The Impact of Prescribing Safety Alerts for Elderly Persons in an Electronic Medical Record

An Interrupted Time Series Evaluation

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Background: Considerable effort and attention have focused on medication safety in elderly persons; one approach that has been understudied in the outpatient environment is the use of computerized provider order entry with clinical decision support. The objective of this study was to examine the effects of computerized provider order entry with clinical decision support in reducing the use of potentially contraindicated agents in elderly persons.

Methods: With data from a 39-month period of a natural experiment, we evaluated changes in medication dispensing using interrupted time series analysis to estimate changes, controlling for prealert prescribing trends. The setting was a large health maintenance organization in the Pacific Northwest. All adult enrollees of the health plan participated. The intervention was computerized alerts cautioning against using certain medications in elderly persons. The main outcome measure was dispensing per 10,000 members per month.

Results: Following the implementation of the drug-specific alerts, a large and persistent reduction (5.1 prescriptions per 10,000, P=.004), a 22% relative decrease from the month before alert implementation, in the exposure of elderly patients to nonpreferred medications was observed. We found no evidence of a decrease in use of nonpreferred agents for nonelderly patients. The reduction seen in use of nonpreferred agents for elderly persons was driven primarily by decreases in dispensing for tertiary tricyclic agents.

Conclusions: We found that alerts in an outpatient electronic medical record aimed at decreasing prescribing of medication use in elderly persons may be an effective method of reducing prescribing of contraindicated medications. The effect of the alerts on patient outcomes is less certain and deserves further investigation.

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to reduce the use of 2 classes of medications generally contraindicated in elderly persons. We took advantage of a natural experiment and 39 months of data at a large health maintenance organization (HMO), using a strong quasi-experimental design and interrupted time series analysis, to examine the effects of CPOE with clinical decision support in reducing the use of potentially contraindicated agents in elderly persons. To our knowledge, this is the first study examining the effects of medication safety alerts (CPOE with clinical decision support) in a population-based primary care setting.

METHODS

STUDY DESIGN

By using data from a 39-month period, we evaluated changes in the use of medications generally contraindicated in elderly persons, associated with the implementation of a CPOE alert cautioning against using these 2 classes of medications in elderly persons. We used interrupted time series analysis to estimate changes in the use of these medications, controlling for prealert trends.

SETTING AND INTERVENTION

The setting for the study was a group-model HMO in the Pacific Northwest caring for about 450 000 people, with demographic characteristics closely mirroring those of the surrounding metropolitan area. The Research Subjects Protection Office approved the study. The HMO uses an EMR (EpicCare; Epic Systems Corporation, Verona, Wis) for all outpatient encounters, including the ordering of all medications. From September to October 2000, decision support was implemented, which alerted clinicians to preferred alternative medications when they ordered certain nonpreferred agents that carry potential contraindication in elderly persons.19 These nonpreferred agents were certain long-acting benzodiazepines (diazepam, flurazepam, triazolam, and chlordiazepoxide) and tertiary amine tricyclic antidepressants (TCAs) (imipramine, amitriptyline, and doxepin); the shorter-acting and less-sedating alternative benzodiazepines (oxazepam and temazepam), secondary amine TCAs (nortriptyline and desipramine), or other medications (buspirone, trazodone, and paroxetine) were suggested as alternatives. Paroxetine was subject to changes in formulary status during the period of study, leading to large fluctuations in use that were unrelated to the alerts, so we did not include it in any of our analyses.

The alerts (Figure 1) made it possible to change the order by accepting the alternative medication suggested. These alerts were drug specific, meaning that they were presented to the clinician after ordering one of the nonpreferred medications, regardless of patient characteristics, such as age or comorbidities. As Figure 1 illustrates, the alert was constructed so that the warning regarding falls and fractures was prominent. If desired, the user could scroll down the message pane to see the rest of the text, which contained further information on specific preferred alternative agents.

