HHS Public Access

Author manuscript

Ann Longterm Care. Author manuscript; available in PMC 2016 June 21.

Published in final edited form as:

Ann Longterm Care. 2016 March ; 24(3): 37–40.

An Update on Geriatric Medication Safety and Challenges Specific to the Care of Older Adults

Michael Koronkowski, PharmD, CGP[1], **Christine Eisenhower, PharmD, BCPS**[2], and **Zachary Marcum, PharmD, PhD, BCPS**[3]

[1]University of Illinois at Chicago, College of Pharmacy, Chicago, IL

[2]University of Rhode Island, College of Pharmacy, Kingston, RI

[3]University of Washington, School of Pharmacy, Seattle, WA

Abstract

The prescribing of drug therapies in older adults presents a number of safety challenges. The increased complexity of chronic care for older adults has led to polypharmacy and potentially inappropriate medication use, which can contribute to drug-induced diseases, adverse drug reactions, drug interactions, cognitive impairment, falls, hospitalization, and mortality. In this review, the authors discuss recent medication safety literature pertaining to the classes of medications commonly prescribed to older adults: anticholinergics, psychiatric medications, and antibiotics. Safety concerns associated with the use of these medications and the implications for long-term care practitioners are reviewed. The information provided can be used to inform and improve geriatric care delivered by practitioners across health care environments.

Keywords

geriatrics; older adults; medication safety; adverse drug events; drug interactions; postmarketing surveillance

An aging population, so commonly treated by clinical practitioners, is presenting new drug therapy safety challenges. Increased complexity of chronic care among older adults has led to polypharmacy and potentially inappropriate medication use, which can contribute to drug-induced diseases, adverse drug reactions, drug interactions, cognitive impairment, falls, hospitalization, and mortality.[1] It is estimated that adverse drug reactions are approximately 7 times more common in persons greater than 70 years of age than in those younger than 70 years of age.[2] This update discusses how recent medication safety literature can inform and improve geriatric care delivered by practitioners across health care environments, with a focus on the classes of medications commonly prescribed to older adults: anticholinergics, psychiatric medications, and antibiotics. Safety concerns covered in this review include

Address correspondence to: Michael Koronkowski, University of Illinois at Chicago, Department of Pharmacy Practice (MC 886), 833 South Wood Street, 164 PHARM, Chicago, IL 60612-7230, koron@uic.edu, Phone: (312) 996-8865, Fax: (312) 996-0379.

Disclosures:
Dr Koronkowski is a consultant for OptumRx.

cognitive impairment and dementia, adverse drug events, drug interaction, emergency department (ED) visits, hospitalizations, and postmarketing drug safety surveillance.

Anticholinergics: Cognitive Impairment and Incident Dementia

Background

Medications with anticholinergic activity are commonly used and prescribed in older adults for a variety of conditions, including depression, Parkinson's disease, urinary incontinence, muscle spasms, allergies, intestinal motility, and pulmonary disorders. Often, these medications are initiated to manage symptoms rather than to resolve underlying disease pathology. These medications also tend to be nonselective in their mechanisms (leading to unwanted adverse effects) and may be continued without judicious reevaluation of efficacy and safety or de-prescribing considerations. It is important to note that randomized controlled trials evaluating anticholinergic agents are often underpowered to detect infrequent serious cognitive adverse events. Thus, epidemiologic studies are critical to better understanding the relative safety and efficacy of anticholinergic medication use in older adults.

Recent Findings

A recently published, population-based cohort study in adults older than 65 years of age (N = 3434; mean follow-up, 7.8 years) assessed the risk of new-onset dementia following longterm cumulative exposure to anticholinergic medications.[3] Study results indicated the highest risk exposure group (ie, exposure equivalents of oxybutynin 5 mg daily for >3 years) was associated with an increased risk of incident dementia (n=797, 23%) compared with low-risk exposure or no exposure (hazard ratio [HR], 1.54; 95% confidence interval [CI], 1.21–1.96). These findings are consistent with two cohort studies of shorter duration and a recent systematic review.[4]

Cautions

With observational studies of medication use, unmeasured confounding is a potential source of bias. However, this study controlled for a number of factors not usually available in studies only using administrative data, such as selfrated health and depressive symptoms. These new findings are consistent with previous observational studies addressing the association between cumulative use of strong anticholinergic agents and adverse cognitive effects.[5,6]

