Adverse Drug Events Resulting from Patient Errors in Older Adults

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OBJECTIVES: To characterize the types of patient-related errors that lead to adverse drug events (ADEs) and identify patients at high risk of such errors.

DESIGN: A subanalysis within a cohort study of Medicare enrollees.

SETTING: A large multispecialty group practice.

PARTICIPANTS: Thirty thousand Medicare enrollees followed over a 12-month period.

MEASUREMENTS: Primary outcomes were ADEs, defined as injuries due to a medication, and potential ADEs, defined as medication errors with the potential to cause an injury. The subset of these events that were related to patient errors was identified.

RESULTS: The majority of patient errors leading to adverse events (n = 129) occurred in administering the medication (31.8%), modifying the medication regimen (41.9%), or not following clinical advice about medication use (21.7%). Patient-related errors most often involved hypoglycemic medications (28.7%), cardiovascular medications (21.7%), anticoagulants (18.6%), or diuretics (10.1%). Patients with medication errors did not differ from a comparison group in age or sex but were taking more regularly scheduled medications (compared with 0–2 medications, odds ratio (OR) for 3–4 medications = 2.0, 95% confidence interval (CI) = 0.9–4.2; OR for 5–6 medications = 3.1, 95% CI = 1.5–7.0; OR for ≥7 medications = 3.3, 95% CI = 1.5–7.0). The strongest association was with the Charlson Comorbidity Index (compared with a score of 0, OR for a score of 1–2 = 3.8, 95% CI = 2.1–7.0; OR for a score of 3–4 = 8.6, 95% CI = 4.3–17.0; OR for a score of ≥5 = 15.0, 95% CI = 6.5–34.5).

CONCLUSION: The medication regimens of older adults present a range of difficulties with the potential for harm. Strategies are needed that specifically address the management of complex drug regimens. **J Am Geriatr Soc 55:271–276, 2007.**

Key words: patient safety; adverse drug events; medication errors

During recent years, researchers have identified substantial rates of adverse events resulting from medication errors across clinical settings.[1–9] These studies have focused on errors occurring during prescribing of medications and monitoring of their effects by healthcare providers. The patient safety movement has encouraged a shift in focus away from blaming individuals for errors to an emphasis on understanding and preventing system failures. As a result, we have witnessed the development of a range of new approaches to the prevention of adverse events and the reduction of their effect on patients.[10–17]

The activities of patients and their families have rarely been included in these analyses and are usually not considered to be a component of the overall system of medication handling, although in a recent study of adverse drug events (ADEs) in a large population of Medicare enrollees aged 65 and older, 21.1% of preventable ADEs in the ambulatory setting resulted, at least in part, from medication adherence errors by patients and their families.[5] These events had important implications; 47.2% were considered serious and 22.5% life-threatening.

If we are to reduce the rates of these events, it is important to increase our understanding of the role of patient errors in the overall medication system. In response, this study was designed to characterize medication handling by patients, categorize the medication activities in which errors most often occurred, and identify patients at particularly high risk of errors leading to adverse events.

METHODS

Population

This study builds upon previously reported results from a study of more than 30,000 persons aged 65 and older who received health care from a large multispecialty group

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practice and who were followed over a 1-year period.[5] The institutional review board of the University of Massachusetts Medical School approved the project, which did not require explicit consent from the participants, because there was no direct contact by study personnel with patients or healthcare providers during the study.

Identification and Classification of Events

Methods relating to the original identification and classification of ADEs and potential ADEs (pADEs) have been described previously.[5,18] Signals that a possible drug-related incident had occurred were detected via electronic tracking of administrative data, as well as reports from clinicians and summaries of hospital discharges and emergency department visits. After extensive training, clinical pharmacists reviewed the medical records related to these signals and abstracted information on possible drug-related incidents for presentation to pairs of physician reviewers for classification. Agreement between the clinical pharmacist investigators on whether to abstract possible drug-related incidents across 80 signals was tested, and the kappa for agreement was found to equal 0.67, indicating substantial agreement. The pharmacists prepared extensive summary descriptions of all information available in the medical records that was relevant to these incidents.