STUDY SAMPLE

We collected electronic data on monthly outpatient medication dispensings from prescriptions written by primary care providers between October 1, 1999, and December 31, 2002; this period included 12 months before the alerts were imple-mented and 27 months after implementation. We included data from all 15 primary care clinics. Providers were family practitioners and internal medicine clinicians, including physicians (n=152), nurse practitioners (n=25), and physician assistants (n=32) (the numbers are for the 12 months preceding the intervention). All members of the HMO during the observation period were included in the study.

DATA SOURCES AND MEASURES

We were interested in examining the effect of the alerts on initial medication prescribing, because it is during prescribing that alerts are presented to the clinician. Our data source was the prescription-dispensing database. The dispensing database includes prescription refills, but refills are not subject to the alert. Prescriptions are given a unique identification number, and this identification number is associated with the entire stream of prescription refills, making it impossible to directly differentiate between initial dispensings and refills. To minimize inclusion of refills, we included dispensings only when (1) the patient had not been exposed to the medication in the previous 6 months and (2) the prescription was the first in a stream of refills for a given prescription identification number.

The alerts in this analysis were presented when any nonpreferred drug was prescribed, regardless of age or clinical characteristics of the patient. It was left to the prescriber to determine the clinical appropriateness of the advisory. Because of this, we were interested in whether there was any spillover effect in nonelderly persons, so we examined results for patients in the elderly (aged ≥65 years) and nonelderly (aged <65 years) groups.

STATISTICAL ANALYSIS

Outcomes of interest (number of dispensings of nonpreferred and preferred drugs per 10 000 population) were aggregated into 39 monthly intervals. We used interrupted time series regression models (segmented regression) to estimate changes in outcomes that occurred after the alert implementation, controlling for preintervention trends and other autocorrelation (including seasonal effects).20-23 The models included a constant, a baseline slope term to control for secular trends (eg, first-, second-, and higher-order autocorrelation), and terms estimating changes in the level and slope of outcome rates. Analyses were conducted using SAS statistical software (Proc Autoreg; SAS Institute Inc, Cary, NC).

RESULTS

At baseline, patients with a dispensing for the nonpreferred agents were older (nonelderly patients, 44.9 vs 31.4 years; and elderly patients, 75.1 vs 74.7 years) and more likely to be female (nonelderly patients, 72.1% vs 51.7%; and elderly patients, 69.4% vs 56.2%) compared with the general HMO population. Data on the use of nonpreferred and preferred medications at baseline are given in the Table. Controlling for baseline trends, a sudden reduction in the rate of initial dispensing of nonpreferred agents among elderly persons was observed when the alerts were placed (Figure 2A), from 21.9 to 16.8 per 10 000 (P<.01). This decrease of 5.1 prescriptions per 10 000 represented a relative decrease of 22% from the month before alert implementation and was sustained over the entire 2-year postalert observation period. For non-

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elderly persons, no significant \((P=.48)\) changes were observed in the use of nonpreferred agents.

The dispensing rate of preferred agents did not change significantly \((P=.66)\) for elderly persons, but did continue an upward trend throughout the observation period (Figure 2B). Controlling for preintervention trends, the use of preferred agents increased suddenly by 4.0 dispensings per 10 000, a 20% increase from the month before alert implementation. An upward trend continued over the observation period.

Controlling for baseline trend, the rate of use of nonpreferred TCAs for elderly persons decreased abruptly by 4.5 dispensings per 10 000, a 35% decrease from the month before the alert, with a further continued decline of 0.4 prescription per 10 000 per month \((P<.01)\) observed over the entire 39-month study period. The rate of initial dispensing of the nonpreferred TCAs for elderly persons had been increasing at a rate of 0.3 prescription per 10 000 per month \((P=.02)\) before the alerts were placed—this trend was reversed after alert implementation. The rate of overall dispensing for nonpreferred TCAs did not change significantly \((P=.22)\) before or after alert implementation for nonelderly persons.

