International Journal of Medical Toxicology & Legal Medicine Volume 27, No. 4, 2024
e-ISSN: 0974-4614
p-ISSN: 0972-0448

Impact of a Comprehensive Clinical Pharmacist Intervention on Medication Safety in Patients on High-Risk Prescription Drugs Following Hospitalization

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Received: 15.10.2024 Revised: 25.11.2024 Accepted: 08.12.2024

ABSTRACT

Background: Adverse drug events (ADEs) significantly impact patients post-hospitalization, particularly older adults prescribed high-risk medications such as anticoagulants, diabetes treatments, and opioids. This study evaluated the impact of a multifaceted clinical pharmacist-led intervention on medication safety after hospital discharge.

Methods: Patients aged 50 and older, recently discharged and prescribed at least one high-risk medication, were randomized into two groups: an intervention group receiving a pharmacist-led program (home visit, education, EHR documentation, and follow-up calls) or a control group receiving mailed educational materials. Outcomes included ADEs and clinically significant medication errors assessed over 45 days.

Results: Among 361 participants, 27.7% experienced at least one ADE, and 18% had a clinically significant medication error. The intervention group showed no significant reduction in ADEs (IRR 0.97, 95% CI 0.70–1.34) or errors (IRR 0.81, 95% CI 0.53–1.23) compared to controls. Emergency visits and rehospitalizations were similar across groups.

Conclusion: The intervention did not significantly reduce ADEs or medication errors. Further refinement and evaluation of post-discharge medication safety interventions are essential to address this high-risk period.

Keywords: anticoagulants, diabetes treatments, opioids

INTRODUCTION

Adverse events affect up to 20% of patients within weeks of hospital discharge, with a significant proportion being potentially avoidable (1,2). Older adults transitioning from inpatient to outpatient care face a heightened risk of adverse drug events (ADEs), which are defined as harm caused by medications (3,4).

The National Action Plan for Adverse Drug Event Prevention has identified three high-risk medication categories that are critical for minimizing medication-related harm: anticoagulants, diabetes treatments (both insulin and oral medications), and opioids (5). These drug classes are responsible for a significant share of measurable medication-related injuries, and many ADEs linked to these medications are deemed preventable (6,7,8,9). Commonly implicated in emergency visits and hospitalizations, insulins, opioid-based pain relievers, and warfarin pose particular risks, especially for older individuals (6,7,8).

This research involved patients recently discharged from the hospital who were prescribed one or more medications from the three high-priority drug classes. Participants were randomly assigned to either a group receiving a comprehensive pharmacist-led intervention for medication safety or a group provided with educational materials on medication safety sent by mail.

Methods

The research was conducted within a multidisciplinary medical group practice providing care to a large patient population. Participants were selected from among patients discharged from a regional medical and surgical hospital affiliated with the group. Eligible patients were those under the care of the group's primary care clinicians. Routine medication reconciliation was standard at discharge, but no systematic postdischarge medication safety programs were in place. For patients on warfarin, outpatient anticoagulation services were available, but reconnecting discharged patients to this service was the responsibility of their primary care clinicians.

Eligibility Criteria

Participants included individuals discharged from the hospital who were patients of the group's primary care physicians and prescribed at least one high-risk medication—anticoagulants, diabetes medications (insulin or oral agents), or opioids. Additional inclusion criteria required meeting at least one of the following:

1. Use of two or more high-risk medications.
2. Limited health literacy.
3. Poor medication adherence (self-reported).
4. Presence of a caregiver or proxy.
5. Use of more than seven medications.

Exclusion criteria included individuals discharged to hospice care, psychiatric hospitalization, or institutional care (e.g., skilled nursing facilities). Non-English speakers and those unable to provide consent without a proxy were also excluded. Initially, eligibility was restricted to individuals aged 65 or older, but the age criterion was later adjusted to include those 50 and older to improve recruitment numbers (10).

Intervention Design

The intervention comprised several elements:

1. **Home Visit:** A clinical pharmacist visited patients within four days postdischarge to conduct a comprehensive assessment, including a medication review, observation of medication storage and administration, and discussions with the patient and caregiver (if applicable).
2. **Educational Materials:** Printed resources with detailed instructions on high-risk medications were provided, including guidance on timing, dietary precautions, missed doses, and when to contact a clinician.
3. **Electronic Communication:** Findings from the home visit were documented in the electronic health record (EHR) to inform the primary care team about relevant safety concerns. Urgent medication-related issues were communicated directly to clinicians.
4. **Follow-Up Call:** Fourteen days post-visit, the pharmacist conducted a telephone call to address any ongoing issues and reinforce prior instructions.

   Control group participants received educational print materials by mail tailored to the high-risk medications they were prescribed.

Recruitment Process

Recruitment occurred over approximately two years. Potential participants were identified through an automated review of hospital discharge medication lists. Calls to potential participants were initiated soon after discharge to ensure timely scheduling of home visits within four days. Participants providing verbal consent were randomized, and written consent was later obtained during the initial visit (intervention group) or by mail (control group). Participants received a $25 gift card for participation.

