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Medication Misadventures in the Elderly: A Year in Review

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Abstract

Objective—This paper reviews recent articles examining medication misadventures that can be defined as medication errors and adverse drug events in the elderly.

Methods—MEDLINE and International Pharmaceutical Abstracts were searched for articles published in English in 2009 using a combination of the terms *medication errors*, *medication adherence*, *suboptimal prescribing*, *monitoring*, *adverse drug events*, *adverse drug withdrawal events*, *therapeutic failure*, and *aged*. A manual search of the reference lists of the identified articles and the authors' article files, book chapters, and recent reviews was conducted to identify additional publications. Those studies that described unique approaches to evaluating medication misadventures in the elderly were included in the review.

Results—The search identified 5 unique studies relating to medication misadventures in the elderly. A cross-sectional study found that a new 8-item paper-and-pencil adherence survey—the Morisky Medication Adherence Scale—was significantly associated with antihypertensive drug pharmacy refill adherence ($P < 0.05$). A cross-sectional study of medication discrepancies that occurred during transition from the hospital to a nursing home found discrepancies in almost 75% of patients. A randomized controlled trial of a computer-generated decision support intervention to reduce potentially inappropriate prescribing in an emergency department found that the intervention was associated with a significant reduction in prescriptions for such medications ($P = 0.02$). One study found that patients who were taking digoxin and had been hospitalized during the previous 2 months were at significantly increased risk for additional hospitalizations due to digoxin toxicity. A survey study of Medicare beneficiaries found that use of multiple types of inappropriate medications was a risk factor for self-reported adverse drug events, independent of the number of medications taken.

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Conclusion—Data from these recently published studies could be used to guide the development and evaluation of quality improvement, research, or clinical practice initiatives.

Keywords

medication errors; medication adherence; monitoring; adverse drug events; aged; computerized physician order entry

INTRODUCTION

Medication misadventures, which include medication errors and medication-related adverse patient events (MRAPes), remain a leading public health issue among the elderly.¹ Common medication errors include problems with prescribing, order communication, dispensing, administering, and monitoring. MRAPes include adverse drug reactions, therapeutic failures, and adverse drug withdrawal events.² Elderly patients have several factors (eg, advanced age, frailty, increased drug utilization) that place them at greater risk for adverse outcomes from medication use across multiple care settings.³ Despite efforts to improve medication errors in older adults, this issue remains a leading cause of morbidity and mortality among the elderly. Therefore, an updated review of the literature on medication misadventures in the elderly continues to be a timely and relevant exercise.

METHODS

MEDLINE and International Pharmaceutical Abstracts were searched for English-language articles on medication misadventures in the elderly published in 2009, using a combination of the terms *medication errors*, *medication adherence*, *suboptimal prescribing*, *monitoring*, *adverse drug events*, *adverse drug withdrawal events*, *therapeutic failure*, and *aged*. A manual search of the reference lists of the identified articles and the authors' article files, book chapters, and recent reviews was conducted to identify additional publications. Those studies that, in the authors' opinion, described unique approaches to evaluating medication misadventures in the elderly were included in the review. Articles were categorized using a previously described classification of medication errors and MRAPes.² Additional articles of interest published during 2009 that are related to medication errors and MRAPes are listed in the appendix.

RESULTS

The literature search identified several recent studies evaluating medication misadventures. However, the authors deemed 5 of these articles^{4–8} to be particularly note-worthy in their advancement of the current literature and their topics of study. These studies address adherence,⁴ monitoring,⁵ prescribing,⁶ and adverse drug reactions.^{7,8}

Medication Errors

Adherence—Krousel-Wood et al⁴ reported on the concordance between a relatively new self-reported measure of medication adherence and pharmacy fill data in a small sample of older adults with hypertension enrolled in a Medicare managed care plan. The authors randomly selected 100 white and 100 black patients from administrative data, 177 of whom were found to be eligible; 116 patients returned the surveys for a response rate of 66%. An additional 29 patients were excluded for various reasons, leaving a final sample of 87 patients.

Respondents filled out the 8-item Morisky Medication Adherence Scale (MMAS),⁹ an expanded version of the original 4-item scale.¹⁰ The 8 items, all given a weight of 1, were: (1) Do you sometimes forget to take your high blood pressure pills? (2) Over the past 2 weeks, were there any days when you did not take your high blood pressure medicine? (3) Have you

ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it? (4) When you travel or leave home, do you sometimes forget to bring along your medications? (5) Did you take your high blood pressure medication yesterday? (6) When you feel like your blood pressure is under control, do you sometimes stop taking your medicine? (7) Taking medication every day is a real inconvenience for some people; do you ever feel hassled about sticking to your blood pressure treatment plan? and (8) How often do you have difficulty remembering to take all your blood pressure medication?