The medications with the largest observed changes in dispensing rates were the TCA amitriptyline (nonpreferred) and its metabolite, the preferred TCA, nortriptyline. Nortriptyline was specifically suggested in the alert as the preferred alternative to amitriptyline. The rate of dispensings for the nonpreferred TCA (amitriptyline) was
higher than for the preferred TCA (nortriptyline) for both age groups at every time point before the alert (Figure 3). This trend was suddenly reversed after the alerts. Controlling for baseline trends, there was an abrupt and sustained 34% decrease from 9.8 (1 month before alert implementation) to 6.4 dispensings per 10,000 (P < .01) in the use of the TCA amitriptyline for elderly persons, with a further slight decline (−0.3 prescription per 10,000 per month, P = .004) during the follow-up period of observation. Use of the TCA amitriptyline also decreased for nonelderly persons, but not significantly (P = .22) (Figure 3A). Use of the preferred TCA nortriptyline increased suddenly in both age groups, by 3.5 prescriptions per 10,000 for elderly persons (P < .01) and by 1.9 prescriptions per 10,000 for nonelderly persons (P < .01) (Figure 3B).

Although the monthly rate of initial prescribing for nonpreferred benzodiazepines did not change, the monthly initial prescribing rate of flurazepam per 10,000 did decrease immediately following the alert for elderly persons, by 0.3 dispensing per 10,000 (P < .10), with a continued decrease of 0.04 dispensing per 10,000 per month (P = .02), which persisted to the end of the study period; no changes were observed for nonelderly persons. No significant (P = .36) changes were noted in the rate of use of preferred benzodiazepines or “other” preferred agents (buspirone and trazodone) in either age group—the small sample sizes did not produce stable effects.

Following the implementation of drug-specific alerts in an outpatient setting aimed at decreasing the use of medications that are often contraindicated in elderly persons, we found an abrupt, large, and persistent reduction in the exposure of elderly patients to nonpreferred medications. Among elderly persons, we found that the use of nonpreferred agents decreased immediately by 5.1 prescriptions per 10,000 (P < .01), a 22% relative decrease from the month before alert implementation. This reduction was sustained over the entire 2-year postalert period of observation, and was driven primarily by decreases in dispensings for nonpreferred TCAs. The reduction in the use of nonpreferred TCAs was especially striking given that their rate of dispensing was increasing significantly before the intervention, then continued significantly downward at every time point after the intervention. We found no evidence of a decrease in the use of nonpreferred agents for nonelderly patients.

Among all the medications studied, the TCAs amitriptyline and nortriptyline had the largest changes in dispensing rates. Before the alert, the nonpreferred TCA amitriptyline was prescribed more frequently at every time point than the preferred TCA nortriptyline, but after the alert, this finding was exactly reversed. One reason may be that there is a clear therapeutic interchange—amitriptyline is metabolized to nortriptyline—perhaps making the exchange more amenable for clinician and patient acceptance. In addition, for other nonpreferred medications, specifically the long half-life benzodiazepines, there is conflicting opinion on whether they should be avoided in elderly persons.24

We found that while the use of nonpreferred medications decreased for elderly persons, there was no offsetting increase in the use of preferred medications. This finding suggests that the alerts had the effect of decreasing overall exposure of older patients to these types of drugs, nonpreferred and preferred. While this may have been clinically appropriate for some patients, it is possible that others were denied appropriate medication. Alternatively, clinicians may have switched to other medications that we did not include in our analysis.

This research suggests there may be some unexpected consequences from the alerts, namely, that the rates of use of preferred medications increased for people in younger age groups. One reason for this finding may be the high fraction of prescribing encounters with nonelderly patients for whom the alerts were generated. Also, the alert functioned such that it was easy to choose the recommended alternative medication, and the clinicians’ “reward” for choosing the alternative was a completed prescription automatically prepopulated (with dose, directions for use, and refills) that was ready for electronic signature. Anecdotes from clinicians suggest that they would start a prescription with the nonpreferred medication to access the prepopulated prescription.

This study includes alerts with particular characteristics, potentially limiting generalizability. First, even though the premise of the safety message contained in these alerts was related to patient age, because of the functionality constraints of the specific EMR in use at the time of the study, ordering of specific medications, regardless of patient age, triggered the alerts. At the HMO, about 25% of all prescriptions for the nonpreferred drugs are for people older than 65 years. An alert with more patient specificity (ie, only present for elderly patients) would reduce provider burden; whether such an alert would be differentially effective is unknown.