The physician reviewers independently classified incidents using structured implicit review to determine whether an event was present and, if so, whether it was preventable and the categories of drugs involved. Reviewers based their categorizations of events on standard definitions; an ADE is an injury due to a medication, a preventable ADE is an injury that is the result of an error at any stage in medication use, and a pADE is a medication error with the potential to cause an injury but that does not actually cause any injury.[19] For example, if a patient taking warfarin failed to present for scheduled laboratory testing resulting in a dangerously high international normalized ratio but did not suffer a bleeding event, that would be considered a pADE. Events were considered to be preventable if they were due to an error and were preventable by any means available. The kappa for agreement in judgments about the presence of an ADE between physician reviewers across all possible events was 0.81, and the kappa for agreement on preventability was 0.67. By definition, all pADEs were associated with an error and were considered preventable. For events that were judged to be preventable, the physician reviewers responded to a series of questions about the types of errors involved and the individuals responsible for the errors. Available categories included patients and families. The physician reviewers identified medication adherence errors by patients as a factor in 89 (21.1%) of the 421 preventable ADEs and 33 (15.0%) of the pADEs.

Analysis of Patient Errors

Previous studies have developed categories of patient misunderstandings of medication directions[20] and patient medication errors,[21] but no previous literature categorizing the activities involved in patients' handling of their medications could be identified. Therefore, the establishment of a set of categories of medication handling activities in which errors might occur preceded the analysis. These categories were revised throughout the process of reviewing events whenever patient errors that were not included in the existing categories were encountered. The final categories are summarized in Table 1 with examples.

The review of events related to patient errors was begun by identifying all preventable ADEs and pADEs for which either of the physician reviewers had identified a patient adherence error, had selected the patient or family as having any responsibility for the event, or had specified that errors in patient education were a component of the event (n = 188). For each of these events, the original physicians' assessment and the complete event descriptions were read by pairs of reviewers (TSF, KM, BB, KD) who independently

Table 1. Categories of Medication Handling Activities in Which Patient Errors Occurred, with Selected Examples of Errors

Filling and refilling the prescription

A patient who was taking digoxin ran out of 0.125 mg tablets. Rather than refilling the prescription, he took 0.25 mg tablets that were left over from a previous prescription.

Administering the right medication and right dose at the right time

A patient taking warfarin confused her medications and took pravastatin instead. When laboratory tests revealed a low international normalized ratio (INR), and she was told to increase her warfarin dose, she increased the pravastatin. Subsequently she suffered a stroke.

Modifying the medication regimen when advised to do so by clinicians or in response to results of a self-monitoring regimen.

A patient taking insulin was in a hurry and failed to eat breakfast and did not check his blood sugar level but took his usual dose of insulin. He experienced a hypoglycemic reaction while driving, leading to a motor vehicle accident.

Following clinical advice about medication use, such as to use or avoid using over-the-counter medications, alcohol, consistent food and liquid intake, or a bowel regimen.

A patient taking insulin lost her dentures and ceased eating solid food but continued to take the same doses of insulin. The resulting hypoglycemia led to mental status changes and an emergency department visit.

Reporting information to healthcare providers, such as adverse effects of medications and use of over-the-counter medications.

A patient with a previous history of gastrointestinal problems was prescribed naproxen. She did not inform the physician that she was already taking 8 to 10 ibuprofen pills daily and continued taking them after beginning the naproxen.

Adhering to follow-up by keeping laboratory and clinical appointments.

A patient taking warfarin had a busy social schedule and missed three successive appointments for tests of INR levels. The next INR result, 1 month later, was 5.7.

determined whether a patient error was involved in the event and, if so, in what category of medication-handling activities it occurred. When the two reviewers disagreed, they discussed their decisions and reached consensus. For judgments about the presence of a patient error, the kappa for agreement was 0.79. The reviewers also attempted to identify the underlying causes of failures in patients' medication handling, based on information that had been abstracted from medical records.

