A Pharmacist-based Screening Program of Octogenarians Starting New Medications

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ABSTRACT

OBJECTIVE: To measure the impact of clinical pharmacists in primary care practices who closely monitor patients older than 80 years after initiation of new medications.

METHODS: The study was an uncontrolled pilot trial performed at a group-model health maintenance organization in the Pacific Northwest between August and December 1999. Forty-eight patients who were older than 80 years and were prescribed at least one new medication in their primary care clinic were called at home 3 to 6 days after starting a new medication and asked questions focusing on compliance and potential adverse drug events.

RESULTS: More than 20% of patients (10 of 48) had a clinically important change made as a result of the pharmacist telephone monitoring; 42% of patients (20 of 48) either experienced an undesired medication effect (14 of 48) or an inadequate effect (6 of 48). Pharmacists spent an average 11.3 minutes at an estimated cost of $6.40 per patient.

CONCLUSION: A simple, inexpensive pharmacist-based program to screen for medication problems after initiation of new medicines may improve the care to a population older than 80 years.

KEYWORDS: Adverse drug reactions, Adverse drug events, Elderly, Clinical pharmacist, Pharmacist screening

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A dverse drug events (ADEs) and adverse drug reactions (ADRs) are quite common among older patients. The World Health Organization (WHO) has defined an ADR as “… any noxious, unintended and undesired effect of a drug after doses used in humans for prophylaxis, diagnosis or therapy…” An ADE is a broader term that includes ADRs and has been defined as “an injury resulting from medical intervention related to a drug.” For example, an anaphylactic reaction to penicillin would qualify as both an ADE and an ADR, but an injury resulting from the use of an incorrect dose of penicillin would be an ADE only.

While there is a large range in the medical literature of the incidence of ADEs and ADRs due to the variety of definitions used as well as differences in populations studied, the potential for ADEs and ADRs is a significant concern when providing medical care to the aged. A large study in Iowa of relatively healthy patients older than 65 years taking relatively few medications demonstrated a self-reported annual ADR rate of 10%.

In a group of veterans older than 65 years who were not as healthy and taking more medications on average, the annual rate of ADEs was significantly higher at 35%.

The major risk for ADRs (and probably ADEs) seems to be the number of medications used. Age does not appear to be an independent risk factor. However, because age is a risk factor for a variety of chronic diseases (though this may be confounded by a survival effect), polypharmacy, and altered pharmacokinetics, frail older patients may be at increased risk for ADEs. According to data from the General Accounting Office, as many as 1 in 6 hospitalizations in older adults are due to ADRs.

For any prescribing provider, there is tension between the increasing number of effective medical therapies for a number of chronic diseases and the known association between polypharmacy and ADEs. Health care providers who care for seniors are encouraged to actively screen for ADRs, inquire about noncompliance, and review whether prescribed medications are having their intended effect in an effort to minimize the risk of ADEs. Unfortunately, the effectiveness of such monitoring has not been well documented. Waiting for patients to actively complain of ADEs may be inadequate because elderly patients suffering from one or more chronic disease may become accustomed to suboptimal health and less likely to complain if they suspect a drug-related effect.

In settings where patients are at risk for an ADE due to polypharmacy or frailty, clinical pharmacists working closely with prescribing physicians may have a role in monitoring patients.

In a variety of clinical settings, telephone contact has been
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...demonstrated to be a very effective tool in the management of several chronic diseases, including congestive heart failure, depression, and coronary artery disease, and among older men. Von Korff et al. recommend that telephone contact can be a key element in efforts to improve the management of chronic illness. Pharmacist-based telephone care also has been demonstrated to be effective in improving care. A study performed at the Palo Alto Veterans Administration Hospital demonstrated that having clinical pharmacists available to address medication concerns and refill requests resulted in a reduction in walk-in urgent-care visits when the pharmacist is able to satisfy patient needs through telephone assessment and appropriate prescribing as defined by protocol. Cost savings were demonstrated in this study due to fewer urgent-care visits. Six percent of the calls the clinical pharmacist received related to medication concerns (not a refill request), and two thirds of these medication concerns only required education.

In this pilot study, the impact of proactive monitoring of high-risk seniors started on new medications was examined. Rather than waiting for patients to call with complaints, the clinical pharmacists called patients thought to be at risk for ADEs. The authors focused on patients older than 80 years because of a presumed level of frailty and medical complexity that might put them at high risk for polypharmacy and adverse events. Each patient received a phone call from a pharmacist working closely with his or her primary care physician in clinic. Based on the assumption that most adverse events occur soon after initiating a new medication, the phone calls were placed within 3 to 6 days of a new prescription.