Respondents were then categorized into 3 groups: high adherers (perfect score of 8), medium adherers (score of 6 or 7), and low adherers (score <6). The authors collected pharmacy fill data for these patients over the previous year (calendar year 2002) and calculated 3 measures of adherence: the continuous single-interval medication availability (CSA), the medication possession ratio (MPR), and the continuous medication gap (CMG). These measures were averaged across all the antihypertensive drugs a patient was taking over the year to produce 1 score for each of the measures for each patient. *Nonadherence* was defined as a value <0.8 for CSA and MPR or >0.2 for CMG. Finally, the concordance between self-reported and pharmacy fill data was analyzed by measuring the CSA, MPR, and CMG in patients who were low, medium, and high adherers based on the MMAS scale.

Overall, the sample had high self-reported adherence, with 58% of patients having an MMAS score of 8. Only 8 patients (9%) were in the low adherence group, and patients in this group were significantly more likely to be black ($P = 0.04$) and female ($P = 0.03$). There was an association between MMAS category and adherence based on each of the 3 automated adherence measures. After adjusting for age, sex, and race, patients in the low-adherence MMAS group were 6.89 times (95% CI, 2.48–19.10) more likely and patients in the medium-adherence group were 2.58 times (95% CI, 1.08–6.17; $P = 0.001$) more likely than patients in the high-adherence MMAS group to have nonpersistent pharmacy fill adherence by CSA measure. Of the 8 patients in the low MMAS category, 87.5% were nonadherent by CSA, 75% by MPR, and 100% by CMG. Of the 50 patients in the high-adherence MMAS group, 92%, 87%, and 76% were adherent using CSA, MPR, and CMG, respectively.

This study is important for advancing previous work on the internal reliability and predictive validity of the MMAS relating to blood pressure control.⁹ This is the first study to demonstrate concordance between the MMAS and pharmacy fill data for antihypertensive medications. Furthermore, the study used a standardized data collection instrument and included a racially diverse sample (48% black).

There are, of course, limitations to this study. The small sample size and unusually adherent population are the 2 most obvious limitations. This study also averaged adherence across different drugs, which may not capture prescribing nuances that could occur across multiple antihypertensive classes. Finally, the study sample was older community-dwelling adults with managed care insurance; therefore, the instrument should be studied in other populations in the future to increase its generalizability.

Monitoring—Tjia et al⁵ conducted a cross-sectional study to describe the prevalence and sources of medication discrepancies on admission to a skilled nursing facility (SNF) from either a hospital or another SNF. The rationale for conducting this study was that little is known about the prevalence of medication discrepancies on admission to SNFs, despite this being a well-established source of patient harm.^{11–13} The study was conducted from March 1 through June 30, 2007 at 2 community-based SNFs in central Massachusetts. The main outcome measure was the number of medication discrepancies among documented medication regimens, including the hospital discharge summary, patient care referral form, and SNF admission orders. Medication discrepancies have been previously defined as unexplained differences

among documented regimens.¹¹ Tjia et al operationally defined medication discrepancies as any differences in the prescribed dose, route, or frequency noted among the sources of documentation. If elements were present but different in 2 sources, this was also considered a discrepancy.

The abstractors reviewed 100 sequential admissions at each of the 2 SNFs. The total number of medications prescribed on admission ranged from 2 to 24, with a mean (SD) of 11.7 (4.5). Approximately 87% (n = 173) of the patients were managed by hospitalists in the hospital setting. Of 2319 medications reviewed on admission, 495 (21.3%) had a medication discrepancy; ≥ 1 medication discrepancy was identified in 142 (71.4%) of 199 SNF admissions. The discharge summary and the patient care referral form did not match in 104 (52.3%) of 199 SNF admissions and accounted for 307 (62.0%) of all medication discrepancies. Both the dose and route of administration were frequently omitted or discrepant (210 [42.4%] and 208 [42.0%], respectively). In most cases, the medication was continued after medication reconciliation (333 [67.3%]). Cardiovascular agents, opioid analgesics, neuropsychiatric agents, hypoglycemics, antibiotics, and anticoagulants accounted for >50% of all discrepant medications.