Identification of Patient-Level Risk Factors

To identify factors predicting patients who would have errors leading to ADEs and pADEs during the year, these individuals were compared with a control group, randomly drawn from the same population of older adults. For each individual with an adverse event in the original study (N = 1,299), a control had been randomly selected from all individuals aged 65 and older receiving health care from the same multispecialty group practice who had an outpatient visit and drug dispensing within the month before the case's ADE; selection of controls has been fully described in a previously published report.[22] Information including age, sex, all regularly scheduled medications, and Charlson Comorbidity Index was abstracted from medical records as of the date of the case's event.

Analysis

The analysis was begun by examining the categories of drugs involved in the events and summarizing the categories of medication-handling activities in which patient errors occurred across these drug categories. In comparisons of the characteristics of patients experiencing events with the control group, chi-squares and *P*-values were calculated for each variable, and multivariate logistic regression models were constructed using SAS (SAS Institute, Inc., Cary, NC). Separate models were constructed for age and sex, number of regularly scheduled medications, and Charlson Comorbidity Index. Variable groups that were statistically significant at the 0.05 level were then combined in a single model. All interactions were assessed, and none were significant.

RESULTS

Of the 188 events reviewed, 59 did not contain patient errors. The remaining 129 events included 99 ADEs and 30 pADEs. These events represented 23.5% of all preventable ADEs and 13.6% of all pADEs identified during the year. A variety of medication categories were involved in these events. Drug categories associated with more than 10 events were hypoglycemics, cardiovascular drugs, anticoagulants, diuretics, and non-opioid analgesics.

Table 2 presents categories of activities in which medication-handling errors occurred for these medications and all other drugs. Although there were errors in each category, the majority occurred in administering the medication (31.8%), following clinical advice (21.7%), or modifying the regimen when advised to do so (41.9%). Many of the events associated with hypoglycemic medications included a failure to follow clinical advice or an error in modifying the medication regimen. Of errors related to cardiovascular medications and diuretics, most occurred in administering the medication or modifying the regimen. For patients with errors related to anticoagulants, errors most commonly occurred in administering the medication, modifying the regimen, and adhering to follow-up. Errors related to the use of analgesics were most often related to failure to follow clinical advice.

The available information limited the assessment of the underlying causes of patient errors, although the medical records contained some relevant information. In 29 events, there were indications of cognitive limitations, including diagnosed dementia, schizophrenia, bipolar disorder, depression, and clinicians' comments in the medical record about confusion and reduced mental capacity. Sensory problems such as low vision and physical limitations underlay 11 additional events. In 27 cases, the complexity of the medication regimen was specifically noted in the medical record as being responsible for the error. Medication regimens noted as complex included regimens with frequent dose changes; complex or conflicting communications between physicians, pharmacists, other healthcare providers, the laboratory, and the patient; and regimens with complex verbal directions. For a few events, the patient had decided to reject the recommended dosing regimen, continued to use an interacting medication to offset perceived side effects, refused to continue laboratory monitoring, or declined medical advice of any kind.

One hundred thirteen unique individuals experienced the 129 ADEs and pADEs. Twelve patients experienced more than one event. Table 3 compares these 113 individuals

Table 2. Categories of Medication-Handling Activities in Which Patient Errors Occurred, by Type of Medication Involved in the Event (N = 129)

