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POLYPHARMACY in Older Adults

Polypharmacy, by definition, is the concurrent use of several different medications consumed by a person. Often these multiple medications are in the same class and are used to treat more than one chronic condition. Older individuals are often faced with issues of polypharmacy due to multiple chronic conditions and multiple providers. The risks associated with polypharmacy can lead to increased adverse effects, falls, and decreased risk of medication compliance. This paper will discuss the issues surrounding polypharmacy and provide a case example to illustrate the significance of this problem.

Introduction

A common observation when interacting with patients suffering from multiple chronic diseases is an extensive list of medications, which expands phenomenally as people age (Linjakumpu et al., 2002). By definition, the use of five or more medications is considered polypharmacy (Hovstadius & Petersson, 2012). This phenomenon is very common in older patients and has been associated with an increase in geriatric syndromes, decrease in functional outcomes, and increased mortality (Gnjidic et al., 2012). These poor outcomes are related to adverse drug reactions, falls, and medication compliance (Sergi et al., 2011). Several explanations can account for polypharmacy in the older adults; one such explanation is accumulation of comorbidities that results in consulting multiple providers each prescribing medications for a particular condition independent of other prescribers (Randall & Bruno, 2006). The purpose of this paper is to discuss the issues surrounding polypharmacy in older adults and provide a case example to illustrate the significance of this problem.

Case Presentation

M.M. is a 77-year-old woman who saw a primary care provider to establish care. Her daughter wanted one provider who would discontinue medications that weren't essential overseeing M.M.'s care. M.M.'s medical history includes hypertension and hyperlipidemia for 20 years, embolic stroke 15 years ago, stage 3 chronic kidney disease, gout, cataracts, narrowing of the esophagus, beta thalassemia minor, and smoking history of ½ pack per day for 55+ years (27½ pack years). On the initial visit she stated she was fatigued and appeared pale. M.M. provided the primary care provider with a piece of paper with all of her current medications (Table 1). She started on these medications, which were prescribed by four healthcare providers over a period of 20 years. When questioned about each medication M.M. did not know the

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reason for most of her medications but "trusted" her physicians who prescribed them for her. M.M. confirmed her daughter's statement about wishing to eliminate medications she did not need.

Laboratory studies were ordered and revealed an extremely elevated lipid profile, a low hemoglobin and hematocrit, and her glomerular filtration rate (GFR) was abnormal, otherwise all other indices were within the normal range. Her vital signs on initial visit revealed: heart rate 92 beats per minute, blood pressure 180/88 mmHg, respiratory rate 18 breaths per minute, and oxygen saturation 98% on room air.

Polypharmacy in Older Adults

With advances in medical treatment people are living longer. Today someone turning 65 years of age can anticipate living another 18 to 20 years (Kochanek et al., 2011). Because individuals are living longer, there is a higher risk for chronic disease and comorbidities, which often results in an increased number of medications (Linjakumpu et al., 2002). Older adults, age 65 and older consume approximately 34% of prescription medications and purchase 40% of over-the-counter (OTC) medications (Randall & Bruno, 2006) and often take at least five medications (Gnjidic et al., 2012), which is consistent with M.M.'s profile.

The leading causes of chronic illness in older adults are attributed to hypertension, high cholesterol, and pain, which can result in heart disease, stroke, and potential drug dependence (Jett, 2012a). Some of the most common medications prescribed to older adults are cardiovascular drugs, diuretics, nonopioid analgesics, anticoagulants, and antiseizure medications (Field et al., 2004).

Negative Outcomes of Polypharmacy

The three main problems with polypharmacy in the older adult are: (1) adverse drug reactions, (2) falls, and (3) medication noncompliance (Sergi et al., 2011). One explanation for these problems can be attributed to changes in physiology. Aging brings about predictable physiological changes in the body that can result in differences in pharmacokinetic and pharmacodynamics of medications (Jett, 2012b). It is estimated that 40% of older adults experience reduced renal blood flow and GFR, which varies widely among individuals (Jett, 2012b). These changes occur in concert with structural changes, including a decrease in renal mass, which correlates with fewer nephrons present. It appears that normal kidney vasculature is

