Prescribing cascade in an elderly woman

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Background

Prescribing cascades usually occur when signs and symptoms of a patient are inaccurately assessed and an adverse drug reaction (ADR) is misinterpreted as a new condition, resulting in a new medication being prescribed.^{1,2} The prevalence of prescribing cascades is currently unknown. Prescribing cascades often lead to polypharmacy, especially in elderly people. In the United States, one study reported that 57% of women aged 65 years and older take 5 prescription drugs or more and 12% take more than 9.³ Polypharmacy is also a risk factor for ADRs, which cause 12% of all hospital admissions.⁴ Limiting prescribing cascades could therefore help to prevent ADRs.⁵

Case

A 71-year-old, 68.4 kg Caucasian woman with high blood pressure, type 2 diabetes, asthma, hypothyroidism, depression, osteoarthritis and Ménière's disease was admitted to the emergency department following a fall. She had had a stroke 9 days before the admission. The fall was attributed to gait and balance problems from multiple causes (osteoarthritis, deconditioning, drugs and stroke). Multiple fractures were identified in a lumbar spine X-ray.

Four months prior to this event, the patient's family physician had prescribed amlodipine 2.5 mg twice daily to control her blood pressure. Three weeks later, her cardiologist prescribed 2 diuretics: furosemide 20 mg and spironolactone 25 mg, to be taken once daily. The drugs were intended to treat edema of the lower limbs, which she had recently developed. Three more weeks passed and she was prescribed an antimuscarinic, fesoterodine 4 mg once daily, by her urologist, to treat her overactive bladder symptoms. One month after this, she complained of dry mouth to

her family physician, who prescribed anetholtrithion 25 mg 3 times a day. One month later, she lost her balance while washing in the bathroom, fell and knocked her head and back against her bathtub. With severe pain attributable to multiple fractures, she presented herself to the emergency department. The drugs for her other medical illnesses included metformin, fenofibrate, clopidogrel, rabeprazole, levothyroxine, potassium citrate, aripiprazole, citalopram, bupropion, hydroxyzine, ibuprofen and montelukast.

Discussion

This case illustrates the dynamics of a drug prescription cascade. Elderly persons are the most at-risk population for prescribing cascades, since they are often polymedicated. In this population, health problems frequently encountered, such as constipation, edema or urinary incontinence, often overlap with the adverse effects of medications.^{1,6} This patient was diagnosed with hypertension in the ambulatory setting and was prescribed an antihypertensive drug. A few weeks later, the woman experienced a dose-dependent adverse effect of the dihydropyridine calcium channel blockers. She had not been diagnosed with any medical cause of edema, such as heart failure, venous insufficiency or hypoalbuminemia. Peripheral edema is the result of vasodilation of local peripheral arterioles, probably induced in this case by amlodipine, since it was not present prior to the initiation of the drug. The prevalence of peripheral edema for calcium channel blockers is 8.9% and is higher in women. It is therefore important to consider them as a likely cause of peripheral edema, especially in women.^{7,8}

In this case, this symptom was interpreted as a new health issue by the second physician, who

FIGURE 1 Sequence of drug prescriptions

prescribed 2 diuretics (presumably for heart failure). Their pharmacologic effect increased the diuresis frequency and spawned urinary incontinence symptoms.⁹ Instead of attributing these symptoms to an ADR, the third physician diagnosed a new health problem and prescribed an antimuscarinic agent. Fesoterodine is known for its strong peripheral anticholinergic effect, which in this case resulted in dry mouth.¹⁰ Furosemide also possesses an anticholinergic load that could have contributed to xerostomia and could also lead to dehydration.¹¹ This symptom was again misinterpreted as a new health problem by the first physician, who prescribed anetholtrithion (Figure 1), an agent that acts directly on the cells of salivary glands to stimulate salivation.¹¹ Xerostomia may be encountered in 19% to 35% of patients taking fesoterodine, and the effect is dose dependent.

The etiology of falls is often multifactorial. In this situation, fesoterodine and furosemide might have contributed, taking into account their anticholinergic drug load.¹¹ Dizziness and vision disorders reported with fesoterodine could also be a contributing factor.¹² Lying down followed immediately by sitting blood pressure did not show orthostatic hypotension. Finally, aripiprazole, citalopram and bupropion, regular medications of the patient, are also associated with an increased risk of falls.¹³

During the first days of the patient's hospital stay, the clinical pharmacist identified the prescribing cascade, and the lead geriatrician stopped amlodipine, spironolactone, furosemide, fesoterodine and anetholtrithion. A few days later, the patient's urinary symptoms decreased, followed by a resolution of her dry mouth within a week and then resolution of the edema. To reduce blood pressure, amlodipine was replaced with an angiotensin-converting enzyme inhibitor. After a 14-day hospital stay and resolution of her symptoms, the patient was transferred to a geriatric rehabilitation centre.

This article aims to increase prescribers' and pharmacists' awareness of drug-prescribing cascades, an area often neglected in elderly patients. In this case, the involvement of many prescribers and a suboptimal review of drug history at medical appointments and in the community pharmacy potentially contributed to the development of the drug cascade. Until the end of 2014, the province of Quebec did not have a centralized information database of current and past drug prescriptions accessible to physicians and pharmacists. This often led to incomplete information about drug history. To prevent this kind of incident, it is important to consider each new sign and symptom as a potential adverse effect, especially if a new drug was recently started or if a dose was recently changed. A complete review of drug therapy, including prescription, over-the-counter medications and natural health products, should be carried out at each medical appointment and visit to the community pharmacy. In addition, it is essential to evaluate the relevance of a new treatment and to avoid polypharmacy. If the initiation of treatment is deemed necessary, low doses should first be prescribed to reduce the risk of side effects, particularly in elderly patients. Patient education is a key factor in the detection of adverse reactions. Physicians and pharmacists should inform patients of the most likely ones and prompt them to consult a health care provider if these or any other type of reactions occur. At follow-up visits, physicians should question the patient on the efficacy and side effects of drugs.

Prescribing cascades attract little attention from clinicians and investigators despite their potential impact on patients' health and quality of life. As highlighted in this article, physicians and pharmacists should work together in the detection and resolution of prescribing cascades. Research is also needed in this field, as epidemiological data are lacking to determine the possible causes and risk factors of this specific problem. ■

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