Reducing pill burden and helping with medication awareness to improve adherence

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Introduction

Medication nonadherence can be intentional when polypharmacy and high pill burden become overwhelming for patients. At the Bruyère Geriatric Day Hospital (GDH), patients referred for medication review take an average of 15 medications.¹ The resulting complex regimens can lead to confusion about indications for medications, lack of certainty in their effectiveness and frustration. Patients increasingly believe that the multiple medications may not be needed and often elect to stop taking some or all of them.

This case illustrates an approach to reducing the pill burden of polypharmacy that includes eliminating medications that are not working or are potentially harmful, reducing dosing frequency and using fixed combination products. Ultimately, identifying barriers to adherence and enhancing the patient's understanding of the indication and proper use of medications, while reducing pill burden, assisted in improving adherence and disease control during a 12-week admission. A description of the GDH processes and in particular, communication about medication-related care, can be found in Appendix 1 (www.cpjjournal.ca).

Patient case

A 78-year-old woman was referred to the GDH for assessment of cognition and review of her multiple medical problems. Her past medical history included hypertension, diabetes,

dyslipidemia, a recent stroke, hypothyroidism, osteoporosis, gout, restless leg syndrome and psoriatic arthritis. She had recently scored 14 of 30 on the Montreal Cognitive Assessment (MOCA) (normal being ≥ 26) (www.mocatest.org). At the initial assessment, her daughter raised concerns about progressive memory loss and reported a family history of Alzheimer disease. Low mood/unresolved grief, decreased mobility and endurance, and ongoing pain (particularly in her right heel) were also identified as active issues. The patient was independent with her activities of daily living and shared responsibility for household tasks with her spouse but reported increasing difficulty with dressing and cooking, in particular.

The patient was taking 27 medications and had a 4-times-a-day medication regimen. She reported filling and managing her dosette independently but was unable to answer many questions posed about her medications. She stated that she was "tired of taking medications." Her daughter had observed errors such as not reading vial labels and forgetting to put medications in afternoon slots. The patient also brought with her an empty mirtazapine bottle that contained a few ranitidine tablets.

The initial medical assessment identified multiple issues: cognition, mood, pain, mobility and falls, vascular risk factors, polypharmacy and medication nonadherence, lower-extremity edema and need for community integration and

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supports. Hypertension (blood pressure [BP] 166/68 mmHg on admission) and poor glycemic control (hemoglobin A1c 8.5% on admission) were noted despite multiple medications, previous emergency room visits and multiple specialist follow-ups for each. Blood work revealed vitamin B₁₂ levels of 1110 pmol/L; creatinine clearance (CrCl) was 43 mL/min (using the Cockcroft-Gault equation with ideal body weight).

The GDH pharmacist, nurse, social worker, occupational therapist and physiotherapist were consulted. The GDH pharmacist conducted a medication assessment that included a 45-minute comprehensive patient interview, chart review and communication with both the family and the community pharmacy. Each medication was assessed for indication, effectiveness, safety, compliance and patient understanding.² The results of the initial part of this assessment are outlined in Table 1.

STOP HERE: If you are using this case report for group discussion, go to Appendix 2 (www.cpjjournal.ca) for instructions, discussion questions and blank worksheets. You may print out the above case description and Table 1 for discussion prior to moving on to reading about the results of the medication assessment.

Signs and symptoms were assessed to determine potential drug causes, and drug-related problems were identified.³ The complete medication assessment is outlined in Table 2.

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With the patient's agreement, and the optimization of BP and glycemic control identified as priorities, along with reducing pill burden and improving adherence, the following changes were made: tramadol, vitamin B₁₂, aliskiren, hydralazine, pantoprazole and fluticasone were discontinued and the doses of calcium and allopurinol were reduced. Separate metformin and sitagliptin tablets were replaced with combination metformin/sitagliptin. Amlodipine and simvastatin were replaced with combination amlodipine/atorvastatin. Twice-daily labetalol was replaced by once-daily bisoprolol and the gliclazide modified

KNOWLEDGE INTO PRACTICE

- Consider nonadherence and pill burden as possible reasons for suboptimally controlled chronic conditions.
- Reassess each medication for ongoing indication.
- Engage other team members in managing symptoms such as pain.
- Use once-daily dosing options instead of multiple daily doses.
- Use fixed combination tablets where possible to reduce pill burden.

release (MR) was changed from two 30 mg tablets to one 60 mg tablet. A combination hydrochlorothiazide/valsartan pill was added. The result was a previously 4-times-a-day regimen simplified to twice a day.

