Research Article

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Polypharmacy in Very Elderly Hospitalised Patients: A Single Centre Study

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Abstract

Objectives: To quantify the extent of polypharmacy and potentially inappropriate medications (PIMS) in very elderly hospitalised patients.

Method: A retrospective audit of prescribed medications among hospitalised medical patients (≥80 years). The number of regular medications was categorised as: non-polypharmacy (0-4 drugs), polypharmacy (5-9 drugs) and hyper-polypharmacy (≥ 10 drugs).

Results: 318 patient records were reviewed with a mean age of 86.3 years, Polypharmacy was identified in 50.6% of patients and hyper-polypharmacy in 31.2%, while only 18.2% of patients had non-polypharmacy. 62.3% of patients received at least one psychotropic agent, most commonly anti-depressants (26.1%) followed by sedatives (19.5%). Antidepressant use correlated significantly with a history of falls, $P=0.005$. Other commonly prescribed medications were proton-pump inhibitors (53.5%), diuretics (48.1%), statins (45.6%), beta-blockers (34.3%) and anti-coagulation agents (21.7%).

Conclusion: Our study showed that over 80% of hospitalised very elderly patients were exposed to polypharmacy, and many patients were prescribed PIMS.

Keywords: Polypharmacy; Geriatrics; Deprescribing; Hospital; Treatment

Impact Statement

This study identifies that polypharmacy and hyper-polypharmacy are highly prevalent among the very elderly hospitalised patients. Antidepressant use is associated with increased risk of falls in the geriatric population. Proton pump inhibitors, statins for primary prophylaxis and psychotropic medications should be considered as targets for deprescribing in the elderly population.

Introduction

Polypharmacy (the use of five or more regular medications per day) is widely recognised as a potentially significant contributor to morbidity and mortality in the

elderly population [1]. As the proportion of the elderly (80 years and older) population continues to rise, the community burden of medication treated conditions will also increase, along with the risk of adverse drug reactions [2,3]. The geriatric population is especially vulnerable to the effects of polypharmacy due to the age related decline in renal and liver function, which alters drug metabolism and clearance [4,5].

Certain drug classes, such as benzodiazepines, antipsychotics and anticholinergics have been well described in the literature to be associated with harm in the elderly population due to age-related increased sensitivity to adverse effects [3,6]. Furthermore, these drug classes are frequently prescribed for elderly

patients despite evidence of limited therapeutic benefit [2,3,7,8,9]. While other medications are continued in the elderly beyond the treatment duration required for the primary indication, such as proton pump inhibitors for reflux symptoms and antidepressants for depression [2,3]. These drugs may be described as “potentially inappropriate medications” or PIMs [3]. PIMs may add significantly to an elderly patient’s medication burden, which is of concern given that the total number of medications taken has been shown to increase the risk of falls and delirium, especially if anticholinergic and sedating drugs are used [2,3,6].

Another major consideration when assessing prescribing in the elderly is that many treatments initiated for this population are based on limited evidence of benefit. The majority of clinical trials include the geriatric population in their exclusion criteria, with treatment benefits extrapolated from a younger population, despite some benefits taking many years of treatment to become apparent [5].

As the level of polypharmacy at Peninsula Health’s very elderly patients was unknown despite having one of the more elderly cohorts among Victoria’s health-care networks, a cohort study at the network’s tertiary centre was conducted to assess the level of polypharmacy and to identify potential deprescribing targets.

Method

A single centre, retrospective, cohort study at a tertiary hospital in Victoria, Australia was conducted with inclusion of all patients aged 80 years or over admitted between January and April 2016 under general medical teams. Patients admitted under speciality teams such as cardiology, neurology or surgical teams were excluded from this study.

Data were extracted by medical staff, using a data collection sheet, from scanned digitised medical records, such as preadmission medications from pharmacists conducted medication reconciliation forms (MRFs), nursing home medication administration charts, community pharmacy dispensing records or general practitioner prescribing lists. Any pharmacists conducted MRFs utilise at least two sources of information, including patients or their carer as one source. Patient demographics, residential status (assisted living facilities or private residence), falls history, cognitive status (dementia, delirium or minimal cognitive impairment), palliative status and polypharmacy burden were recorded.