Methods

Setting

The study was performed at 3 Group Health Cooperative (GHC) primary care clinics in Seattle, Washington. GHC is a group-model HMO serving approximately 500,000 enrollees. Six pharmacists who were employed by GHC in primary-care clinics participated. At the time of the study, their practices included a total of 12 physicians and 4 physician assistants with a patient base of 21,650. The Human Subjects Committee of GHC approved the study.

Patient Selection and Enrollment

Any patient older than 80 years who received a new prescription during the enrollment period was eligible. Clinical pharmacists enrolled patients at the time their new medication was dispensed between August 22, 1999, and December 1, 1999. Informed consent was obtained by the pharmacists at the time of enrollment. Pharmacists also asked patients for their phone number and the best time to reach them during the following 3 to 6 days.

Questionnaire

The clinical pharmacists used a script to conduct their phone interviews. The authors developed the script to elicit answers that would help determine whether potential adverse events were related to the medication that was recently started. They attempted to avoid using sophisticated medical jargon and reviewed the script with the participating pharmacists. The script asked several questions regarding the recently prescribed medication:

1. Have you been able to take the new medication?
2. Have you missed any doses?
3. Have you noticed any problems since you started taking it?
4. Did the problems start before or after you began taking the medication?
5. Do you think the problem is related to the medication?
6. Did you stop taking the medication because of the problems you were having?
7. If you stopped taking the medication, have the problems gone away?

Pharmacists recorded data on forms that corresponded to the script. They responded to questions, provided counseling on the effects of medications, and referred appropriate concerns to the prescribing physician. Pharmacists also recorded the number of attempts made to contact each patient and the amount of time spent, including the consent process. Phone calls were not taped or monitored.

Evaluation of Reported Adverse Drug Events

Adverse events were reviewed by a geriatrician (Seevak) and pharmacist (Kent) and determined to be probable if the reaction was well known, if there was a temporal relationship between starting the new medication and the perceived effect, and whether symptoms resolved when the suspected medication was stopped. This assessment was based on criteria adopted by the WHO for assessing causality. The 2 reviewers were in agreement on all suspected ADEs. With the exception of 2 patients, the authors did not have adequate follow-up to determine if symptoms resolved when medications were stopped. The authors were not involved in any rechallenges of suspected medications.

Results

Enrollment and Patient Characteristics

Fifty-four patients were asked to enroll in the study, and 48 patients agreed to participate. Several of the pharmacists commented that because of competing demands, they were...
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unable to enroll many patients who may have met entry criteria during the enrollment period. The mean age of participants was 85 years, and they were taking an average of 6 medications at the time of enrollment (Table 1). Women slightly outnumbered men. During the predetermined follow-up period of 3 to 6 days, 46 of 48 patients were contacted.

There were at least 15 patients who were not offered enrollment because they had dementia or hearing loss, had a caregiver who dispensed their medications, or were non–English-speaking. However, several patients with hearing loss, dementia, or a caregiver were offered enrollment.

Compliance With Physician Recommendations
Four percent of patients (2 of 46) who were contacted reported to the pharmacist that they had not started the recently prescribed medication. One of these patients had been prescribed 2 new medications and wanted to start one at a time so that she would be aware of any side effects. The second patient did not want to take the antidepressant she was prescribed because of a previous bad experience with antidepressants. She was not planning to tell her physician that she was not taking the antidepressant.

Undesired and Inadequate Effects
Forty-two percent of patients (20 of 48) either experienced an undesired effect attributed to the medication (14 of 48) or an inadequate effect (6 of 48).

Table 2 describes the actions that were taken after the pharmacist call. Three patients had their dose changed as a result of the pharmacist call. Three patients had a medication changed to another medication within the same class. One patient had her medication stopped by the pharmacist. As a result of the phone calls, 3 patients were scheduled to be evaluated by a physician within a day or two, including a patient seen in urgent care for urinary retention after starting naproxen.

The conversation between the patient and pharmacist revealed significant information for several patients. Actions taken as a result of the calls is described in Table 2. One patient taking nasal steroids developed epistaxis that resolved spontaneously. Six patients were encouraged by the clinical pharmacist to continue taking their recently prescribed medication despite a report of no benefit. One patient was reassured that the lightheadedness he was experiencing with an ACE inhibitor would resolve.