Once the new regimen was established, the nurse worked with the patient to have her practise filling the dosette. The pharmacist met routinely with the patient to improve medication awareness using a written medication chart that included reasons for use, goals, changes and progress. The patient was subsequently observed by the nurse to make fewer and eventually no errors in filling her dosette. Both BP control (BP = 148/65 on last visit) and glycemic control (postprandial blood sugar 6.4-9.9 mmol/L) improved. A 5 kg weight loss was also recorded. The occupational therapist addressed the foot pain by recommending orthotics and a 4-wheeled walker, eliminating the need for additional analgesics. Endurance improved with twice-weekly physiotherapy and exercises (6-minute walking distance increased from 770 to 1050 feet). The patient reported improved mood as a result of supportive counselling with the social worker in addition to increased opportunities for socialization during her visits. She gradually became more actively involved in and confident about the management of her conditions. Cognition was retested before discharge. The patient's Mini-Mental State Examination score was 28 of 30 (with spelling) and 24 of 30 (with calculation). Her MOCA score had improved to 21 of 30 with intact delayed recall and points primarily lost on visuospatial/executive tasks. These findings were felt to represent mild vascular cognitive impairment.⁴ These deficits, made worse by anxiety over multiple medication changes and coupled with a long-standing history of tending to "rush" through tasks, might have contributed to previous errors in filling the dosette, as well as nonadherence. To ensure continued adherence,

TABLE 1 History of medication experience

#	Drug	Reason for use (if known)	Knowledge, efficacy, compliance, goals, safety assessment	Duration* (if known)
1	Amlodipine 10 mg daily	Hypertension	166/68 mmHg on admission	?
2	Aliskiren 300 mg daily	Hypertension		~1 year?
3	Valsartan 320 mg daily	Hypertension	Dose doubled recently because of high BP	7 months
4	Labetalol 200 mg twice daily	Hypertension	Changed from acebutolol for more vasodilation due to high BP	7 months
5	Hydralazine (directions unknown)	Hypertension	Added by internist because of high BP; not taking routinely	6 months
6	Furosemide 40 mg daily	Bilateral leg + ankle edema	Patient states feet and legs swollen; feels legs are not as hard now	6 months
7	ASA 81 mg daily	CVA 9 months previously	Had taken previously but stopped, restarted after CVA Patient currently has some bruising	~9 months
8	Simvastatin 10 mg daily	CVA 9 months previously	Recent LDL = 1.7 mmol/L, total cholesterol = 3.7 mmol/L	~2 years
9	Metformin 500 mg, 2 twice daily	Diabetes	No gastrointestinal side effects reported; HbA1c = 8.5%	?
10	Gliclazide MR 30 mg, 2 daily	Diabetes	Patient did not recall the drug during interview	?
11	Sitagliptin 100 mg daily	Diabetes	Patient did not recall the drug during interview	2 months
12	Fluticasone 250 mcg, 2 puffs twice daily	Cough and wheezing	Patient states started for cough after pneumonia; now uses when needed for morning wheezing; states has never had asthma or emphysema and never had inhalers prior to this	1 year
13	Salbutamol when needed	?	Patient states uses with fluticasone	1 year
14	Risedronate 35 mg on Wednesday	Osteoporosis	Patient thinks for back pain and states it does not work; takes appropriately	?
15	Calcium twice daily (dose unknown)	Osteoporosis	Patient thinks calcium purpose is to improve brittle nails	?
16	Vitamin D daily (dose unknown)	Osteoporosis		?
17	Levothyroxine 0.088 mg each morning	Hypothyroidism	TSH = 0.66 mIU/L	?
18	Pramipexole 0.25 mg at bedtime	Restless leg syndrome	Patient states has helped significantly with leg cramping at night	?
19	Psyllium twice daily	Constipation	Patient states has no problems with constipation	?
20	Acetaminophen + methocarbamol 325/400 mg 2 each morning	Pain	Takes 2 each morning and back pain is "good for the day"	?

#	Drug	Reason for use (if known)	Knowledge, efficacy, compliance, goals, safety assessment	Duration* (if known)
21	Tramadol (dose unknown)	Pain	Patient states she often forgets to take tramadol as it "doesn't do much for pain"	?
22	Allopurinol 250 mg daily	Prevention of gout	Patient describes 2 gout attacks in past; ankles affected and couldn't walk	Years
23	Betamethasone cream	Psoriasis	Patient states does not help with psoriasis	?
24	Calcipotriene at bedtime	Psoriasis	Patient unsure if helping with psoriasis	?
25	Vitamin B ₁₂ daily (dose unknown)		Recent B ₁₂ levels = 1110 pmol/L	?
26	Pantoprazole 40 mg daily	Unclear	Patient does not have heartburn or history of ulcer	?
27	Ranitidine 150 mg when needed	Unclear	Patient carrying in old mirtazapine bottle but not using	?