Table 1. M.M.'s Medication List and Potential Adverse Effects

Medication/Dosage	Classification	Reason for Taking Medication	Adverse Effects
Atorvastatin 20 mg/1 tab at bedtime	Statin	Cholesterol	GI upset, headaches, myalgia, arthralgia, elevated serum transaminases, rhabdomyolysis with renal dysfunction, increased glucose, cognitive impairment
Fenofibrate 160 mg/1 tab once daily	Peroxisome proliferator receptor alpha agonist	Cholesterol	Abnormal liver function tests, elevated CPK, rhinitis, myopathy, cholelithiasis, pancreatitis, increased BUN or creatinine
Lovaza 1 g Cap/2 capsules twice daily	Lipid-regulating agent	Cholesterol	Eructation, dyspepsia, rash, taste perversion, increased ALT, AST, LDL-C
Clopidogrel 75 mg/1 tab once daily	Platelet inhibitor	Blood thinner	Bleeding (may be fatal), epistaxis, hematuria, bruising, ulcers, rash, thrombotic thrombocytopenic purpura
Aspirin 81 mg/1 tab once daily	Antithrombotic	Blood thinner	GI upset/bleed, prolonged bleeding time, anaphylaxis
Nifedipine ER 30 mg/1 tab once daily	Calcium channel blocker	Blood pressure	Edema, headache, fatigue, dizziness, flushing, constipation, nausea, palpitations, muscle cramps
Atenolol 100 mg/1 tab at bedtime	Beta-blocker	Blood pressure	Heart failure, bronchospasm, bradycardia, heart block, dizziness, fatigue, fluid or electrolyte imbalance, hyperuricemia, orthostatic hypotension, GI upset, cold extremities
Lisinopril 40 mg/1 tab once daily	ACE inhibitor	Blood pressure	Headache, dizziness, cough, hypotension, chest pain, hyperkalemia, renal impairment, angioedema, liver dysfunction, blood dyscrasias
Furosemide 20 mg/1 tab once daily	Loop diuretic	Fluid pill	Excessive diuresis, fluid or electrolyte imbalance, GI upset, dizziness, vertigo, paresthesias, orthostatic hypotension, hyperglycemia, tinnitus, hearing loss, blood dyscrasias, renal calcification
Klor-Con 8 mEq/1 tab once daily	Potassium supplement	Potassium pill	Hyperkalemia, GI discomfort and irritation, diarrhea, rash
Cetirizine hydrochloride 10 mg/1 tab once daily	Antihistamine	Allergy pill	Drowsiness, somnolence, fatigue, dry mouth, pharyngitis
Allopurinol 100 mg/1 tab once daily	Xanthine oxidase inhibitor	Gout	Rash, GI disorders, acute gout, ecchymosis, fever, headache, hepatic necrosis, drowsiness, Stevens-Johnson syndrome, renal failure
Citalopram 10 mg/1 tab once daily	SSRI	Mood	GI upset, dry mouth, somnolence, insomnia, anorexia, sexual dysfunction, fatigue, dose-dependent QT prolongation, neuroleptic malignant syndrome
Baclofen 10 mg/½ tab three times a day	Gamma-aminobutyric acid-ergic agonist	Esophagus spasms	Transient drowsiness, confusion, dizziness, weakness, fatigue, headache, hypotension, seizures and hallucinations on abrupt withdrawal
Epitol 200 mg/1 tab once daily	Mood stabilizer/ antiepileptic agent	Headache	Blurred or double vision, back and forth eye movements, confusion, agitation
Amitriptyline 10 mg/1 tab at bedtime	Tricyclic antidepressant	Esophagus spasms	Drowsiness, anticholinergic effect, CNS overstimulation, arrhythmias, stroke, coma, confusion, extrapyramidal symptoms, hypo- or hypertension, nausea, fatigue, headaches
Ferrous Sulfate 325 mg/3 times a day	Iron supplement	Anemia	Nausea, abdominal discomfort and pain, constipation, masks occult bleeding, black stools, stains teeth and dentures

Note: ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CPK = creatine phosphokinase; GI = gastrointestinal; LDL-C = low-density lipoprotein cholesterol. Adapted from: Monthly Prescribing Reference (2013). http://www.empr.com/

maintained until the fourth decade of life whereby a 10% loss in vascular flow occurs each decade. Approximately one-half of older individuals eventually develop chronic kidney disease (Wiggins, 2003). These changes in kidney function can affect how medications are excreted from the body.