Pharmacist Effort and Cost
Pharmacists contacted 96% of patients (46 of 48) enrolled in the study after an average of 1.46 calls (Table 3). The pharmacists contacted the majority of patients on the first attempt. The pharmacists reported spending an average of 11.3 minutes per patient contacted, including time spent obtaining patient consent. Assuming a salary of $35 per hour, the estimated cost of this intervention was $6.40 per patient.

Discussion
This pilot study of telephone monitoring by pharmacists indicates that adverse effects commonly may appear in patients older than 80 years very soon after starting a new medication, and as a result of active pharmacist involvement, important clinical changes can be made in the medical regimen of a significant portion of these patients. These include changes due to ineffective medications, unwanted effects, and incorrect usage.
As a result of the simple intervention described in this pilot study, 21% of patients (10 of 48) had a significant change, and 30% of patients (14 of 48) described a problem with a new medication that met criteria for a probable ADR.

Because this is a small, uncontrolled pilot study with variable adherence to protocol, the results must be interpreted with some caution. In a relevant study by Hanlon et al., a group of veterans in North Carolina older than 65 years, each taking more than 5 medications a day, reported a one-year ADE incidence of 35%. Hanlon et al. defined ADEs as "noxious and unintended patient events...caused by a drug," and the ADEs were self-reported in a close-out interview. The participants in Hanlon’s study had a mean age of 69 and were taking 8 chronic medications compared with a mean age of 85 and 6 chronic medications in the pilot study described here. With a comparable degree of polypharmacy and significantly increased age, it should not be a surprise that participants in this pharmacist intervention experienced a high rate of adverse events. Unfortunately, Hanlon et al. did not report the timing of the ADEs in relation to when the offending medications were started. It would be interesting to learn if the majority of ADEs experienced in Hanlon’s study occurred soon after initiation of a new medication. If so, that would reinforce the value of an early clinical pharmacist intervention.

Patients, in general, were very happy to receive a call from a pharmacist to see how they were doing with their new medication. Anecdotal reports from the clinical pharmacists regarding patient responses were very positive. Numerous patients expressed their pleasure when they received a call from their pharmacist. Several physicians initially expressed concern that this intervention might create more work for them by uncovering insignificant or factitious drug effects that would be brought to their attention. Physicians did not voice these concerns to their pharmacist colleagues during the study period, and it appears that the pharmacist interventions did not create more work for physicians. Whether or not this is true could be evaluated in greater detail in further studies with longer follow-up.

Whether the results of this study overestimate the problem of ADEs by soliciting feedback from the participants, as several of the participating physicians were concerned it might, is a reasonable concern. As with all studies reporting the incidence of ADEs and ADRs, it is important to view the data in the context of the study. Clearly, if the participants in this study were asked to call with problems instead of receiving an inquiring call from a pharmacist, the results would be less impressive and fewer actions would have been taken that altered patient care. The authors felt that the most significant result of this study was the number of actions (see Table 2) taken by the pharmacists as a result of the intervention, not the number of probable ADEs discovered.

A more rigorous approach to evaluating the criteria for causality in ADEs would require assessment of the benefit of a dechallenge (withdrawal of the drug) and the consequences of a rechallenge, if performed.

Malone has described several threats to the reliability of studies of clinical interventions, including self-selection bias. In our study, 89% of the patients who met the inclusion criteria agreed to participate in the study. However, there may have been some selection bias on the part of the pharmacists in enrolling patients. For example, several patients with dementia were not included in this study. While demented patients actually may be at increased risk of experiencing an ADE, they might require more pharmacist effort and time to enroll and then interview over the phone. A follow-up study should take this into account and establish strict entry criteria. A long follow-up period would be required to assess the benefit of this intervention. Measurable benefits might include decreased utilization, with fewer ER visits, hospitalizations, and clinic calls over the subsequent 12 months, attributable to better compliance, early detection of adverse reactions, and early detection of inadequate therapeutic effect. A larger study also might confirm the potential for cost savings that were demonstrated in a telephone-care pharmacy program at the Palo Alto Veterans Administration Hospital. Of course, in addition to addressing biases and having a long follow-up period, a control group, as part of a randomized, controlled trial, would be needed to establish the value of this intervention in any follow-up studies.

