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Original Study

Adverse Outcomes in Relation to Polypharmacy in Robust and Frail Older Hospital Patients

Arjun Poudel PhD [a,b,*], Nancye M. Peel PhD [c], Lisa M. Nissen PhD [a,b], Charles A. Mitchell MBBS [b], Leonard C. Gray PhD [c], Ruth E. Hubbard MD [c]

[a] School of Clinical Sciences, Queensland University of Technology, Brisbane, Australia
[b] School of Pharmacy, The University of Queensland, Brisbane, Australia
[c] Centre for Research in Geriatric Medicine, The University of Queensland, Brisbane, Australia

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A B S T R A C T

Objective: To explore the relationship between polypharmacy and adverse outcomes among older hospital inpatients stratified according to their frailty status.
Design and setting: A prospective study of 1418 patients, aged 70 and older, admitted to 11 hospitals across Australia.
Measurements: The interRAI Acute Care (AC) assessment tool was used for all data collection, including the derivation of a frailty index calculated using the deficit accumulation method. Polypharmacy was categorized into 3 groups based on the number of regular drugs prescribed. Recorded adverse health outcomes were falls, delirium, functional and cognitive decline, discharge to a higher level of care and in-hospital mortality.
Results: Patients had a mean (SD) age of 81 (6.8) years and 55% were women. Polypharmacy (5–9 drugs per day) was observed in 48.2% (n = 684) and hyper-polypharmacy (≥10 drugs) in 35.0% (n = 497). Severe cognitive impairment was significantly associated with nonpolypharmacy compared with polypharmacy and hyper-polypharmacy groups combined ($P = .004$). In total, 591 (42.5%) patients experienced at least 1 adverse outcome. The only adverse outcome associated with polypharmacy was delirium. Within each polypharmacy category, frailty was associated with adverse outcomes and the lowest overall incidence was among robust patients prescribed 10 or more drugs.
Conclusion: While polypharmacy may be a useful signal for medication review, in this study it was not an independent predictor of adverse outcomes for older inpatients. Assessing the frailty status of patients better appraised risk. Extensive de-prescribing in all older inpatients may not be an intervention that directly improves outcomes.

Aging is associated with the development of chronic illness and the implementation of guidelines for the management of these conditions has resulted in an increase in the cost and number of prescribed medications. Global spending on prescription medications is growing and is likely to reach $1 trillion by 2017.[1] In Australia, for example, medications account for more than 14% of the annual $140.2 billion health care expenditure.[2] Older people are the major recipients of medications[3] with those older than 65 contributing to more than half of all Pharmaceutical Benefits Scheme expenditure.[4]

There is increasing concern that the prescription of multiple drugs for older people can cause significant harm.[5] Pharmacokinetic and pharmacodynamics changes with chronological age increase the risk of adverse drug events.[6] In community-dwellers, polypharmacy (defined as the use of 5 or more medications per day) is associated with falls, functional decline, and mortality.[7] Among older inpatients, polypharmacy is widely cited as a risk factor for falls[8] and delirium,[9] geriatric syndromes that independently predict nursing home admission.[10]

On the other hand, medication can be of considerable value to older people, improving quality of life through symptom control, preventing cerebrovascular morbidity, and reducing cardiovascular mortality. The absolute benefits of primary and secondary prevention are greatest in the oldest old,[11] and the systematic underprescription of potentially beneficial medicines has been implicated in adverse outcomes.[12] Definitive evidence to support deprescribing is currently

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* Address correspondence to Arjun Poudel, PhD, School of Clinical Sciences Faculty of Health, Queensland University of Technology Q Block (Level 9), Brisbane, QLD 4000, Australia.
E-mail address: a3.poudel@qut.edu.au (A. Poudel).

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lacking. Recent Cochrane reviews conclude that interventions to reduce polypharmacy improve prescribing practice with no clinically significant improvement in outcomes[13] and that medication review in hospital may reduce emergency department contacts but with no effect on mortality or hospital readmissions.[14]

The relationship between polypharmacy and adverse outcomes is likely to be complex rather than linear. Comorbidity is a clear mediating factor; that is, patients taking multiple drugs may be at greater risk because of the disease conditions triggering prescribing. The frailty status of patients may be another important confounder. A recent study suggested that frail older people are more vulnerable to the impact of fall-risk-increasing drugs than their more robust peers.[15] Hence, in this study we aimed to determine the prevalence of polypharmacy and its association with adverse outcomes in hospitalized older patients and to assess the additional role of frailty.

