised knowledge base to determine if the resulting alerts might have allowed a clinician to prevent or lessen harm related to medication toxicity. We randomly selected 11% (n = 58, of which 56 were available) of charts deemed to be high- or critical-priority alerts, based on the likelihood of the alerts being associated with injury, to determine the frequencies of ADEs and preventable ADEs.

Results: In 6 months, there were 8829 activations of the rule set, generating a total of 3547 alerts. Of these, 528 were of high or critical priority, 664 were of medium priority and 2355 were of low priority. Chart review among the sample (56 charts) of high- or critical-priority alerts found five non-preventable and two preventable ADEs, suggesting that among the total high- or critical-priority alerts alone, there would be approximately 94 non-preventable ADEs and 37 preventable ADEs annually in this hospital that could be detected using this method.

Conclusions: Computer-based rules engines have the potential to identify and, with clinical intervention, mitigate preventable ADEs, and implementation is feasible in community hospitals without an advanced information technology application.

Introduction

Medical injuries are common, and drugs are their most frequent cause.[1] In the inpatient setting, adverse drug events (ADEs) result in significant injury to patients, significantly increase healthcare costs[2-4] and are often preventable.[5] However, since most organisations still rely on spontaneous reporting to detect ADEs, they obtain very little information about the frequency, severity or cause of these events within their own institutions.

In one study, spontaneous reporting identified only about one in twenty ADEs detected by chart review.[6] As a result, other approaches, including computerised ADE monitoring, have been developed to enable active surveillance.[6-10] With this method, the computer system is used to screen for signals that suggest that an ADE might be present, such as the use of an antidote or an abnormal laboratory test, which can then be followed up by a pharmacist. An additional advantage of this approach is that problems may be detected early on in the course of the event, so that it may be possible to prevent or ameliorate an injury.[11]

We previously reported on results obtained with an ADE monitor that we built at a large academic hospital,[6] which was modelled on an ADE monitor developed at Latter-Day Saints Hospital, Salt Lake City, Utah, USA.[7] Another approach has been to utilise laboratory values to monitor for ADEs, without linking the laboratory information to specific medication use.[12] All these studies took place in relatively large hospitals.

However, most hospital care is delivered in community hospitals, which tend to have relatively unsophisticated computer systems. Systems developed for large academic centres are not easy to implement in these community settings. Nonetheless, since most community hospitals do have medication lists and laboratory data online,[13] even though these data are often not electronically linked, a system designed to exploit these data may be useful.

The development of a targeted ADE monitor at a community teaching hospital has previously been described.[14] We wished to utilise a monitor that could screen a larger number of medications than had been included in this previous monitor. Therefore, we evaluated the capacity of a commercially available application that is intended for implementation in community hospitals to detect ADEs early and to ameliorate these events. The Vigilanz Corporation (Minneapolis, MN, USA) has developed a tool, the Dynamic Pharmaco-Monitoring™ System. The Dynamic Pharmaco-Monitoring™ System is a surveillance and feedback tool that actively monitors for potential ADEs by combining medication and laboratory results with patient demographic information. We evaluated the utility of this application for identifying ADEs and evaluated the burden such a system might place on the resources of a community-based hospital.

Methods

We used data from a community-based teaching hospital in Boston, Massachusetts, USA. The hospital has 140 medical and surgical beds, and there are approximately 7200 discharges every year. We used retrospective data from a 6-month period from 1 July 2002 to 31 December 2002. We filtered all laboratory, medication and patient demographic data against a set of rules designed as a real-time event engine. These rules were retrospectively evaluated, and the rule engine generated 'alerts' that could be potentially associated with ADEs. The study was submitted to and accepted by the institution's independent review board.

Rules

The rules were developed using combinations of drugs, laboratory data and patient demographic data that met certain conditions. For example, a patient on gentamicin with a rising serum creatinine level would trigger an alert. Drugs were identified by a pharmacy order (as opposed to a medication administration), and the rules allowed for linking of multiple drugs and laboratory tests. An example of this would be a potential bleed due to an order for heparin in conjunction with a recent abciximab order. The use of these drugs together would activate the second part of the rule, in which the application monitored the laboratory results for evidence of

testing of haematocrit and associated red blood cell counts or a haemoglobin levels.

The rule set also designates the alerts with a low, medium, high or critical priority based on how likely the alert is to be associated with injury, and a baseline level is established for the key laboratory parameter within the rule. In the previous gentamicin example, a serum creatinine level >1.3 mg/dL but ≤2.47 mg/dL would be a low-priority alert. A serum creatinine level >2.47 mg/dL but ≤3.51 mg/dL would constitute a medium-priority alert, whereas a high-priority alert would require a serum creatinine level >3.51 mg/dL but ≤3.9 mg/dL. Finally, any serum creatinine level >3.9 mg/dL would be classified as a critical alert. The system is designed with the flexibility to allow individual institutions to increase or decrease these values based on local practice and priorities.