A remaining unanswered question is the relationship of the intervention to patient outcomes. The alerts may have decreased the use of nonpreferred medications, but that decrease does not necessarily translate into improved outcomes (eg, decreased rate of daytime sedation and fewer falls). In addition, there is some contro-

Table. Use of Nonpreferred and Preferred Medications at Baseline*

<table>
<thead>
<tr>
<th>Medication</th>
<th>Nonelderly Persons</th>
<th>Elderly Persons</th>
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<td>Nonpreferred prescriptions</td>
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<td></td>
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<td>Tricyclic antidepressants</td>
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<td>Benzodiazepines</td>
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<td>Total</td>
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<tr>
<td>Preferred prescriptions</td>
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<td></td>
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<td>Tricyclic antidepressants</td>
<td>5.2</td>
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</tr>
<tr>
<td>Benzodiazepines</td>
<td>5.9</td>
<td>22.5</td>
</tr>
<tr>
<td>Other preferred agents</td>
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</tr>
<tr>
<td>Total</td>
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<td>53.3</td>
</tr>
</tbody>
</table>

*Data are given as number of prescriptions per 10,000 enrollees. Data were calculated at 1 month prealert. The different types of drugs included in each category are described in the “Setting and Intervention” subsection of the “Methods” section.
versy surrounding the clinical appropriateness of recommendations regarding some of the medications targeted by the alerts in this analysis. Specifically, some research has suggested that long half-life benzodiazepines are less likely than short half-life benzodiazepines to be associated with hip fractures. This literature may have had some effect on the effectiveness of the alerts if, for example, clinicians chose to ignore the alerts because of their awareness of the controversy. However, these medications remain on recent lists of medications to avoid in elderly persons. A recent study suggests that elderly nursing home patients who are exposed to potentially inappropriate agents (including those in our study) experience a higher risk of hospitalization and death. That study examined a broader array of agents and a more frail population, but does suggest that decreasing exposure to these agents is beneficial.

The alerts were not entirely successful in eliminating the use of these medications in elderly persons. Some use of these drugs in elderly persons is probably clinically appropriate, however, so we would not expect to see the use of the drugs decline to 0. For example, it might be reasonable for a patient who has successfully used diazepam for relief of anxiety in the past to use it again at a low dosage for the short term, particularly if the patient has not responded well to an alternative preferred agent, such as oxazepam or buspirone.

Compared with studies conducted in the inpatient setting of CPOE with clinical decision support, our results suggest a similar direction of effect for the outpatient environment (ie, toward decreasing contraindicated prescribing). Comparing the results of these studies is difficult because of differing clinical topics, study designs, and outcome measures. However, the reduction of 22% in potentially inappropriate prescribing of nonpreferred agents in those older than 65 years that we observed is consistent with findings from studies of inpatient CPOE with clinical decision support.

One small Canadian study in the outpatient setting that examined the effectiveness of clinical decision support (but without CPOE) found a reduction of 13% (relative rate, 0.77; 95% confidence interval, 0.59-1.00) in inappropriate prescribing of long-acting benzodiazepines and active metabolite TCAs. Our results reinforce that finding in a larger population with a mature EMR.
There are alternative explanations for our findings that should be considered. Specifically, the issue of avoiding certain drugs in elderly persons has gained press in recent years, raising awareness in the clinical community. However, given our strong quasi-experimental methods, and the sudden decrease we observed contemporaneous with the alert initiation, this is an unlikely explanation for the observed changes in medication use. In addition, we are unaware of any ongoing cointervention that could explain these results. We did investigate this possibility thoroughly by directly inquiring with appropriate personnel in pharmacy and other relevant departments at the HMO.

In conclusion, we found that alerts in an outpatient EMR aimed at decreasing prescribing of medication use in elderly persons may be an effective method of reducing prescribing of contraindicated medications. Additional work on the impact of more patient-specific clinical decision support will be useful to determine whether an intervention method with less clinician burden can have similar effects in the outpatient setting. More important, the effect of the alerts on patient outcomes is less certain and deserves further investigation.

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