*Duration of therapy difficult to ascertain in many cases as patient gave conflicting information.

Past medications included Tylenol #3, indapamide, iron supplement, pioglitazone, acebutolol, hydroxychloroquine, Symbicort and mirtazapine. ASA, acetylsalicylic acid; BP, blood pressure; CVA, cerebrovascular accident; HbA1c, glycosylated haemoglobin; LDL, low-density lipoprotein; MR, modified release; TSH, thyroid stimulating hormone.

her daughter was engaged to observe filling of the medication organizer during their regular Sunday visits. Steps taken to implement the action plan are outlined in Table 3, and a final medication list is presented in Box 1.

Discussion

The large number of medication doses, in addition to multiple recent medication changes, were likely contributing to our patient's anxiety, confusion and subsequent lack of adherence. These concerns were addressed using a systematic approach. Medications with no clear indications were stopped, along with those that were ineffective and not associated with adverse drug withdrawal events. Medications that increased the risk of adverse drug reactions were also stopped. Fixed combination formulations were used to further reduce pill burden. The strategy employed was to group changes in a way that did not interfere with monitoring for potential adverse effects. Throughout, medication understanding was increased by having the patient agree to each change, understand the underlying reason, monitor the impact and report back to the team. In addition, repeated teaching to facilitate filling of the dosette and medication taking resulted in fewer dosing errors.

Reducing use of unnecessary medications and doses

Continued use of medically unnecessary medications contributes to polypharmacy and carries with it an increased risk of falls, adverse drug events and mortality.⁵ Physicians are often reluctant to stop medications when they have been started by a colleague, when their length of use or original indication is unclear, or if the patient perceives this to signify that the physician is giving up on him or her.⁶ Medications may be unnecessary if they are continued despite lack of evidence for symptomatic effectiveness, when treatment is complete, when indications for ongoing use of medications are unclear or when doses are too high and have not been individualized.

The patient was unsure about the effectiveness of the tramadol in controlling her pain, and it was stopped with no subsequent worsening of pain. Her high B₁₂ level suggested no further need for B₁₂ supplementation, and it was stopped. The benefit of continuing the pantoprazole was unclear as the patient did not have heartburn, an ulcer history or other indication. It was tapered by changing to rabeprazole 10 mg daily (the only low-dose proton pump inhibitor covered by the Ontario Drug Benefit Program) and subsequently stopped with no heartburn

TABLE 2 Medication care plan

#	Drug-related problem	Action plan	Monitoring (team)
1	Pain not relieved by tramadol; not needed	Stop tramadol	Pain
2	B ₁₂ level = 1110 pmol/L; B ₁₂ not needed	Stop B ₁₂	
3	Pantoprazole may not be needed (no heartburn, ulcer history or NSAID use)	Stop pantoprazole and start rabeprazole 10 mg daily for 2 weeks; use ranitidine as needed for rebound heartburn	Heartburn (2-4 weeks afterward)
4	Patient does not have asthma or COPD; no need for ongoing fluticasone or salbutamol	Stop fluticasone; reassess need for salbutamol	Wheezing or coughing
5	Twice-daily calcium not needed as dietary intake is 500 mg	Decrease calcium to 1 daily; will find calcium/vitamin D combination acceptable to patient	
6	Due to low CrCl, decrease allopurinol to 200 mg daily	Decrease allopurinol to 200 mg daily (ask pharmacist to dispense one 200 mg, not two 100 mg tablets)	
7	Increased risk of hypotension, hyperkalemia, renal complications secondary to combination of aliskiren and valsartan	Stop aliskiren	BP target: <130/80 mmHg
8	BP control suboptimal; consider adding HCTZ 12.5 mg daily in combination with valsartan (risk of gout associated with HCTZ is dose related)	Change valsartan to valsartan/HCTZ 320/12.5 mg daily	BP target: <130/80 mmHg Avoid HCTZ dose >12.5 mg daily
9	Reconsider need for hydralazine given not taken routinely	Stop hydralazine	BP target: <130/80 mmHg
10 11 12 13	To reduce pill burden: • Switch labetalol to bisoprolol • Combine metformin and sitagliptin • Combine amlodipine and statin • Change gliclazide to 1 instead of 2 pills	<ul style="list-style-type: none"> • Stop labetalol and start bisoprolol 10 mg daily; confirm with internist BP was only labetalol indication • Stop metformin, stop sitagliptin; start metformin/sitagliptin 1000/50 mg twice a day • Stop amlodipine, stop simvastatin; start amlodipine 10 mg/atorvastatin 10 mg daily • Stop gliclazide MR 30 mg; ask pharmacist to dispense gliclazide MR 60 mg daily 	BP target: <130/90 mmHg HbA1c <7% Fasting BG: 4-7 mmol/L PP BG: 5-10 mmol/L