From an initial pool of 7075 potentially eligible patients, 4539 were deemed eligible after record review. Of these, 3755 were contacted by phone, 3606 were eligible, and 459 provided verbal consent and were randomized (230 intervention, 229 control). Ultimately, 361 participants (180 intervention, 181 control) completed written consent and were enrolled. Recruitment and enrollment details are elaborated elsewhere (11).

Outcome Definitions

Two primary outcomes were assessed:

1. **Adverse Drug-Related Incidents:** This included both preventable and non-preventable adverse drug events (ADEs) and potential ADEs.
2. **Clinically Important Medication Errors:** These encompassed preventable or ameliorable ADEs and potential ADEs. Preventable ADEs referred to medication-related harm due to errors, while ameliorable ADEs were instances where harm could have been mitigated (12, 13).

   Outcomes were not limited to high-risk medications but included all prescribed drugs. Events were categorized based on severity (e.g., less serious, serious, life-threatening, or fatal) and preventability (e.g., preventable, probably preventable, or non-preventable).

Event Identification

Two clinical pharmacists reviewed patient records and conducted telephone interviews five to six weeks postdischarge to identify potential drug-related incidents. They were blinded to the patients' group assignments. A summary of each potential event was prepared for review by two independent, masked physician reviewers who classified events by type, severity, and preventability. Disagreements were resolved through consensus.

Data Analysis

Group differences in baseline characteristics were assessed using statistical tests, including t-tests for continuous variables and χ^2 tests for categorical variables. Incidence rates of adverse events and medication errors were calculated as events per 100 person-days. The intervention's impact was analyzed using Poisson binomial regression, adjusting for factors such as age, sex, and home nursing services. Emergency department visits and rehospitalizations were also compared between groups.

The study's sample size was calculated to detect a 19% reduction in the incidence rate of clinically important medication errors, assuming a baseline rate of 0.95 events per patient over 30 days postdischarge (12). Despite adjustments to eligibility criteria, the recruitment goal of 500 participants was not achieved.

RESULTS

Participants in the study had an average age of 68.7 years (SD 9.3), with an age range of 50 to 94 years. Of these, 49% (177 participants) were women. The study achieved a reasonable balance of demographic and clinical characteristics between the intervention and control groups, except for the significantly differing factor of having visiting nurse services (Table 1).

Pharmacist reviewers identified 191 potential drug-related problems, with physician reviewers confirming 153 of these (80%) as adverse drug-related events. Among all participants, 27.7% (100 individuals) encountered at least one adverse drug-related event, and 18% (65 individuals) experienced at least one clinically significant medication error. Adverse drug-related events totaled 81 in the intervention group and 72 in the control group. The intervention group accumulated 7392 follow-up days, while the control group contributed 7447 days. The incidence of adverse drug-related events was 1.10 per 100 person-days in the intervention group versus 0.97 per 100 person-days in the control group. No significant difference in the per-patient rate of adverse drug-related events was observed, with an unadjusted incidence rate ratio of 1.13 (95% CI, 0.83–1.56) and an adjusted incidence rate ratio of 0.97 (95% CI, 0.70–1.34).

Clinically significant medication errors, which included preventable or ameliorable adverse events as well as potential events, were observed in 18% (65 participants). These errors were nearly evenly distributed between the groups, with 44 events in the intervention group and 45 in the control group. Both groups had an identical incidence rate of 0.60 clinically significant medication errors per 100 person-days. The intervention showed no significant impact on the rate of such errors, with an unadjusted incidence rate ratio of 0.99 (95% CI, 0.65–1.49) and an adjusted incidence rate ratio of 0.81 (95% CI, 0.53–1.23).

Regarding emergency department visits within the 45-day post-discharge follow-up period, 18.3% (33 participants) from the intervention group visited the emergency department, compared to 18.8% (34 participants) in the control group. A total of 16.1% (29 participants) in the intervention group failed to complete the 45-day follow-up due to either rehospitalization (28 participants) or death (1 participant), compared to 14.4% (26 participants) in the control group, all of whom were rehospitalized.

For adverse drug-related events classified as adverse drug events (ADEs), gastrointestinal issues were the most prevalent in both groups (Table 3). Other commonly observed ADE categories included cardiovascular issues, kidney/electrolyte/fluid imbalances (e.g., kidney insufficiency, hyperkalemia, hypokalemia, and dehydration), bleeding episodes, and metabolic/endocrine problems (e.g., hypoglycemia).

Table 4 outlines the medication types most frequently linked to adverse drug-related events and clinically significant medication errors across both groups. Opioids were the most commonly associated medication class in both the intervention and control groups. Other frequently implicated categories included cardiovascular drugs, anticoagulants, and diuretics.

Table 1. Characteristics of Enrolled Participants.

