Prescribing Cascades in Older Adults

By Benjamin Webster, PharmD

Introduction
As patients age, the number of health care providers they see and comorbidities they are diagnosed with will inevitably grow. Because of this, drug therapy in geriatric patients can become complicated, often resulting in lengthy medication lists or polypharmacy. One factor that can increase this confusion is the phenomenon known as a "prescribing cascade." When an adverse event of one medication is inadvertently misdiagnosed as a new medical condition, a new medication may be prescribed to treat that condition. This unnecessarily increases a patient's pill burden, contributing to polypharmacy and increasing the risk for adverse events. Recognizing common prescribing cascades and eliminating unnecessary prescriptions can impact patient outcomes and decrease medication spending. This newsletter will review evidence on the significance and prevalence of one such prescribing cascade and identify other prescribing cascades that may be of concern in older patients.

DH-CCB/Loop Diuretic Cascade: A Case Report

In 2016, Nguyen and Spinelli described a prescribing cascade which contributed to a fall in an elderly woman. A 71-year-old woman was diagnosed with hypertension, and her family physician prescribed the dihydropyridine calcium channel blocker (DH-CCB) amlodipine. Three weeks later, the patient developed lower limb edema, a common dose-dependent adverse effect of DH-CCBs. While she had no diagnosed medical causes of edema, her cardiologist interpreted this as a new condition and prescribed two diuretics, furosemide and spironolactone.

Within three weeks, the patient developed urinary incontinence. As diuretics increase urinary frequency, they could potentially cause or exacerbate this condition. Her urologist again interpreted this as a new condition and prescribed fesoterodine, an anticholinergic drug. One month later, she had developed dry mouth, a well-established adverse effect of anticholinergic drugs, for which her family physician prescribed anetholtrithion.
After one more month, she lost her balance and fell while in the bathroom, resulting in multiple fractures. This fall was likely multifactorial, including causes such as medications, osteoarthritis, and a stroke from nine days prior.²

During the hospital stay following this patient's fall, a clinical pharmacist identified this prescribing cascade, and these five medications were discontinued. Following discontinuation, her urinary symptoms decreased. Then her dry mouth resolved. Lastly, her edema resolved. For treatment of her blood pressure, an angiotensin-converting enzyme inhibitor was prescribed instead of amlodipine.²

**DH-CCB/Loop Diuretic Cascade: Prevalence Study**

In a recently published observational study, Vouri et al. estimated the prevalence of this same prescribing cascade (DH-CCB resulting in peripheral edema then treated with a loop diuretic). Researchers used the National Ambulatory Medical Care Survey database to assess the percent of patient visits where a loop diuretic was started or continued in patients who were already on a DH-CCB. To limit visits to those without medical causes of lower extremity edema, patients were excluded if they had the following comorbid conditions: congestive heart failure (CHF), venous thromboembolism, obstructive sleep apnea, chronic kidney disease, end-stage renal disease, obesity, or resistant hypertension. A more sensitive secondary definition was also used, where only patients with CHF were excluded. Prevalence and factors associated with the prescribing cascade were assessed.⁶

The authors identified a potential prescribing cascade in 2.2 to 5.6 million patient visits out of the 47.5 million visits in which a patient continued taking a DH-CCB (4.6-11.8%). Visits with a potential prescribing cascade comprised 33.5-85.1% of visits with patients taking both a DH-CCB and a loop diuretic. The odds that patients between 65 and 84 years of age had this potential prescribing cascade were 2.56 times that of younger patients (OR 2.56, 95% CI 1.20-5.43), and patients over 85 had 3.89 times the odds (OR 3.89, 95% CI 1.76-8.61). Additionally, patients taking higher numbers of medications had increased odds of a prescribing cascade compared with those taking 0-4 additional medications. This was especially apparent in patients taking over 12 medications (OR 5.23, 95% CI 2.29-11.94).⁶

While this study explored the prevalence of prescribing cascades in the ambulatory care population, the patients at the highest risk of falling into this prescribing cascade were those of increased age taking a greater numbers of
medications. It is important to note that this study could only estimate the prevalence of potential prescribing cascades, as a true prescribing cascade can only be determined if the offending drug is withdrawn and the adverse event resolves. Nevertheless, this study highlights the importance of investigating patients taking both a DH-CCB and a loop diuretic to ensure that they have a true medical need rather than a drug therapy problem.

Other Prescribing Cascades
Many additional prescribing cascades have been identified in the literature. A selection of prescribing cascades which are potentially concerning in older adults are listed in the table below.¹

**Table. Selected Prescribing Cascades¹**

<table>
<thead>
<tr>
<th>Initial Drug Therapy</th>
<th>Misdiagnosed Adverse Event</th>
<th>New Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipsychotic</td>
<td>Parkinsonism</td>
<td>Antiparkinsonian agent</td>
</tr>
<tr>
<td>Cholinesterase inhibitor</td>
<td>Urinary incontinence</td>
<td>Urinary anticholinergic agent</td>
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<tr>
<td>Dihydropyridine calcium channel blocker</td>
<td>Edema</td>
<td>Loop diuretic</td>
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<tr>
<td>Nonsteroidal anti-inflammatory drug</td>
<td>Hypertension or increased hypertension</td>
<td>Antihypertensive agent</td>
</tr>
<tr>
<td>Thiazide or thiazide-like diuretic</td>
<td>Gout</td>
<td>Anti-gout agent</td>
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</tbody>
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Conclusion
The case report above illustrates how a prescribing cascade can come about and demonstrates why it should be of concern. As many practitioners and specialists take part in one patient’s care, they may interpret symptoms as a new medical condition without realizing that it could be a drug therapy problem, and so prescribe more medications. As was the case for this elderly woman, this cascade can increase the risk for more adverse events and continue to multiply the patient’s list of medications and comorbidities. The exploratory study above demonstrated that these prescribing cascades are especially prevalent in older patients and those taking a great number of medications. As over 30% of patients with both a DH-CCB and a loop diuretic may have a prescribing cascade, pharmacists should carefully consider whether there is a true medical need for these drugs, or whether alternative therapy may be simpler and safer. In addition to the DH-CCB/loop diuretic prescribing cascade, pharmacists should review patient medication lists for other potentially bothersome prescribing cascades (see Table above) and intervene as necessary.
References


   https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5be745f0-8ae7-4c3c-9962-37d6263326f1