Results of this study have significant clinical implications in that they improve our understanding of medication discrepancies during a high-risk transition period. The study highlights the importance of improving communication between providers during transitions of care from the hospital to the SNF. It also provides us with a list of medication classes that should draw immediate attention in an effort to improve medication discrepancies during transitional care.

This study has some potential limitations that are worth noting. First, the study omitted discrepancies based solely on differences between the home medication list and prior medication administration record because they may have been intentional omissions based on the patient's hospital course. However, medication discrepancies that may have arisen either on admission or during the course of hospitalization would likely have been useful if they had been included in the study. Second, the study did not evaluate which source of information (ie, the hospital discharge summary, patient care referral form, or SNF admission orders) was the most accurate or clinically useful in providing medication information in the SNF after hospitalization. Third, the authors did not directly measure harm attributable to medication discrepancies as others have done.^{14,15} Therefore, it is unclear to what degree these medication discrepancies are associated with medication-related problems, which may include any of the MRAPs such as adverse drug reactions, adverse drug withdrawal events, and therapeutic failures.²

Prescribing—Terrell et al⁶ reported the results of a randomized, controlled trial evaluating the effectiveness of computer-decision support (CDS) in reducing potentially inappropriate prescribing for older adults discharged from the emergency department (ED). The primary outcome was the proportion of ED visits by older adults that resulted in ≥ 1 prescription for a targeted inappropriate medication. The authors focused on 9 medications (ie, promethazine, diphenhydramine, diazepam, propoxyphene with acetaminophen, hydroxyzine, amitriptyline, cyclobenzaprine, clonidine, and indomethacin) from the most recent version of the Beers list.¹⁶ These medications were selected because they represented >80% of the inappropriate medications prescribed to seniors at the study's ED in the previous year. Sixty-three emergency physicians were randomized to receive computer-generated alerts that advised against the use of the 9 potentially inappropriate medications while suggesting potentially safer substitute therapies. Physicians in the control group did not receive CDS, but the computer system tracked their prescribing. Prescribing data were collected from the intervention and control groups from January 2005 to July 2007. The study compared the proportion of ED visits by older adults

that resulted in the use of ≥ 1 inappropriate medication between the intervention and control groups.

Adjusting for within-physician correlation resulted in a significant reduction in the proportion of potentially inappropriate prescriptions for the intervention group compared with the control group. Specifically, physicians receiving CDS prescribed ≥ 1 inappropriate medication during 2.6% of visits compared with 3.9% of the visits managed by physicians in the control group (odds ratio [OR] = 0.55; 95% CI, 0.34–0.89; $P = 0.02$). However, the absolute risk reduction of 1.3% was not statistically significant. The authors concluded that the CDS intervention led to a significant reduction in potentially inappropriate prescribing for older adults leaving emergency care. Overall, 43% of 114 CDS recommendations were accepted by physicians. The most common reasons for rejecting these recommendations were that the patient had no problems with the medication in the past (40%), it was a medication refill (17%), no adequate substitute for the medication was available (16%), the physician lowered the dose (13%), and the patient insisted on receiving the medication (6%).

Although the results of previous studies in the out-patient setting^{17,18} provide evidence that CDS is effective in reducing inappropriate prescribing for older adults, this study appears to be the first randomized study to test whether this intervention is appropriate in the ED setting. Another strength of this study is that it included an analysis of the reasons for rejecting CDS prescribing recommendations. This is particularly important because 57% of the system's recommendations were not accepted by physicians. The primary reason reported by prescribers for rejecting a recommendation was that a given patient had tolerated the inappropriate medication in the past. Other studies examining medication CDS with alerting functionality have found that alerts are often perceived as irrelevant and that this can lead to a negative view of the CDS system by clinicians.¹⁹ In addition, the randomized controlled trial design is unique for CDS interventions in the ED setting.

This study has limitations worth noting. First, the study did not examine whether an association existed between the observed reduction in potentially inappropriate prescribing and specific clinical or economic outcomes. This would have been particularly useful because previous studies have shown mixed results between prescribing potentially inappropriate medications and increases in health care costs,¹⁶ hospitalization,^{20,21} falls,²² and mortality,²⁰ as well as a decline in functional status.²³ However, the authors do note that studies examining the effect of the CDS intervention on specific outcomes will be important future research. This was a single-site study with a small sample of academic physicians and residents, thus limiting its generalizability. Finally, the clinical impact of a 1.3% absolute difference in the rate of prescribing potentially inappropriate medications is debatable and, ultimately, would depend on the clinical setting in which this number is viewed.