Discharge destinations were collected as either patients returning to primary residence, transfer to rehabilitation site or another hospital, admission to a higher level care facility, or in-hospital mortality. Additionally, statin dose, potency and indication (primary or secondary) were recorded as part of this study [10]. Pill burden for regular medications was recorded separately to the medication burden.

The primary outcome was the level of polypharmacy, which was defined as five or more regular medications prescribed per day, with hyper-polypharmacy being defined as taking 10 or more regular medications prescribed per day [1]. Secondary outcomes were associations between the use of opioids, benzodiazepines, statins, gastric acid suppression therapies, anticholinergic drugs, antihypertensive therapies, polypharmacy, pill burden and the risk for falls, dementia, delirium and mortality.

Statistics

All bivariate outcomes were analysed using Fisher’s exact, and continuous variables were analysed using student t-test or Mann-Witney U test. Multivariate analyses were carried out for additional associations between medication use and the secondary outcomes. All results with a p-value of less than 0.05 were considered to be statistically significant. All statistical testing was completed using SPSS Computer Program, Version 19.0. (SPSS Inc, Chicago, IL, USA).

Results

Over the study period 318 patients met the inclusion criteria, 189 (59.4%) were female with the median age for the cohort of 86 years (95% CI 85.8-86.8), and a range of 80 to 101 years. The majority of these patients were admitted from private residences, while 14.5% came from a residential care facility (Table 1). Over 25% of patients had a history of cognitive impairment, including dementia and delirium. Nearly half the population had a history of falls, and 1 in 10 required palliative care. At the end of this cohort’s admission 68.2% of patients were discharged back to their homes or residential care facilities, while 6.3% of patients died during the admission. Additionally, 4.1% of patients were discharged to a new residential care facility, 18.9% were discharged to subacute care sites and 2.2% required transfers to other hospitals.

Table 1: Patient characteristics

Characteristics	Patients (N=318)
Age [years]	86.3 (95%CI 85.8-86.8)
Range [years]	80-101
Female	189 (59.4%)
Admitted from:	
Residential Care Facility	46 (14.5%)
Home alone	99 (31.1%)
Home with Others	165 (51.9%)
Other	8 (2.5%)
Past history:	
Dementia	33 (10.4%)
Delirium	29 (9.1%)
Both delirium and dementia	15 (4.7%)
Minimal cognitive impairment	14 (4.4%)
Normal cognitive function	227 (71.4%)
Falls history	149 (46.9%)
Palliative care	30 (9.4%)
Medication history:	
Anticoagulants	69 (21.7%)
Warfarin	44 (13.8%)
Dabigatran	1 (0.3%)
Rivaroxaban	11 (3.5%)
Apixaban	13 (4.1%)
Statins	145 (45.6%)
Low potency	5 (1.6%)
Moderate potency	83 (26.1%)
High potency	57 (17.9%)
Primary prophylaxis	53 (16.7%)
Secondary prophylaxis	90 (28.3%)
Cardiovascular drugs	
Digoxin	46 (14.5%)
ACEI†	61 (19.2%)
A2RA‡	63 (19.8%)
Combination of ACEI and A2RA	3 (0.9%)
Calcium Channel Blocker	59 (18.6%)
Beta blocker	109 (34.3%)
Diuretics	153 (48.1%)
Other antihypertensives	15 (4.7%)
Gastric acid suppression therapy	201 (63.2%)
Proton pump inhibitors	170 (53.5%)
Histamine receptor 2 inhibitors	19 (6.0%)
Both	12 (3.8%)
Opioids	76 (23.9%)
Regular	36 (11.3%)
When required	22 (6.9%)
Both	18 (5.7%)
Central nervous system drugs	
Antidepressants	83 (26.1%)
Antipsychotics	17 (5.3%)
Sedatives	62 (19.5%)