Implications for Practice

Given this emerging body of literature, use of medications with strong anticholinergic properties should be minimized, continued for the shortest duration possible, and prescribed at the lowest effective dose necessary to manage the symptoms and conditions commonly seen in older adults. Clinician, patient, and caretaker decisions should balance risk/benefit with re-evaluation, de-prescribing considerations, and alternative treatment strategies as supported by the 2015 Beers Criteria Update and Screening Tool of Older People's Prescriptions (STOPP) explicit criteria.[7,8]

Antipsychotics: Hospitalization and Acute Kidney Injury

Background

Evidenced-based guidelines caution against the use of atypical antipsychotic agents (AAPs) for the management of behavioral disturbances in dementia, except for short-term use in certain acute situations.[9] Randomized controlled trials demonstrate only modest benefit to patients at the price of increased morbidity and mortality. Despite these cautions, off-label AAP drug prescribing for older adults with dementia remains a common practice. An estimated 13.9% of older adults with Medicare Part D who live outside the nursing home setting and have a diagnosis of dementia are prescribed an antipsychotic agent. Therefore, a recent Government Accounting Office report aimed to extend efforts to curtail inappropriate use of AAPs beyond nursing homes to include other settings.[10]

Recent Findings

Hwang and colleagues examined a range of adverse outcomes in almost 100,000 older adult outpatients starting AAPs. The outpatients were followed for 90 days and were compared with a similar sample of nonusers via 5 linked Canadian administrative databases.[11] As expected, those treated with AAPs had a greater overall mortality (relative risk [RR], 2.39; 95% CI, 2.28–2.50) and a higher risk of pneumonia. In addition, AAP use was associated with a statistically significant increase in likelihood for hospitalization with acute kidney injury (n = 3592; odds ratio [OR], 1.70; 95% CI, 1.22–2.38) compared with no AAP use. Antipsychotic-induced hypotension (RR, 1.91; 95% CI, 1.60–2.21), and urinary retention (RR, 1.98; 95% CI, 1.63–2.4) are thought to contribute to this association.[11]

Cautions

Although large observational studies can provide insight into more specific and less common outcomes such as the findings outlined by Hwang and colleagues, there are reasons to be cautious in applying these findings to clinical practice. With observational studies, we can never be completely confident that matching or adjustment adequately accounts for unmeasured risk factors or confounders. For example, the acute agitation that prompts an AAP prescription may be triggered by an underlying illness that is the true cause of increased risk for acute kidney injury, hospitalization, and mortality. In addition, the study by Hwang and colleagues examined only three antipsychotic agents in a sample of older adults. Therefore, these results are not generalizable to younger adults or across all antipsychotic medications.

Implications for Practice

Clinician and caregiver decisions regarding the use of AAPs in the management of agitation and behavioral disturbances in dementia remains a challenge. Given the findings of Hwang and colleagues regarding hospitalization and acute kidney injury, more selective use of these drug treatment options should be considered. AAPs should only be used as a last resort when behavior poses a risk of harm to the patient and/or others and after nonpharmacologic interventions have been trialed.[7] The findings of Hwang and colleagues suggest the need to expand educational outreach efforts beyond nursing homes.

Antibiotics: Drug Interactions and Mortality

Background

Trimethoprim-sulfamethoxazole (TMP-SMX) is commonly prescribed to treat various infections in older adults with multiple chronic conditions, including renal impairment. TMP-SMX induces hyperkalemia by blocking sodium channels in the distal nephron.[12] Inhibitors of the renin-angiotensin-aldosterone system have become the mainstay of therapy for managing hypertension and heart failure, and they are also sometimes used with proteinuric kidney disease. Drug-drug interactions are more likely to occur with advancing age, increased serum creatinine, and a rising number of concurrently administered potassium-increasing drugs.[13]

Recent Findings

Fralick and colleagues examined the association between sudden death and exposure to antibiotics, including TMP-SMX, in participants 66 years of age or older treated with angiotensin-converting-enzyme inhibitors (ACE-I) or angiotensin receptor blockers (ARB) using a population-based nested cohort design. Results demonstrated TMP-SMX initiation to be associated with an increased likelihood of sudden death at 7 days (OR, 1.38; 95% CI, 1.09–1.76) and 14 days (OR, 1.54; 95% CI, 1.29–1.84), respectively.[14] A study by Antoniou and colleagues showed a similar association between TMP-SMX treatment and sudden death at 14 days (OR, 2.46; 95% CI, 1.55–3.90) in patients older than 66 years of age concurrently prescribed spironolactone.[15]

Caution

With observational studies of medication use, unmeasured confounding is a potential source of bias. Also, both of these studies evaluated older individuals with health problems, so the findings may not be generalizable to healthier or younger populations.