We could have created new rules based on gender, age or patient unit, but we chose to utilise only the rules from a previously created rule set. The structure of a rule set varies based on the intent of the specific rule (i.e. the rule can look for either a rising or falling laboratory parameter level) and can include parameters based on gender, age and weight. The operating system utilised was Windows® 2000 server, and the database was Microsoft SQL server 2000 and Transact® SQL (Microsoft Corporation, Redmond, WA, USA). The application services ran in .NET® framework with C# assemblies. The web application was run with .NET® middleware framework with Internet Information Services and asp.net (Microsoft Corporation, Redmond, WA, USA).

A rule was considered to be activated if all of the rule's criteria were met. The activated rule could change to an 'alert' if a designated amount of time, called the Good Medical Practice interval, had passed and the medication had not been stopped, a new test had not been ordered or the dose of the drug of interest had been decreased. The Good Medical Practice interval can be different for every rule. There were 787 rules in the library for use in the rules engine, but nearly half of them required the incorporation of a patient's weight to accurately calculate creatinine clearance. Because our information system did not reliably capture patient weight, we were only able to use 358 rules. In addition, some rules that utilised glucose levels were eliminated due to the fact that bedside glucose values were not recorded in the hospital's laboratory reporting system. The alerts were stratified into critical, high, medium and low priority.

Selection of Charts for Review

We randomly selected 11% (n = 58) of the high- and critical-priority alerts for further chart review, using a random number generator. We over-sampled because in any chart review process some charts are not available and we wished to obtain a minimum sample of 10% of all high-priority alerts. To assess how often high- or critical-priority alerts were associated with ADEs, we randomly selected 58 charts, of which 56 were available for review; this sample of 56 charts included 48 unique patients.

Results

During the 6-month period, there were 90 053 pharmacy medication orders and 841 028 laboratory results among the 3428 patient admissions to the medical or surgical services. There were 8829 activations of the rule set, generating a total of 3547 alerts among 1108 unique patients during the time period. Of these 'alerts', 528 in 215 patients were considered to be high or critical priority, 664 were considered to be medium priority and 2355 were considered to be low priority. Demographic information for the patients who received high- or critical-priority alerts is listed in table I.

A total of 135 (26%) of all high- or critical-priority alerts resulted from nephrotoxic drugs and rising creatinine levels. The second most common

Table I. Demographics of patients (n = 215) with high- or critical-priority alerts between 1 July 2002 and 31 December 2002

Demographic	Number (%)
Male	116 (54.0)
Age in years	
≥81	61 (28.4)
61–80	98 (45.6)
24–60	56 (26.0)

alerts were from the use of hepatotoxic drugs and an elevated ALT or AST level, which represented 96 (18%) of all high- or critical-priority alerts. Examples of some of the rules that created high- or critical-priority alerts were the use of celecoxib and an elevated creatinine level; the use of digoxin and an elevated serum digoxin concentration; the use of amiodarone and an elevated ALT level; the use of risperidone and an elevated ALT level; the use of heparin and a decreased platelet count; the use of furosemide (frusemide) and a decreased magnesium level; the use of metformin and an elevated creatinine level; the use of simvastatin and elevated ALT level; the use of warfarin and an elevated international normalised ratio; and the use of a potassium supplement with an elevated potassium level. Selected other drug/laboratory test combinations are also listed (table II).

The reviewed population included 48 unique patients representing the 10% of all high- and critical-priority alerts. Of these, 27 (56.2%) were female and 21 (43.8%) were male. The demographics and diagnoses of the reviewed patients with high-priority alerts are listed in table III. The available charts were reviewed following the criteria utilised in previous studies.[5] The overall results of our review are listed in table IV and the specific case results from these chart reviews revealed there were five non-preventable ADEs and two preventable ADEs, one related to an elevated digoxin level and one related to administration of enoxaparin sodium and a subsequent drop in red blood cell count due to bleeding. Summing the number of events and dividing by the total number of random charts gives a positive predictive value (PPV) of 0.125 for any ADE appearing in a chart having been signalled by an alert. In addition, the PPVs were calculated for all events. The PPVs were 0.125 for all events, 0.089 for non-preventable ADEs and 0.036 for preventable ADEs.

We present the two cases of preventable ADEs detected by the system. The first was that of an elderly woman admitted for congestive heart failure.