† ACEI; angiotensin converting enzyme inhibitors,

‡ A2RA: angiotensin 2 type 1 receptor antagonist

The average number of medications taken by patients in this cohort was 7.7 (range of 0 to 21) and 11.1 pills per day (range 0 to 38). The primary outcome of

polypharmacy was identified in 50.6% of patients, with hyper-polypharmacy in 31.2% (figure 1). The number of medications taken per day was directly associated with a higher Charlson comorbidity index ($p<0.001$). Due to the high prevalence of cardiovascular disease in such an elderly population there was a high use of cardiovascular medications including: 21.7% using anticoagulants, 45.6% on statins and over 40% on antihypertensive drugs. Among statin users, 16.7% were indicated for primary prophylaxis, the majority of which were on moderate to high potency statins.

In addition to high use of cardiovascular medications, more than half the population was on gastric acid suppressive therapy with 53.5% of patients taking proton pump inhibitors (PPIs). Opioid use was also common with nearly 1 in 4 patients using this class of analgesics. Psychotropics were frequently prescribed with over 25% of patients taking antidepressants, of which nearly 20% were on sedatives and 5.3% were on antipsychotics.

Figure 1: Polypharmacy levels

Secondary outcomes for the study showed that the Charlson comorbidity index and antipsychotic use were associated with increased mortality during the index admission ($p=0.094$ and $p=0.016$ respectively), while statin use was associated with reduced mortality ($p=0.085$), although not statistically significant. A history of dementia, delirium or both was weakly associated with risk for falls ($p=0.062$), but not individually. Neither statin use nor potency were associated with falls, ($p=0.654$ and $p=0.382$ respectively), and there was no association between statin use and risk of delirium ($p=0.726$), but

there was a trend towards a lower dementia history (2.1% vs 6.9%, $p=0.062$). The risk for falls was not identified among patients using sedatives ($p=0.671$), opioids ($p=0.602$), diuretics ($p=0.432$), antipsychotics ($p=0.330$), those with polypharmacy ($p=0.305$) or the number of antihypertensive drugs ($p=0.702$). However, the use of antidepressants was significantly associated with an increased risk of falls ($p=0.005$), including after conducting a multivariate analysis ($p=0.012$). The number of pills per day, among patients taking 20 or more, was weakly linked with higher falls history ($p=0.066$) in this patient cohort.

Discussion

This study has identified high levels of polypharmacy among the very elderly hospitalised population. The degree of polypharmacy is comparable to that reported in previous Australian studies of patients aged over 70 and 85 years, with levels of polypharmacy in these studies at 52.2% for those aged over 70, and at 51.9% for those aged over 85 versus 50.6% in this study population [1,11]. The level of hyper-polypharmacy in this study and the recent study of those aged 85 and older was significantly greater compared to the results among those aged over 70 years, 31.2%, 34.2% versus 23.8% respectively [1,11]. The medication burden in this population (7.7 medications per day) was similar to those aged over 85 years (8.3 medications per day) and higher than for those aged over 70 years (7.1 medications per day) [1,11]. PIMs identified in this cohort were comparable to those previously reported at levels of 15-46.8%, with PPIs and statins for primary prophylaxis, as well as antidepressants and sedatives being potential targets for deprescribing [2]. The levels of these medications used in this cohort was again higher than in those aged over 70, with statin use at 45.6% versus 38.7%, opioid use at 23.9% versus 13.1%, antipsychotic use at 5.3% versus 5.0%, and sedatives use at 19.5% versus 10.3% [1]. These results are concerning as the median age in this cohort was only 5 years older, but the rates of hyper-polypharmacy increased by 7.4%.