Aging causes changes in liver volume, as well as blood flow through the liver and enzymatic function (Jett, 2012a). Reduction in liver function associated with aging can compromise the first pass effects of medications like warfarin, benzodiazepines, and opiates resulting in higher than normal or toxic levels of these substances. On the contrary, prodrugs such as enalapril and perindopril are activated in the liver so their first pass activation may be delayed or reduced.

Medications that are protein bound have a high affinity for albumin. However, serum albumin decreases by 15% to 20% with aging and may be even lower with illness (Wiggins, 2003). Levels of medications that are albumin bound can also be reduced by malnutrition from food restrictions, poorly fitting dentures, or meal preparation difficulties, which can result in higher drug blood levels.

These physiological changes in conjunction with multiple medications can lead to increased adverse drug effects, which relate significantly with the number of geriatric syndromes, decrease in functional outcomes, and increased mortality rates among this population (Gnjidic et al., 2012). The risk for adverse effects increases every time a new medication is started. For example, the risk of an adverse event is 15% when two medications are being taken but this risk increases to 58% with five medications and 82% with seven or more medications (Maher et al., 2014). Seventeen percent of those suffering from an adverse drug event are hospitalized, and this rate increases to 33% for adults 75 years of age or older (Frazier, 2005).

Polypharmacy is a major risk factor for falls (Lai et al., 2010). The risk for falls significantly rises in relationship to the number of medications a person consumes, regardless of age or existing disability. Drugs directly related to this increased risk are diuretics, benzodiazepines, and anticholinergics (Ziere et al., 2006). Therefore, when changing or adding a new medication to the treatment regimen for older adults the concept of how the drug works in the body as well as how the body uses the drug is critically important.

Poor medication compliance is also a major complication of polypharmacy. Compliance with medications is vital to the treatment of chronic disease. However, polypharmacy can inhibit compliance with medication due to the complicated regimens and number of medications needing to be managed by the person. A significant decrease in medication compliance is directly related to the number of medications a person takes (Claxton et al., 2001). As the number of medications or the number of times per day it has to be taken increases, the nonadherence rate can increase up to 79% (Veehof et al., 2000). In a longitudinal study, Veehof et al. found approximately 125,000 deaths per year are linked to medication nonadherence and an increase of healthcare cost of approximately 177 billion dollars.

Strategies to Address Polypharmacy

Healthcare professionals working with patients have a responsibility to help prevent polypharmacy from occurring. This can be done by helping patients to maintain an accurate list of medications that contain the following information: both the generic and brand names of each medication, the dosage and frequency, who prescribed the medication (their contact information is also helpful), and the reason for taking the prescribed drug. Because older adults purchase approximately 40% of all OTC medications and are three times more likely to be taking one or more (Jett, 2012a, 2012b), exploring with patients their use of OTC medications is also prudent. In the home healthcare setting this list should be updated and reviewed with the patient monthly and after each provider visit. The medication review can help reduce duplicate medications, medications that are contraindicated for older adults, and provide ways to ensure patients understand why they are taking the medications as well as how to take them correctly. During the routine medication review home healthcare clinicians also have the opportunity to assess if patients are using multiple pharmacies to fill prescriptions. Older patients should use one pharmacy to help reduce the risk of polypharmacy.

Additionally, home healthcare clinicians can assess adherence to medications during the routine reviews and advocate for patients if a medication regimen is too complex, especially for patients who may be suffering from dementia or are depressed. Generally the rule is to minimize the number of prescribed medications with simple dosing schedules, with the assurance the right drugs are given for the right circumstance to treat the right disease.

Home healthcare clinicians should use a valid and reliable tool to conduct a periodic medication assessment using one of the three available assessment tools to help decrease polypharmacy. The Beers Criteria is the most commonly used assessment tool initiated by healthcare providers to improve medication safety for older adults. Beers and colleagues published a consensus document to establish criteria to identify inappropriate medications for older adults (Fick et al., 2003). In 2001, Zhan et al. modified Beers criteria by identifying medications that: (1) should always be avoided (due to known adverse effects where the risk outweigh the benefits), (2) are rarely appropriate, and (3) are frequently misused but have clinical indication. In the process of revising their assessment tool, Beers et al. found 21.3% of older adults were on at least one inappropriate medication and 2.6% received at least one "absolutely avoid" medication. Overall, 66 medications were identified as having the potential of severe adverse outcomes when used by older adults (Fick et al.).