Methods

Study Sample and Setting

This was a secondary analysis of 3 cohorts of older patients (n = 1418), aged 70 and older, admitted to 11 acute care hospitals in Queensland and Victoria, Australia, between 2005 and 2010, for whom data were collected prospectively. Most (n = 1220) were admitted to general medical units, with 71 in orthopedic wards and 127 in surgical wards. The study sites were diverse, from small secondary care centers with 120 to 160 beds to major tertiary referral centers with more than 650 beds. Recruitment was restricted to weekdays and discharge assessment completed on the day of discharge. Maximum daily recruitment was limited to 4 patients based on assessor resources. When more than 4 patients were eligible, a computer-generated random-sample selection method was used to minimize potential selection bias. Patient recruitment has been described in detail elsewhere.[16–18] Patients were excluded if they were admitted to coronary or intensive care units, for terminal care only, or were transferred out of general medical units within 24 hours of admission to inpatient wards.

Data Collection and Measurement Tools

The interRAI Acute Care (AC) assessment tool was used for data collection. This instrument has been specifically developed for use in the acute setting to support Comprehensive Geriatric Assessment of older inpatients.[19,20] It collates information across a large number of domains, including sociodemographic data, physical, cognitive and psycho-social functioning, medications, medical diagnoses, advance directives, and discharge destination. Nurse assessors who were trained to use the interRAI AC instrument gathered data at admission (within 24 hours in the ward) and at discharge. To obtain information for each item in the interRAI instrument, patient and family interviews, direct observations, staff interview, and medical records were used. A number of scales embedded in the interRAI instruments combine single items belonging to domains such as activities of daily living (ADL), instrumental activities of daily living, and cognition; these are used to describe the presence and extent of deficits in these domains.[19]

For each patient, the medication lists were documented by the interRAI assessors who transcribed or photocopied the patients' drug charts. All prescribed medications were recorded approximately 24 hours after admission to hospital and again at discharge from hospital. Data were entered by pharmacists or pharmacy students and verified by a second pharmacist or geriatrician.

Polypharmacy

Polypharmacy was categorized into 3 groups based on the number of regular drugs prescribed. Medications used for a finite period to manage acute medical conditions in hospital (eg, intravenous antibiotics, diuretics, and subcutaneous anticoagulants) were not included in the number of regular prescribed medications. Complementary and as-required medications were also excluded. Hyper-polypharmacy was defined as concurrent prescription of 10 or more drugs per day; polypharmacy was defined as prescription of 5 to 9 drugs, and non-polypharmacy represented patients prescribed 4 or fewer drugs concomitantly. These cutoff points were based on previous studies.[21,22]

Adverse Outcomes

Fall in hospital

In-hospital fall was defined as having at least 1 fall during the period of hospitalization. These data were collected prospectively by the research nurses using all available sources of information (interviewing the patient and medical staff, daily ward visits to review medical records, and checking the forms or systems for recording adverse events).

Delirium in hospital

As part of the interRAI AC, varying mental function and acute changes in mental status from baseline were evaluated by the nurse assessors at admission and discharge. The 2 items were combined to screen for delirium. This screener has been validated in a prospective observational study with good positive predictive value of delirium.[23] Delirium in hospital was recorded if the interRAI delirium screen was positive at the admission or discharge assessments or if delirium and/or any acute change in cognitive function was noted in the hospital records on daily ward visits by the nurse assessor.

In-hospital ADL function decline

This was assessed using change in the ADL short-form scale that consists of 4 items (personal hygiene, walking, toilet use, and eating). Scores on the ADL scale range from 0 to 16, with higher scores indicating greater impairment.[17] In-hospital functional decline was defined as having a worse (higher) ADL score on discharge compared with admission.

In-hospital cognitive function decline

The Cognitive Performance Scale (CPS) was used to measure cognitive impairment.[17] Scores range from 0 to 6, with higher scores indicating greater impairment. In-hospital cognitive decline was defined as having a higher CPS score on discharge compared with admission.

Discharged to a higher level of care

The residential status on admission was classified on an ordinal scale as community (independent), community (supported), institutional care (hospice, low- or high-level residential aged care). Discharge to a higher level of care was defined as change to higher score on the ordinal scale at discharge, for example change in permanent living arrangement from a community to an institutional setting, and within the institutional environment from a low-care to a high-care setting. Those who died in the hospital were excluded.

In-hospital mortality

In-hospital mortality was recorded for those patients who died during the hospital episode.

Composite Adverse Outcome

To explore the association of polypharmacy with adverse outcomes, a composite adverse outcome (CAO) was derived as the presence of at least 1 adverse outcome.

Frailty Measurement

A Frailty Index (FI) was calculated using a well-defined methodology.[24] Data collected using the interRAI assessment tool were coded