Categories of Medication-Handling Activities	All	Hypoglycemic Medications n = 37	Cardiovascular Medications n = 28	Anticoagulants n = 24	Diuretics n = 13	Analgesics n = 11	Other Medications n = 23
	n (%)						
Filling the prescription	2 (1.6)	0 (0)	1 (3.6)	0 (0)	2 (15.4)	0 (0)	0 (0)
Administering the drug	41 (31.8)	3 (8.1)	14 (50.0)	10 (41.7)	3 (23.1)	1 (9.1)	10 (43.5)
Following clinical advice	28 (21.7)	16 (43.2)	0 (0)	5 (20.8)	0 (0)	6 (54.5)	3 (13.0)
Modifying the regimen	54 (41.9)	25 (67.6)	11 (39.3)	7 (29.2)	7 (53.8)	2 (18.2)	5 (21.7)
Reporting clinical information	12 (9.3)	4 (10.8)	0 (0)	0 (0)	1 (7.7)	4 (36.4)	3 (13.0)
Adhering to follow-up	12 (9.3)	0 (0)	2 (7.1)	7 (29.2)	1 (7.7)	0 (0)	2 (8.7)

with the controls. Patients with medication-handling errors leading to ADEs and pADEs differed from this comparison group in several ways. Their scores on the Charlson Comorbidity Index were higher, and they were taking more regularly scheduled medications. Differences in age or sex were small and did not reach statistical significance. In a multivariate analysis, there was a dose–response association between patient errors leading to ADEs and pADEs and regularly scheduled medications; compared with zero to two medications, the odds ratio (OR) for three to four medications was 2.0 (95% confidence interval (CI) = 0.9–4.2), for five to six medications was 3.1 (95% CI = 1.5–7.0), and for seven or more medications was 3.3 (95% CI = 1.5–7.0). However, the strongest association was with the Charlson Comorbidity Index; compared with a score of 0, the OR for a score of 1 to 2 was 3.8 (95% CI = 2.1–7.0), for a score of 3 to 4 was 8.6 (95% CI = 4.3–17.0), and for a score of 5 or more was 15.0 (95% CI = 6.5–34.5).

DISCUSSION

In summary, the process of medication handling by patients was found to be complex, including a variety of activities in which errors occur. The patient errors leading to adverse events most often occurred in administering the drug, modifying the medication regimen, and failure to follow clinical advice about medication use. The most common underlying reasons for errors identified in this study related to the demands that complex medication regimens and changes in those regimens placed on patients and the presence of dementia, confusion, and sensory problems. Patients with medication errors did not differ from other older adults in age or sex but were taking more regularly scheduled medications and had more chronic conditions.

Efforts to reduce ADEs in ambulatory patients should focus on the activities in which errors leading to such events most often occur. ADEs were often associated with patient errors in administering medications and following clinical advice about medication use, suggesting that some patients may require assistance in developing and maintaining safe medication-management systems. The large proportion of errors leading to ADEs and pADEs that occurred when patients were advised to modify their medication regimens suggests the need for enhanced surveillance and follow-up when changes in medications are made.

The underlying reasons for the errors identified suggest that there is a need to carefully weigh the risks and benefits of prescribing medications requiring complex handling for confused or demented patients, as well as those with psychiatric problems, depression, or inadequate support systems. Whenever patients develop medical or health conditions that weaken their ability to cope with medication regimens, a fresh review of the risks and benefits of their medications may be required. Because hospitalizations and emergency department visits frequently lead to changes in medications and development or worsening of medical conditions, newly discharged patients should receive special attention.

Issues that have been identified in the literature as increasing the complexity of prescribed regimens include medications with conflicting administration patterns, frequent changes in administration schedules, the inclusion of as-needed drugs and those for which dose and frequency are based on patient monitoring, and medication handling that produces disruptions in patients' lifestyles.[23,24] An important contributor to the complexity of medication regimens is the number of providers with whom patients interact. In this study, ADEs and pADEs were identified in patients who had received conflicting information about their medications from pharmacists, nurses, multiple physicians, hospitalists, laboratory technicians, emergency medical technicians, and emergency department staff. Whenever a patient is known to have had a recent hospital stay or emergency department visit or is seeing multiple providers,

Table 3. Characteristics of Patients with Events Compared with Those of a Random Sample of Patients Served by the Same Medical Group