Implications for Practice

In older patients with several risk factors (impaired renal function, poor health, receiving multiple potassium-increasing drugs and receiving ACE inhibitors, ARBs, or spironolactone), the addition of TMP-SMX was associated with an increased likelihood of sudden death at both 1 week and 2 weeks. This finding may reflect sudden death from unrecognized hyperkalemia. As a precaution, clinicians should either select antibiotics that do not contain trimethoprim, or limit the dose and duration of trimethoprim-based therapies, while closely monitoring potassium concentrations in at-risk patients.

Psychiatric Medications: Adverse Events, Sedatives, and Healthcare Utilization

Background

Psychiatric medications such as antidepressants, antipsychotics, and sedatives are frequently used in older adults, yet they can often cause significant adverse outcomes. Recent data from studies,[16] the US Food and Drug Administration (FDA)[17,18] drug safety communications,

and the Drug Abuse Warning Network[19] have shown that ED visits for adverse drug events in patients using sedatives have risen. In addition, the use of sedative agents is associated with a substantial increased risk of falls. Although efforts to reduce inappropriate dosing and use of sedative agents have been strengthened through label changes[17,18] and incorporation into explicit Beers and STOPP criteria,[7,8] persistent overtreatment continues.[20]

Recent Findings

Hampton and colleagues evaluated ED visits resulting in hospitalizations due to psychiatric medication adverse events from 2009 to 2011 using a national emergency department public health surveillance dataset.[21] Their findings suggested that adults aged 65 years and older accounted for 17.3% of ED visits for an adverse drug event (ADE), with adverse drug reactions and unintentional overdose being the most likely cause of these reactions (85% of ADEs). Additionally, projection estimates of annual ED visits per 10,000 outpatient prescription visits demonstrated that sedatives and anxiolytics resulted in a 32% rate of hospitalization. While three-fifths of psychiatric medication ADE-related ED visits were due to 10 drugs, zolpidem alone accounted for more than 1 in 5 visits among adults 65 years and older.

Caution

Registry datasets, such as those detailing ED visits, are valuable to project trends and forecast population estimates. However, because datasets are often incomplete, clinicians are limited in the conclusions they can draw from them. In the ED dataset evaluated by Hampton and colleagues, attribution of ADEs to a particular medication is based on probability of cause and effect. In addition, inherent in this study design, physicians were asked to explicitly attribute the presenting symptom or diagnosis to a medication without knowing the patient's complete medications and comorbid conditions.

Implications for Practice

Recent postmarketing surveillance, FDA initiatives, and explicit criteria such as the Beers and STOPP criteria have heightened awareness of the risks of psychiatric medications, especially sedative use in older adults.[7,8] These findings support the need for strengthening measures targeting the use of "potentially inappropriate" sedative medications. Clinicians, patients, and caregivers should incorporate strategies such as sleep hygiene education, sleep restriction, relaxation training, and cognitive behavioral therapies into treatment plans before considering drug therapy. If psychiatric medications are used in older adults, efforts to limit the dose and duration of sedative medications, while closely monitoring for adverse outcomes, are essential.

Conclusion

This evidence-based medication safety literature update suggests that clinicians are continuing to prescribe medications to older adults that may result in overtreatment and adverse outcomes. These prescribing practices may contribute to possible preventable drug-induced diseases, adverse drug reactions, drug interactions, cognitive impairment, increased health care utilization, hospitalization, and mortality in older adults. Research shows that

overtreatment of older adults occurs across the full spectrum of primary care and institutionalization, and these findings reinforce how important it is for clinical practitioners to incorporate comprehensive medication management programs to address these challenges and enhance medication safety practices in the care of the elderly.