Characteristic	Intervention (n = 180)	Control (n = 181)	P value
Age, mean (SD)	69.44 (9.4)	68.03 (9.3)	.15
Age category, y			.31
50-54	9 (5.0)	13 (7.2)	
55-59	24 (13.3)	18 (9.9)	
60-64	22 (12.2)	34 (18.8)	
65-69	34 (18.9)	39 (21.5)	
70-74	33 (18.3)	30 (16.6)	

75-79	28 (15.6)	28 (15.5)	
≥80	30 (16.7)	19 (10.5)	
Sex			
Women	96 (53.3)	81 (44.8)	.10
Men	84 (46.7)	100 (55.3)	
Prescribed >1 high-risk medication	97 (53.9)	98 (54.1)	.96
Prescribed a high-risk medication at discharge			
Anticoagulant	98 (54.4)	86 (47.5)	.19
Diabetes agents	71 (39.4)	64 (35.4)	.42
Opioid	105 (58.3)	118 (65.2)	.18
Prescribed a new high-risk medication at discharge	154 (85.6)	151 (83.4)	.58
Anticoagulant	88 (48.9)	78 (43.1)	.27
Diabetes agents	62 (34.4)	50 (27.6)	.16
Opioid	98 (54.4)	111 (61.3)	.19
Taking ≥7 medications of any kind	165 (91.7)	169 (93.4)	.54
Has caregiver	117 (65.0)	118 (65.2)	.97
Low health literacy level	61 (33.9)	49 (27.1)	.16
Has visiting nurse services			
Yes	99 (55.0)	88 (48.6)	.004
No	64 (35.6)	53 (29.3)	
Unknown	17 (9.4)	40 (22.1)	
Reason for admission			
Medical	104 (57.8)	94 (51.9)	
Surgical	43 (23.9)	45 (24.9)	.63
Orthopedic	30 (16.7)	39 (21.6)	
Medical procedure	3 (1.7)	3 (1.7)	
Admitted through emergency department	104 (57.8)	109 (60.2)	.64
Length of stay, mean (SD), d	2.59 (2.2)	2.87 (2.9)	.31

[a] Racial category of other comprised Asian, Native Hawaiian/Pacific Islander, and American Indian/Alaska Native.

DISCUSSION

Transitional care interventions led by clinical pharmacists are often regarded as a promising strategy to improve medication safety after hospital discharge. Patients prescribed high-risk medications, such as anticoagulants, diabetes treatments, and opioids, are considered ideal candidates for these interventions. However, in this randomized trial evaluating a comprehensive pharmacist-directed program, no significant reduction in adverse drug-related events or clinically significant medication errors was observed during the immediate post-hospitalization period. Recruitment challenges were encountered despite extending the enrollment period by an additional year (11), and event rates were substantially lower than anticipated based on previous research (12), which reduced the study's statistical power to detect differences between the intervention and control groups.

Few robust studies have thoroughly assessed pharmacist-led interventions for medication safety in outpatient settings. A systematic review by Lee et al. (25) focusing on older adults included 20 studies, only six of which were randomized trials. Of these, only one directly addressed adverse drug events (ADEs) and medication safety. While that study demonstrated reductions in inappropriate prescribing, it did not find a statistically significant difference in ADE rates between intervention and control groups (26).

More recent reviews have underscored the scarcity of studies evaluating pharmacist-directed interventions for medication safety after hospital discharge (27, 28, 29). Some investigations have suggested that pharmacist involvement during inpatient care can improve medication safety at discharge (30, 31), while others have found no significant impact. For instance, a randomized trial involving patients hospitalized for acute coronary syndromes or heart failure showed that a multicomponent intervention, including pharmacist-supported medication reconciliation, did not significantly reduce clinically important medication errors (12). Researchers from that trial noted the challenges of improving medication safety during the hospital-to-home transition (12), attributing their findings to factors like inadequate communication and coordination with primary care providers, a limitation that this study sought to address. Among pharmacist-led transitional care studies, only one has reported a significantly lower risk of "medication-related problems" (33). However, that study employed a pre-post design without adjudicated outcomes, limiting its generalizability.

Strengths and Limitations

This study had notable strengths, including its randomized design, comprehensive intervention, and rigorous outcome adjudication process. Nevertheless, several limitations must be acknowledged. The intervention began after hospital discharge, preventing early involvement during the critical transition from hospital to home. Clinical pharmacist visits to patients' homes did not occur immediately following discharge, delaying the opportunity to address medication safety concerns during this key period.

Moreover, a significant portion of participants, particularly those in the intervention group, received visiting nurse services, which could have skewed the results by favoring the intervention group. Another potential bias arose from the intervention's emphasis on identifying and reporting medication safety issues, which may have led to heightened detection and documentation of these events in the intervention group compared to the control group.

Additionally, control group participants received high-risk medication educational materials through the mail, which could be considered enhanced usual care and may have diminished the perceived impact of the intervention. Lastly, the study focused on a short 45-day post-discharge period. Extending follow-up to include ongoing care from community pharmacists over a longer timeframe, such as up to one year, might yield additional insights into reducing medication-related harm (34, 35).

CONCLUSIONS

Despite these findings, efforts to design, test, and optimize interventions for improving medication safety during the high-risk post-discharge period remain vital. These initiatives are inherently challenging and resource-intensive, requiring a clear demonstration of their effectiveness to justify investment and address implementation barriers. Rigorous research and evaluation are critical to refining these approaches and ensuring their adoption with confidence across healthcare systems.

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