One of the PIMs contributing to polypharmacy is primary prophylaxis with statins, which was found in 16.7% of our patients, who were mainly prescribed moderate to high potency statins. There was a lack of association between statin use and in-hospital delirium in our cohort, but a trend suggesting patients on statin therapy were less likely to have a history of dementia. This finding does not necessarily indicate causality, with a recently published review identifying no benefit from statin use on cognitive decline based on a longitudinal study [12]. The use of moderate to high potency statins for primary

prophylaxis in this study population may stem from the results of previous studies showing no benefit from low potency statins such as pravastatin in the ALLHAT-LLT study [13]. However, the benefits from higher potency statins have been suggested in the HOPE-3 study with a reduction for cardiovascular causes ($p<0.005$), including stroke ($p=0.01$) and myocardial infarction ($p=0.09$), but with no mortality reductions in any age subgroups [14]. Then again, high potency statins in the elderly carry with them additional risk of statin associated muscle adverse events, with interactions with other drugs, older age with reduced clearance being an established risk factor [15,16].

Another class identified as a PIM is PPI therapy, which is frequently used beyond the primary indication and is associated with an increased risk of multiple adverse events including chronic kidney disease, dementia, osteoporotic fractures, micronutrient deficiencies, as well as bacterial infections of the bowel and lungs, and mortality when used beyond a year [17,18,19]. This class of drugs is commonly identified as a target for deprescribing [18], and should be reviewed at every healthcare team-patient interaction; especially as previous studies have identified that up to 40% of patients have no documented reason to use PPIs [19]. We have previously shown in a cohort of patients admitted to the same tertiary hospital for falls, that PPI use was over 40%, with 42.9% use among those who sustained an osteoporotic fracture, and as high as 56.2% in those with a fracture while on osteoporosis treatment with antiresorptive therapy [20]. The fact that over half the population in this general medical cohort was on PPI therapy is troubling given the known long term complications, not to mention the unnecessary addition to the overall pill burden and the potential to compromise the efficacy of bisphosphonate therapy in an already high risk population [20].

The psychotropic group of medications was commonly used in the studied population with over a quarter of the patients taking antidepressants and almost one in five patients using sedatives. Psychotropic medications are associated with falls and fracture risk [3, 6, 8, 20], with antidepressant use being a strong association with a falls history in the studied cohort. The use of antipsychotics preadmission was found to be associated with a higher inpatient mortality in our study, with previous research identifying that this class of medications is frequently overused with poor efficacy for management of delirium and known increased risk of stroke [3,20].

The scope for deprescribing in the studied cohort is high, but the opportunity to undertake this process is limited by the time that these patients spend in the acute hospital settings, as well as the availability of time for general medical clinicians to undertake this process collaboratively with general practitioners who manage them in community settings. Previous studies indicated similar factors affecting the likelihood of deprescribing, including reluctance of junior medical staff to stop therapies without senior approval, while sub-specialists and general practitioners do not frequently stop therapies initiated by specialists without clear communication [1,21,22]. Multidisciplinary team approaches, with pharmacists' medication reviews and consultations with geriatricians have been shown to improve outcomes in polypharmacy reduction, however implementation of these methods in acute care is limited [1,18,21]. Many approaches and tools have been developed to undertake the deprescribing process with validation of these tools [2,3,6]. However, there is reluctance to undertake this process during an acute hospitalisation of the elderly patients with the acute medical and surgical teams applying their time and skills to the management of the primary admission problem rather than the potential polypharmacy contributors for the admission. Systematic approaches such as using the drug burden index [6] should be considered to increase the likelihood of deprescribing or at least identification and documentation of PIMs for community general practitioner to consider for deprescribing.

The results of this study are limited by the short period of data collection, single site and concentration on admissions under the general medical teams; however, the results are in line with similar studies conducted in Australia and other developed countries. The results follow the expected trajectory for polypharmacy in this age group, increasing our confidence in the results obtained.

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Ethics

This study received an exemption from Human Research Ethic Committee review due to low-risk retrospective nature of the study.

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Declarations

The authors declare that the study received no funding and that there are no conflicts of interest to declare.

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Conclusion

Polypharmacy among the elderly hospitalised patients was identified in more than 80% in the studied cohort with substantial exposure PIMs. PPIs, antidepressants, antipsychotics and statins for primary prophylaxis should be considered as commonly overused drugs in this population and are therefore ideal targets for deprescribing at every encounter with healthcare providers.

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