Table II. Selected high- and critical-priority alerts that occurred between 1 July 2002 and 31 December 2002

Medication	Laboratory test	Number of alerts	Proportion of all high- or critical-priority alerts (%)[a]
Furosemide	Serum creatinine level	51	9.66
Enoxaparin sodium	Red blood count	40	7.58
Heparin	Platelet count	38	7.20
Clopidogrel	Haematocrit level	31	5.87
Amiodarone	ALT, AST level	22	4.17
Amiodarone	Prothrombin time	17	3.22
Warfarin	INR	14	2.65
Methylprednisolone	Serum glucose level	8	1.52
Glibenclamide (glyburide)	Serum creatinine level	7	1.33
Lisinopril	Serum creatinine level	7	1.33
Digoxin	Serum digoxin concentration	6	1.14
Celecoxib	Serum creatinine level	4	0.76
Simvastatin	ALT, AST level	3	0.57
Metformin	Serum creatinine level	2	0.38
Naproxen	Serum creatinine level	2	0.38
Potassium chloride	Serum potassium level	1	0.19
Captopril	Serum potassium level	1	0.19
Dexametasone	Serum glucose level	1	0.19
Sodium valproate	Serum valproate level	1	0.19
Total		**256**	

a A total of 528 high- or critical-priority alerts occurred during the 6-month study period.

INR = international normalised ratio.

Table III. Demographics of reviewed patients (n = 48)

Parameter	Number (%)
Male	21 (43.8)
Ethnicity	
Caucasian	38 (79.2)
African-American	6 (12.5)
Hispanic	2 (4.2)
Asian-American	1 (2.1)
Age in years	
≥81	14 (29.2)
61–80	19 (39.6)
24–60	15 (31.3)
Diagnosis	
infection, various	8 (16.7)
pneumonia	7 (14.6)
other	7 (14.6)
lung, various	5 (10.4)
gastrointestinal, carious	5 (10.4)
MI; rule in and rule out	3 (6.3)
cardiac arrest	2 (4.2)
congestive heart failure	2 (4.2)
endocrine	2 (4.2)
ethanol-related	2 (4.2)
gastrointestinal bleed	2 (4.2)
vascular, various	2 (4.2)
fracture	1 (2.1)

MI = myocardial infarction.

At the time of admission, the woman was receiving glibenclamide (glyburide)/metformin 5/500mg for the treatment of diabetes mellitus; she had a serum creatinine level of 3.3 mg/dL. She continued to receive both glibenclamide and metformin for another 2 days after admission and experienced an episode of hypoglycaemia. At 1:00am on the third hospital day, she was noted to have a blood glucose level of 39 mg/dL. She was given one ampoule of dextrose 50% in water, and she subsequently improved. No further episodes of hypoglycaemia were noted during the admission. If the event engine had been operating in a prospective manner at the time of the event, it is likely that it would have alerted the clinicians to the risks associated with glibenclamide/metformin in the setting of renal dysfunction, and the hypoglycaemic episode might have been averted.

In another case, an elderly woman with a recent history of digoxin toxicity was admitted for treatment of hypernatraemia. Her potassium level on admission was 4.6 mEq/L, and she was prescribed captopril 25mg three times daily for control of hypertension. During the hospitalisation, she became anorexic with poor oral intake. On hospital day 7, the laboratory noted a potassium level of 6.9 mEq/L. She continued to receive captopril throughout the next hospital day, despite this life-threatening hyperkalaemia. An alert could have resulted in earlier cessation of captopril therapy.

Although we did not formally evaluate the cost effectiveness of this intervention, we did do a rough assessment. Given an average cost for a preventable ADE of $US4685 (1997 values),[15] and 37 potentially preventable ADEs per year, the annual cost of these events would be $US173 345. In addition, 94 non-preventable ADEs could have been detected. In terms of personnel utilisation, the pharmacy staff estimated that about 1.5 hours of pharmacist time per day were needed to triage, follow up and report results. Utilising a labour cost of $US40/hour, this labour cost would be approximately $US15 600 annually. Labour costs for the information technology implementation and maintenance were estimated to be approximately $US10 000 per year. We also estimated the setup, administration and operation of the system to be $US99 000 for the first year of operation and $US56 350 for subsequent years, not allowing for inflation. Thus, the total first-year cost would be $US124 600, with a cost in subsequent years of $US81 900, compared with the annual benefits of $US173 345. As a result, in addition to the patient safety benefit, it is likely that this approach would be financially beneficial for payers and providers.