Characteristic	Patients with Events (n = 113)	Comparison Group (n = 1,299)	*P*-value
	n (%)		
Age			
65–69	16 (14.2)	281 (21.6)	.07
70–74	27 (23.9)	378 (29.1)	
75–79	30 (26.5)	289 (22.2)	
≥80	40 (35.4)	251 (19.3)	
Female	68 (60.2)	747 (57.5)	.58
Charlson Comorbidity Index score			
0	15 (13.3)	675 (52.0)	<.001
1–2	52 (46.0)	485 (37.3)	
3–4	31 (27.4)	109 (8.4)	
≥5	15 (13.3)	30 (2.3)	
Number of regularly scheduled medications			
0–2	10 (8.8)	411 (31.6)	<.001
3–4	25 (22.1)	393 (30.3)	
5–6	38 (33.6)	291 (22.4)	
≥7	40 (35.4)	204 (15.7)	

it is important to review with them their current understanding of their medication regimen.

In this study, the number of regularly scheduled medications and the Charlson Comorbidity Index, a weighted summary score of serious medical conditions, were both associated with higher risk of patient errors. As health information technology becomes a component of ambulatory health systems, it could be used to identify and track the experience of patients whose medication regimens and medical conditions indicate that they are at particularly high risk.

Prior studies that focused on patient medication errors[21,25] and patient misunderstandings of medication directions[20,26] have identified problems such as multiple prescribers, retention of discontinued medications, lack of a medication routine, lack of knowledge about medications, and passivity during interactions with prescribers. However, no previous study focused on errors in medication handling by patients that were responsible for adverse effects could be identified. By far the largest component of the existing body of research on attempts at assisting patients with handling medication regimens does not adequately address the errors identified in this study. The major focus of this work has been on compliance or adherence, with most studies on patient education and enhanced instructions, sometimes accompanied by a wide variety of behavioral interventions.[23,27–33] Given the components of medication handling in which most errors were identified, it is unlikely that education alone will substantially reduce dangerous errors in elderly patients. Education has rarely been found adequate to prevent errors in clinicians,[34] and technological supports are being promoted.[11,12,16,17]

Only a few technological assists have been developed for medication handling by patients, including Web-based monitoring, telemonitoring, blister packs, personal digital assistant–based reminders, and electronic monitoring via "trackcaps." The primary low-tech solution currently available is pillboxes, although this study identified five ADEs associated with their use, usually involving incorrect filling followed by a week of consuming the wrong medications. A further technical problem for patients is the similarity of appearance of drugs and of differing strengths of the same drug; this problem was a component of many of the errors in administering medications. There is enormous opportunity for the development of new technological solutions for patients, including special packaging, automatic dispensing of accompanying drugs, and dispensing of drugs cut to appropriate dose when required. With the increase in size of the population taking prescribed medications coupled with the increase in valuable drugs requiring long-term use, the field is ripe for the creative development of new technological systems for patient use.

This study describes the elements of the patient medication-handling system that are most closely associated with important errors leading to adverse effects. There are several limitations to the study. The method used to identify and classify ADEs and pADEs was based on evaluations of a range of data or warnings from the clinical system; all accompanying information was drawn from medical records. This approach limited identification of events to those that came to the attention of the healthcare system. Possible drug-related incidents for which the necessary information was not documented in the medical records were not considered in this study. Inclusion of ADEs depended on the interpretations of the available information by clinical pharmacists and initial physician reviewers. Patients and their families were not interviewed. This limited the ability to determine all of the underlying reasons for errors. Future studies should expand the sources of information to more fully characterize errors. Strengths of this study include its setting in a large, defined group of ambulatory older people with a comparison group drawn from the same population.

CONCLUSION

Although much attention has been focused on medication errors in the clinical setting, the goal of this study was to highlight an overlooked set of errors leading to adverse events. The results demonstrate the large range of problems patients encounter in managing their medication regimens. Further development of technological solutions may enhance the ability of patients to customize and safely manage their use of medications.

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