Original Article

The Burden of Polypharmacy in Patients Near the End of Life

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Abstract

Context. Patients with advanced illness are prescribed multiple medications in the last year of life, intensifying the risk of negative consequences related to polypharmacy.

Objectives. To describe the medication burden of patients near the end of life and identify potential areas for improvement in clinician prescribing practices.

Methods. This was a prespecified secondary analysis of data from a prospective trial. Eligible participants were adults with less than 12 months estimated prognosis taking a statin medication for primary prevention of cardiovascular disease. Participants were enrolled from 15 sites, randomized to continue or discontinue statin medications, and followed for up to a year. Concomitant medications were recorded at least monthly from study enrollment through death. Prescribed medications were categorized by class and subclass. Descriptive statistics were calculated.

Results. On average, participants ($n = 244$) were 74.3 years old (SD 11.5) and lived 264 days (SD 128); 47.5% of the patients had a primary diagnosis of malignant tumor. This population was exposed to medications across 51 classes, 192 subclasses, and 423 individual medications. Patients took an average of 11.5 (SD 5) medications at the time of enrollment and 10.7 (SD 5) medications at death or study termination. The five most common classes of medications prescribed near the end of life were antihypertensives, broncholytics/bronchodilators, laxatives, antidepressants, and gastric protection agents.

Conclusion. There is a significant medication burden placed on patients with advanced illness. Although most medications were prescribed for supportive care, we observed a high prevalence of medications for managing non−life-threatening comorbidities. J Pain Symptom Manage 2015;■:■−■.

Key Words

Palliative care, end of life, polypharmacy

Introduction

Clinicians who provide care to patients near the end of life are challenged with managing the expanding medication portfolios of these patients. These medications include four types of interventions. First, medications for the primary prevention of disease (e.g., hypertension medications for prevention of strokes) are often continued despite changes in relative risk of these potential diseases to impact quality of life. Second, medications are often continued to control non−life-threatening comorbidities present concomitant to life-limiting illness (e.g., warfarin for known atrial fibrillation). Third, disease-directed treatments may add to the total medication burden, such as oral tyrosine kinase inhibitors for advanced cancer or immunologic agents for neurologic conditions.

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Fourth, and most commonly actively managed by palliative care clinicians, is medications to address the symptom burden that increases along the trajectory of serious illness (e.g., laxatives to counter the constipating effect of many medications).[1,2] It is, therefore, common for patients to experience a gradual increase in the total medication burden near the end of life. For example, studies demonstrate that up to 20% of patients receiving palliative care services regularly take more than eight medications.[1,3–5]

The imperative for palliative care clinicians to address the expanding portfolio of medications is highlighted by several common harms. For example, the complex interplay of concomitantly managing life-threatening illnesses (e.g., heart failure), non–life-threatening comorbid conditions (e.g., hypertension, atrial fibrillation), and symptoms (e.g., dyspnea, pain) creates challenges for both the clinicians and patients. Also, as medication lists grow, the risk for drug-drug interactions, drug-food interactions, and other adverse drug events (ADEs) increases.[6–8] Naturally, it becomes difficult for even experienced and attentive clinicians to not become overwhelmed with simultaneously managing multiple medications during brief clinical visits. Additionally, as medication lists grow, patients are faced with challenging medication administration regimens (e.g., four times daily dosing, nightly before bed dosing), increasing the risk for nonadherence. Furthermore, patients with advanced illness frequently experience anorexia, swallowing difficulties, and early satiety, so taking multiple pills per day becomes significantly more difficult. Finally, patients and families are often burdened by high out-of-pocket costs associated with the use of multiple medications.[9]

The Palliative Care Research Cooperative Group conducted a randomized clinical trial assessing the impact of discontinuing statins in patients near the end of life. This study demonstrated improved quality of life in patients with a life-limiting illness without an adverse impact on morbidity and mortality.[10–13] Records of patient medication profiles were collected during the study. We aim to describe the breadth and depth of polypharmacy burden among patients within this clinical trial.

Methods

Overview

This study is an observational analysis of medication records from patients enrolled in a multicenter statin discontinuation clinical trial performed by the Palliative Care Research Cooperative Group.[11] Institutional review board approval was obtained for each site participating in the trial. A total of 381 patients were enrolled in the clinical trial that serves as the source of data for these analyses.

Patient Population

Patients eligible for this trial were those who had received a life-limiting diagnosis where at least one physician indicated he/she "would not be surprised if the patient died in the next year," had a life expectancy greater than one month, had been taking statins for three months or more, and had recent deterioration in functional status. Outcomes, which were measured at baseline and at least monthly, included concomitant medications, quality of life, cardiovascular events, performance status, and symptoms.

Data Collection

As a part of this trial, the medications being taken by study participants were recorded at baseline and at Weeks 2, 4, 8, 12, 16, 20, and 24 to document changes in medication use over the course of the trial. Patients for this secondary analysis were included if they had medication data from at least two time points and were alive for at least 30 days after enrollment in the trial ($n = 244$). Spelling mistakes were corrected, and trade names were converted to generics. Medications were then coded as to class, subclass, and individual medications by one of the authors (M. J. M.) (Appendix I). An expert panel of palliative care, oncology, geriatrics, and primary care physicians guided medication categorization. Medication classes were based on prior studies and the World Health Organization's "Guidelines for Anatomic Therapeutic Class (ATC) Classification and Defined Daily Dose (DDD) Assignment."[3,14] Dosing and route of administration were not evaluated in this analysis. Because half of the study population was randomized to discontinue statins in accordance with the parent trial protocol, statin medication use is excluded from these analyses.

Calculations and Analysis

Data were analyzed using descriptive statistics. Noting parametric distribution of data during the data visualization step, we report means and frequencies.

Results

We included 244 patients who met inclusion criteria for this analysis. Mean (SD) age was 74.3 (11.5) years. One hundred ten patients (45.1%) were female. The most common life-limiting illness was malignant tumor ($n = 116$, 47.5%); the mean (SD) Charlson Comorbidity Index[15] was 4.8 (2.8). Eighty-seven patients (35.7%) were enrolled in hospice at baseline, and 132 (54.1%) participated in hospice at some point in their care. A total of 104 of the 244 patients in the cohort died during the study, with the mean (SD)