The results of this study are promising enough to merit a larger, more rigorous study. Currently, the approach described in this pilot has been incorporated into a significantly larger, randomized, controlled study of an intervention employing team care for geriatric patients. Team care is a multidisciplinary, collaborative approach to providing health care that is patient-focused and includes physicians and pharmacists trained in geriatrics. As in the pilot study, participants in this study will receive a phone call from a pharmacist screening for medication-related problems soon after receiving a new prescription from their health care provider. The primary goals of this larger

<table>
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<tr>
<th>TABLE 3</th>
<th>Pharmacist Effort</th>
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<tbody>
<tr>
<td>Number of patients reached</td>
<td>46 (96%)</td>
</tr>
<tr>
<td>Average number of attempts</td>
<td>1.46 (±0.7)</td>
</tr>
<tr>
<td>Number reached on first attempt</td>
<td>30 (65%)</td>
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<tr>
<td>Average time spent per patient following enrollment</td>
<td>11.3 minutes (±5.1)</td>
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study are improvements in resource utilization and functional outcome and improving physicians’ comfort and competence in caring for elderly patients. Similar to the study described in this paper, the investigators in the larger intervention have chosen to focus on a population (patients older than 75 years) rather than a disease.

A follow-up study also may include the use of identifiers in the information system that would warn physicians and clinical pharmacists when high-risk drugs are prescribed for the first time, encouraging discussion among patients, pharmacists, and physicians. A recent study by Bieszk et al. used published guidelines for chronic disease management, including hypertension, diabetes, and congestive heart failure as a basis to develop a medication regimen review process to improve quality of care and reduce polypharmacy.18

Guidelines for prescribing in the elderly, such as the list of inappropriate medications that was developed by Beers with a panel of experts,19 could have a role similar to chronic disease management guidelines. Instead of focusing on a disease, this set of guidelines, like the pilot study described in this paper, focuses on medication use among a population. Pharmacists could refer to this list of inappropriate medications when reviewing prescriptions. If physician order entry is used, clinical decision support could identify and flag medications from this list, when they are ordered, that are considered inappropriate for seniors.20 There were several medications (Table 4), including lorazepam, propoxyphene, and doxepin, that were prescribed during the enrollment for this study that would have triggered such an alert.

Conclusion

This pilot study has demonstrated the potential benefit of using clinical pharmacists to actively monitor, via telephone, adverse events in elderly patients starting new medications. More than 40% of the patients (20 of 48) in our study had an undesired effect or lack of effect that they revealed to the inquiring clinical pharmacist. The inquiry resulted in a medication change or physician visit for at least 21% of the patients (10 of 48) called. Currently, the value of this inexpensive intervention is being tested more thoroughly on a larger scale.

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Disclosures

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Table 4

| List of Medications That Triggered Enrollment |
| (When a patient received more than one new prescription at the time of enrollment, both new medications are listed.) |

| 1. Lisinopril | 25. Pantoprazole |
| 2. Lisinopril | 26. Pantoprazole |
| 3. Lisinopril and sertraline | 27. Ranitidine |
| 4. Lisinopril and levothyroxine | 28. Cimetidine and triamcinolone nasal |
| 5. Captopril | 29. Triamcinolone nasal |
| 6. Losartan | 30. Triamcinolone nasal spray and triamcinolone inhaler |
| 7. Hydrochlorothiazide/triamterene | 31. Triamcinolone nasal spray and triamcinolone cream |
| 8. Furosemide | 32. Triamcinolone nasal spray |
| 9. Losartan | 33. Triamcinolone inhaler |
| 10. Furosemide | 34. Hydrocortisone cream |
| 11. Furosemide/amiodarone | 35. Lorazepam |
| 12. Atenolol | 36. Morphone SR |
| 13. Furosemide | 37. Propantheline |
| 14. Furosemide | 38. Rofecoxib |
| 15. Atenolol | 39. Naproxen |
| 16. Atenolol and furosemide | 40. Choline magnesium trisalicylate and dienesterol |
| 17. Losartan and furosemide | 41. Sulindac and tylexol with codeine |
| 18. Lisinopril and furosemide | 42. Dosepin and sulindac |
| 19. Lisinopril and levothyroxine | 43. Venlafaxine |
| 20. Lisinopril | 44. Donepezil |
| 21. Lisinopril and levothyroxine | 45. Carbidopa/levodopa |
| 22. Atenolol | 46. Promethazine |
| 23. Atenolol | 47. Mesalamine |
REFERENCES