Teachable Moment | LESS IS MORE

Missed Opportunities for Deprescription
A Teachable Moment

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Story From the Front Lines

An 88-year-old man presented to the emergency department with episodic light-headedness and dizziness of 4 days' duration without vertigo. He had experienced these symptoms 3 years earlier during an episode of hypoglycemia. His medical history included diabetes, hypertension, chronic renal insufficiency without proteinuria (estimated glomerular filtration rate [eGFR] by Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] equation, 20 mL/min/1.73 m^2), dyslipidemia, atrial fibrillation, and gout. Prior to arrival, multiple home capillary glucose measurements confirmed hypoglycemia of less than 3.9 mmol/L (reference range, 3.9-11.1 mmol/L). (To convert glucose from mmol/L to mg/dL, multiply by 18.) Medications included warfarin, atorvastatin, acarbose, metformin, gliclazide, valsartan, perindopril, and indapamide.

On examination, his blood pressure was 160/60; pulse was 65 bpm and irregularly irregular. He was not hypoxemic on ambient air, was afebrile, and the remaining findings of a focused physical examination were normal, apart from a low jugular venous pressure seen at the level of the sternal angle. Laboratory investigations revealed an elevated serum potassium level of 6.1 mEq/L (reference range, 3.5-5.5 mEq/L), acute on chronic kidney injury with serum creatinine level of 593 µmol/L (reference range, 70-120 µmol/L; CKD-EPI eGFR <10 mL/min/1.73 m^2), and capillary glucose level of 1.7 mmol/L. Glycosylated hemoglobin (HbA_{1c}) reading from 1 month earlier was 7.4% (reference range, 4.0%-5.6%).

Following investigations, these hypoglycemic episodes were believed to be caused by decreased renal clearance of the oral hypoglycemic agent gliclazide. It was noted that for the past 2 years, the patient had been simultaneously prescribed an angiotensin converting enzyme inhibitor (ACEi) and an angiotensin receptor blocker (ARB). Treatment with both of these medications was discontinued, and after he was intravenously rehydrated with a dextrose-containing solution, the hypoglycemia resolved, and renal function returned to baseline.

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Combination therapy with ACEi and ARB was first recommended for patients with diabetes and proteinuria on the basis of several clinical trials showing reductions in proteinuria. Some of these publications have since been retracted, and despite early enthusiasm, combination therapy has subsequently not been shown to improve morbidity or mortality.[1] Prescribing both classes of drugs concurrently is associated with adverse drug events (ADEs) including acute kidney injury and hyperkalemia.[1] Recognizing this, professional societies now recommend against combination therapy for the treatment of hypertension, diabetic nephropathy, and heart failure.[1]

The present patient's diabetic regimen included metformin and a sulfonylurea, which in the context of preexisting renal disease carry an elevated risk of hypoglycemia. Based on the patient's age and renal function, these oral hypoglycemic agents are potentially inappropriate medications, according to expert-derived consensus lists created to guide medication appropriateness in older adults.[2] Although an individualized HbA_{1c} target reading of 7.5% to 8.5% may avoid overtreatment in vulnerable populations, an estimated 50% of older adults with comorbid conditions placing them at risk for hypoglycemia still have tight glycemic control (HbA_{1c}, <6% to 7%).[3]

Through more in-depth chart review of the present case, it became apparent that other physicians had recognized that this patient's ACEi and ARB were no longer recommended in combination. Nonetheless, when he was treated as an outpatient with his blood pressure well controlled, in the absence of an ADE, his prescriptions were not adjusted. Therapeutic inertia is a common occurrence perpetuated by the belief that the absence of a prior adverse event implies that a future one is unlikely to occur coupled with a fear of negative consequences occurring as a direct result of change. In retrospect, this older patient taking 5 or more medications met the definition for polypharmacy, and there were several missed opportunities for deprescribing. Stopping either the ACEi or ARB treatment along with 1 or both of the oral hypoglycemic agents might have avoided 3 life-threatening ADEs (hypoglycemia, hyperkalemia, and acute kidney injury). In light of possible diminishing returns from tighter blood pressure and glucose control, this patient might have benefited from deprescribing.

Scott et al define *deprescribing* as the "systematic process of identifying and discontinuing drugs in instances in which existing or *potential* harms outweigh existing or *potential* benefits [emphasis added]."[4(p827)] They outline a stepwise approach to managing polypharmacy. While the evidence of benefit from systematic deprescribing remains in its infancy, it is generally believed to be beneficial. Prescribing based on clinical trial evidence is well taught throughout medical training; however, for many programs there is less emphasis placed on discontinuing potentially inappropriate medications or those with diminishing returns.

The present case highlights the importance of a regular, formalized reappraisal of patient medications with deintensification or deprescription for those patients for whom the risks of ADEs (even for events that have not yet occurred) likely outweigh the benefits. With an estimated 9.7 per 1000 emergency department visits by older adults occurring as a direct result of an ADE,[5] deprescribing is one means by which we can begin to improve patient care. Factoring in the present patient's favorable attitude toward a reduced pill burden, he was discharged on a regimen appropriate for his age, comorbidities, and renal function: linagliptin, warfarin, atorvastatin, and amlodipine.

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