Table IV. Adverse drug events (ADEs) in reviewed charts containing high- and critical-priority alerts

	No. of alerts
Selected results	56
Total ADEs	7
Non-preventable ADEs	5
Preventable ADEs	2
Positive predictive value	12.5/100 alerts

Discussion

We retrospectively applied a structured rule set based on both medication orders and laboratory results in a 140-bed community hospital and found that alerts were common and potentially associated with an ADE. We project that, based on our sample, there would be 140 ADEs every year for this hospital, of which slightly less than one-third would be preventable. There were many more activations than alerts, but the programme was able to remove 60% of these activations by monitoring for additional clinical data. The generation of 3547 total alerts over the 180 days of the study period yields a rate of 20 alerts every day, of which 3.2 were high- or critical-priority alerts. The rough analysis of costs and benefits suggest that the application would likely be cost-saving, in addition to providing safety benefits for the institution.

Based on our extrapolation, this system could have identified and potentially prevented up to 37 ADEs per year by focusing on high- or critical-priority alerts alone. The 3.2 high- or critical-priority alerts per day would likely take >1 hour for a pharmacist to review and decide whether action was necessary. In addition, as systems are rolled out to be utilised prospectively, a pharmacist might further reduce the number of alerts after initial review by telling the programme to show no further alerts for a specific rule and a specific patient. In this way, the number of alerts generated can be reduced if used in real time.

This type of ADE monitoring tool appears to complement other approaches to improving medication safety. For example, computerised physician order entry (CPOE) can reduce the medication error rate substantially.[16] However, it has also been shown that in addition to CPOE, systems that lack decision support such as monitoring continue to be associated with high rates of ADEs.[17] In addition, bar-coding of unit dose medication[18] and infusion pumps with integrated decision support[19] may help prevent harm due to medication errors. Furthermore, most CPOE applications target ordering only at the time a drug is started, and adjustment may be needed later, especially in patients with changing renal or hepatic function.

An ADE surveillance system may be helpful either as a stand-alone system or as an adjunct to other information technology systems for intercepting and decreasing events. The use of a computer-based system, as demonstrated at the community-based hospital in this study, can alert the pharmacist or clinician to a situation where a patient is at risk for injury while the event is occurring, allowing a pharmacist to consult with the physician and potentially modify therapy. While some of the triggering drugs have not historically been considered to be 'high-alert' medications, such as corticosteroids causing elevated glucose levels, these drugs may contribute to harm in a less acute sense. Moreover, increasing evidence suggests that improving glycaemic control in hospitalised patients improves outcomes in a variety of conditions.[20-22]

Although only one of the 3457 alerts was related to a patient receiving a potassium supplement and experiencing an elevated potassium level, this high-priority alert is an example of one that could have life-threatening consequences if not corrected quickly. In one study of patients with life-threatening laboratory abnormalities, the mortality rate was 7.4% for the intervention group versus 13.3% for the control group, although this difference was not statistically significant.[23] There were a large number of renal and hepatic high-priority alerts, and acute renal failure in particular is associated with a high inpatient mortality rate.[24] Overall, ADE surveillance, if properly performed, can assist providers in delivering safer care. Although not all rules triggered alerts, the rules that were triggered often related to what are considered 'high-alert' medications,[25] such as warfarin and enoxaparin sodium.

The analysis of costs and benefits suggested that this application would likely be cost-saving, especially after the first year. Again, although we did not perform a formal sensitivity analysis, this conclusion would likely be sensitive to the number of events identified, and their costs. Undoubtedly, some ADEs were associated with medium- or low-

priority alerts, and further evaluations should explore these classes of ADEs as well.

We believe that this type of clinical role is already important for pharmacists and that it is likely to be even more so in the future. Other types of providers such as nurses could also review such alerts, but pharmacists are probably best equipped to do so, given their training. The major limitation that pharmacies have faced in implementing tools such as this have been making sure that adequate pharmacist time is available to intervene, and this can be difficult given the national pharmacist shortage.

Our study was limited by the fact that we utilised retrospective data and the alerting system was designed to be utilised as a real-time application. However, our retrospective analysis provides a glimpse of the performance of such a system. In addition, we sampled only a small number of charts and made determinations of the presence of ADEs based on what was recorded in those charts. Because of budgetary limitations, we did not review medium- or low-priority alerts. In addition, we did not have bodyweights for patients, nor could we closely monitor glucose levels, which limited our ability to detect potentially preventable events relating to insulin use.[26] Some information that is pertinent to the categorisation of the cases may not have been recorded in the charts and therefore we might have missed important events. We also did not calculate estimates of sensitivity, specificity and negative predictive value. Combined, these factors suggest that the estimate we reached of ADE frequency was undoubtedly conservative.

In summary, this study demonstrates that computer-based rules engines can identify both preventable and non-preventable ADEs and perhaps allow intervention around these events in a community-hospital setting. Since it may be possible to prevent or mitigate the severity of some ADEs, the potential safety benefits are substantial and there might also be additional cost savings to the hospital and payers. Such applications can be utilised in sites that do not have fully developed information technology systems and they represent an important complement to other approaches that can be used to improve medication safety.

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