Other tools that attempt to address the issue of polypharmacy include the Screening Tool of Older Persons Potentially inappropriate Prescriptions (STOPP) and the Screening Tool to Alert doctors to the Right Treatments (START) (Gallagher et al., 2008). These tools were developed to address errors of omission and commission. As a refinement of the Beers the STOPP/START tools focus on common prescribing patterns observed in older adults; these include: (1) duplication of drugs in the same class without optimizing monotherapy, (2) the use of furosemide for lower extremity edema without heart failure, (3) vasodilators in patients with persistent postural hypotension, and (4) the use of tricyclic antidepressant such as amitriptyline in patients with glaucoma.

The Assess, Review, Minimize, Optimize and Reassess (Hague, 2009) was developed more recently to consolidate recommendations in a tool that is easily implemented to address polypharmacy. Taking into account the patient's clinical profile and functional status this tool strives to balance evidence-based practices with altered physiological states. This tool also takes an interprofessional approach whereby input is obtained from healthcare professionals (i.e., physicians, nurses, physical therapists, occupational therapists, and pharmacist) to consider all aspects of the patient to maximize quality of life and patient preferences.

Utilizing assessment tools to evaluate patients' risk for adverse effects is a proactive way to prevent medication complications. Every healthcare professional caring for older adults can play a role in evaluating medications on a regular basis, be it in their homes or in the clinical setting. The healthcare professional needs to have a heighten level of suspicion when a new sign/symptom occurs in older individuals on multiple medications or when a new medication is added, especially if the individuals are on five or more medications.

Addressing Polypharmacy in the Case Presentation

M.M.'s medication regimen is concerning for a variety of reasons. First, she is taking an anticoagulant (clopidogrel) and aspirin, which can synergistically result in unexpected bleeding. She is on a potent diuretic (furosemide) despite the fact she has gout and is taking a gout medication, and no documented history of lower extremity swelling. Diuretics can exacerbate gout and should be avoided in this population if possible. She is also on two antipsychotic medications, one to treat her mood disorder and the other to treat her esophagus spasms. These medications in addition to her muscle relaxant can cause instability in balance rendering her at greater risk for falls. Further, amitriptyline and antihistamines could lead to excessive drowsiness, which may be a problem if she is taking them during the daytime hours. She is taking an anticonvulsant medication for her stroke without evidence of seizures. Her low hemoglobin and hematocrit levels are possibly due to her thalassemia trait so her ferrous sulfate is not effective in correcting her low blood indices. Additionally, she is on multiple medications, which could lead to headaches as an adverse effect. To treat her headaches she is taking additional medications. The only way to know if her headaches are due to an adverse effect of her medications is to wean her off these medications.

Based on the new guidelines for blood pressure treatment, M.M. may not need as many antihypertensive medications. At age 77, she would be prescribed medication therapy if her systolic blood pressure is 150 or greater and/or her diastolic pressure is 90 or greater. In addition, the November 2013 hyperlipidemia treatment guidelines advocate for statins (at low, moderate, or intense doses) as the only class of medication used to treat elevated lipid

levels. The fibrates, according to the new guidelines, have been relegated to the sideline and there are no guidelines to treat individuals 75 years and older and those with chronic kidney disease. Implementing this guideline M.M. might have her statin dose adjusted and her fenofibrate discontinued.

It should be noted M.M. did not report the use of herbal medications. Assessment of the use of herbals is necessary since individuals continue to believe herbals and supplements are safe and most are unaware of potential adverse effects when mixed with prescription medications. For example, herbal antidepressants are related chemically to monoamine oxidase inhibitor and if used in combination with a selective serotonin reuptake inhibitor (SSRI) can lead to a hypertensive crisis. Patients should be told not to mix herbals, supplements, and prescription medications without first inquiring with their primary care provider and pharmacist. Lastly, her antiepileptic medication might have been discontinued upon discharge from the hospital after her stroke if it was given to her as prophylaxis to prevent seizures.

Conclusion

Home healthcare clinicians can play a pivotal role in the prevention of adverse effects due to polypharmacy. Frequent reviews of medications should be carried out to verify current needs and should be augmented with education of patients and families about safe medication administration. It is important to remember medication adverse effects may not be obvious until medications are used for many years. The maxim in the care of geriatric patients is: less is sometimes more. ⌂

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