References

1. Steinman MA, Hanlon JT. Managing medications in clinically complex elders: “There’s got to be a happy medium”. JAMA. 2010; 304(14):1592–1601. [PubMed: 20940385]
2. Beard K. Adverse reactions as a cause of hospital admission in the aged. Drugs Aging. 1992; 2(4): 356–367. [PubMed: 1504448]
3. Gray SL, Anderson ML, Dublin S, et al. Cumulative use of strong anticholinergics and incident dementia: a prospective cohort study. JAMA Intern Med. 2015; 175(3):401–407. [PubMed: 25621434]
4. Ruxton K, Woodman RJ, Mangoni AA. Drug with anticholinergic effects and cognitive impairment, falls, and all-cause mortality in older adults: a systematic review and meta-analysis. Br Clin Pharmacol. 2015; 80(2):209–220.
5. Carriere I, Fourrier-Reglat A, Dartigues JF, et al. Drugs with anticholinergic properties, cognitive decline, and dementia in an elderly general population: the 3-city study. Arch Intern Med. 2009; 169(14):1317–1324. [PubMed: 19636034]
6. Jessen F, Kaduszkiewicz H, Daerr M, et al. Anticholinergic drug use and risk for dementia: target for dementia prevention. Eur Arch Psychiatry Clin Neurosci. 2010; 260(Suppl 2):S111–S115. [PubMed: 20960005]
7. The American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2015; 63(11):2227–2246. [PubMed: 26446832]
8. O’Mahony D, O’Sullivan D, Byrne S, O’Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older adults: version 2. Age Ageing. 2015; 44(2):213–218. [PubMed: 25324330]
9. Malone, M.; Ruelez, Maher A.; Hu, J., et al. Off-label use of atypical antipsychotics: an update. Agency for Health-care Research and Quality; Rockville, MD: Sep. 2011 Comparative effectiveness review No. 43
10. U.S. Government Accounting Office. Antipsychotic drug use: HHS has initiatives to reduce use among older adults in nursing homes, but should expand efforts to other settings. U.S. Government Accounting Office; 2015. GAO-15-211
11. Hwang YJ, Dixon SN, Reiss JP, et al. Atypical antipsychotic drugs and the risk for acute kidney injury and other adverse outcomes in older adults: a population-based cohort study. Ann Intern Med. 2014; 161(4):242–248. [PubMed: 25133360]
12. Velázquez H, Perazella MA, Wright FS, Ellison DH. Renal mechanism of trime-thoprim-induced hyperkalemia. Ann Intern Med. 1993; 119(4):296–301. [PubMed: 8328738]
13. Eschmann E, Beeler PE, Kaplan V, Schneemann M, Zünd G, Blaser J. Patient-and physician-related risk factors for hyperkalemia in potassium-increasing drug-drug interactions. Eur J Clin Pharmacol. 2014; 70(2):215–223. [PubMed: 24150532]
14. Fralick M, Macdonald EM, Gomes T, et al. Co-triamoxazole and sudden death in patients receiving inhibitors of renin-angiotensin system: population based study. BMJ. 2014; 349:g6196. [PubMed: 25359996]
15. Antoniou T, Hollands S, Macdonald EM, et al. Trimethoprim-sulfamethoxazole and risk of sudden death among patients taking spironolactone. CMAJ. 2015; 187(4):e138–143. [PubMed: 25646289]
16. Budnitz DS, Lovegrove MC, Shehab N, Richards CL. Emergency hospitalizations for adverse drug events in older Americans. N Engl J Med. 2011; 365(21):2002–12. [PubMed: 22111719]
17. U.S. Food and Drug Administration Drug Safety Communication. FDA approves new label changes and dosing for zolpidem products and a recommendation to avoid driving the day after

using Ambien. [safety announcement]. U.S. Food and Drug Administration. May 14. 2013 http://www.fda.gov/Drugs/DrugSafety/ucm352085.htm. Accessed on July 27, 2015

18. U.S. Food and Drug Administration Drug Safety Communication. FDA warns of next-day impairment with sleep aid Lunesta (eszopiclone) and lowers recommended dose. [safety announcement]. U.S. Food and Drug Administration. May 15. 2014 http://1.usa.gov/1l6FCs0. Accessed July 27, 2015
19. The DAWN Report: Emergency Department Visits for Adverse Reactions Involving Insomnia Medication Zolpidem. Center for Behavioral Health Statistics and Quality; Rockville, MD: May 1. 2013 [news release]
20. Top therapeutic classes by dispensed prescriptions (US). IMS Health. http://www.imshealth.com/files/web/IMSH%20Institute/Reports/The%20Use%20of%20Medicines%20in%20the%20United%20States%202010/Use_of_Meds_in_the_U.S._Review_of_2010.pdf. Accessed February 28, 2016
21. Hampton LM, Daubresse M, Chang HY, Alexander GC, Budnitz DS. Emergency department visits by adults for psychiatric medication adverse events. JAMA Psychiatry. 2014; 71(9):1006–1014. [PubMed: 25006837]