MRAPES

Adverse Drug Reactions—Haynes et al⁷ reported the results of a prospective cohort study of 2030 older adults who were taking digoxin and enrolled in the Pennsylvania Pharmaceutical Assistance Contract for the Elderly program from May 2002 to June 2003. The aim of this study was to identify characteristics of health care coordination between physicians, pharmacists, and patients that influence the risk of digoxin toxicity in older adults, focusing on the transition from inpatient to outpatient care. They found that patients who had been hospitalized during the previous 2 months were at >4 times increased risk for additional hospitalizations related to the use of digoxin than were patients who had not been hospitalized (adjusted incidence rate ratio = 4.27; 95% CI, 1.97–9.26) after controlling for baseline characteristics, measures of comorbidity, complexity of health care, and patient self-reports of having received instructions on medication usage. Specifically, expert reviewers identified 34 hospitalizations that were directly related to digoxin toxicity. This resulted in an overall risk

of hospitalization due to digoxin toxicity of 1.12 events per 1000 person-months of exposure (95% CI, 0.78–1.57). Of the 34 hospitalizations due to digoxin toxicity, 8 patients had been hospitalized within the previous 2 months. The authors reported narrative results of the discharge summary reviews of these 8 patients, and many of the hypothesized errors occurred because of communication issues.

This study is important for several reasons. Previous studies have assessed medication-related hospital admissions and have effectively described the frequency of, and risk factors for, such admissions.^{24–26} However, this is the first study to link the high-risk posthospitalization period to a specific type of medication error, thus highlighting a potential area for targeted interventions. In addition, the prospective nature of the study is a major strength. The use of 2 blinded expert reviewers to assess the discharge summaries (with a third reviewer if opposite conclusions were reached) is another strength.

Some limitations to this study are worth mentioning. Pharmacy claims data were used to measure digoxin exposure, but such data might not reflect how the patient was actually taking the medication. Furthermore, this study included mostly community-dwelling, white females who met income eligibility for a statewide pharmaceutical assistance program and may not be generalizable to other populations. Further research is needed to evaluate interventions (eg, using health information technology) to improve the coordination of care from the inpatient to the outpatient setting with a focus on improving communication regarding prescribing and monitoring of medications with a narrow therapeutic index during this critical transition period.

Adverse Drug Events—Chrischilles et al⁸ reported the results of a cohort study of 626 Iowa Medicare beneficiaries. The primary outcome measure was self-reported adverse drug events (ADEs), and they examined their relationship with specific types of suboptimal prescribing. They found that after controlling for age, mobility limitations, and number of drugs, the use of “drugs to avoid” (adjusted OR = 1.62; 95% CI, 1.01–2.61) and the occurrence of “drug–disease interactions” (adjusted OR = 1.67; 95% CI, 1.02–2.75) both independently and significantly increased the risk of the occurrence of ≥ 1 self-reported ADE ($P < 0.05$). Although the point estimates for the prescribing problems of drug–drug interactions and therapeutic duplication were not statistically significant, they suggested an association with an increased risk of ADEs. A dose-response relationship was found when these 4 measures were summated to calculate the number of different domains of inappropriate use; this relationship was the most predictive measure of self-reported ADEs.

This is the first study to examine multiple aspects of inappropriate prescribing and ADEs. The study demonstrated that drug–drug and drug–disease interactions increased the risk of ADEs. These findings are consistent with results of other studies,^{23,27} which found that these types of prescribing problems increased the risk of functional status decline and the number of outpatient physician visits. Other investigators have examined the risk of using potentially inappropriate drugs according to the Beers criteria and found mixed results with ADEs.²⁸

Some study limitations are worth noting. The validity of the self-reported ADEs being truly adverse drug reactions was not established. The 1997 version of the Beers “do not use drugs” and “drug–disease interactions” was used; more recent consensus lists have been published that may be more suitable for future use.^{16,29,30} Finally, this group of mostly white, highly educated, older adults from Iowa, who were selected because of mobility limitations, may not be representative of other populations.

CONCLUSIONS

This review identified several unique approaches to the evaluation and critical assessment of potential medication misadventures in the elderly. Data from these recently published studies could be used to guide the development and evaluation of quality improvement, research, or clinical practice initiatives.

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Appendix. Other “medication misadventures in the elderly” articles of interest*

MEDICATION ERRORS

Adherence

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Administration

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Monitoring

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Prescribing

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