BG, blood glucose; BP, blood pressure; COPD, chronic obstructive pulmonary disease; CrCl, creatinine clearance; HbA1c, glycosylated hemoglobin; HCTZ, hydrochlorothiazide; MR, modified release; NSAID, nonsteroidal anti-inflammatory drug; PP, postprandial.

within the 2- to 4-week usual rebound period.⁷ The ongoing indication for fluticasone was unclear and it was stopped with no worsening of respiratory function. The calcium supplement dose was reduced to once daily after dietary intake of calcium was assessed.

Optimizing medication choices according to risk/benefit

Optimizing medication use in the elderly can be challenging on a number of fronts. Changing pharmacodynamics can make older

people more sensitive to the adverse effects of medications, such as orthostatic hypotension with antihypertensives.⁸ Changes in absorption, distribution, metabolism and excretion mean that medication choices and doses need to be carefully checked to minimize risk of adverse effects.⁹ As in this case, periodic nonadherence can also make assessing medication effectiveness difficult.

Two medications identified as being potentially more risky than beneficial were hydralazine and aliskiren. Hydralazine had

BOX 1 Medication schedule at GDH discharge**Breakfast**

Amlodipine/atorvastatin 10/10 mg
 Valsartan/hydrochlorothiazide 320/12.5 mg
 Bisoprolol 10 mg
 Furosemide 40 mg
 Acetylsalicylic acid 81 mg
 Metformin/sitagliptin 1000/50 mg
 Gliclazide modified release 60 mg
 Calcium 500 mg
 Vitamin D 1000 units
 Levothyroxine 0.088 mg
 Acetaminophen/methocarbamol 325/400 mg

Bedtime

Metformin/sitagliptin 1000/50 mg
 Pramipexole 0.25 mg
 Allopurinol 200 mg

Every Wednesday

Risedronate 35 mg

As needed only

Ranitidine 150 mg
 Salbutamol 1-2 puffs every 4 hours
 as needed for wheeze or increased shortness of breath
 Restart regular psyllium if constipation becomes a problem

been added recently by the patient's internist in an attempt to control blood pressure. However, widely variable readings, ranging from as low as 115/61 mmHg to as high as 229/86 mmHg, despite use of 5 antihypertensives, strongly suggested inconsistent medication use. The hydralazine was likely added when nonadherence to the other medications resulted in high BP readings. Given the known risks of orthostatic hypotension and our suspicion that the hydralazine was not taken consistently, it was stopped. In renally impaired, diabetic patients (CrCl <60 mL/min) taking an angiotensin receptor blocker (ARB), the addition of aliskiren can increase the risk of hyperkalemia, hypotension and renal complications and is unlikely to be of benefit in preventing cardiovascular or renal events.¹⁰ When the internist was contacted regarding its potential discontinuation, he was surprised that it was still being taken, as he previously verbally instructed the patient to stop it. This highlights the need for effective written communication

between health care professionals and patients regarding stoppage of a medication.

Amlodipine was initially thought to be contributing to bilateral lower extremity edema and was therefore tapered as well. However, an increase in blood pressure prompted us to reincrease the dose to 10 mg daily with no worsening of the edema noted.

To optimize blood pressure control and reduce risk of renal complications from diabetes, hydrochlorothiazide (HCTZ) was added and given in combination with valsartan (valsartan/HCTZ tablet). This combination has been shown to confer significant renal benefits in patients with type 2 diabetes mellitus and also has blood pressure lowering effects.¹¹ It is possible HCTZ was not prescribed previously because of the patient's gout history; however, doses of HCTZ less than 25 mg daily have not been shown to increase the likelihood of needing acute gout treatment.¹²

Finally, in collaboration with the internist, a sleep study was organized and a new diagnosis of sleep apnea was confirmed. This may have been an additional contributor to her hypertension.¹³

The risk/benefit of acetaminophen/methocarbamol was also examined. Methocarbamol can worsen cognition, but the patient found the combination extremely effective in controlling pain and, as a result, elected to continue the medication despite this risk.

Strategies to reduce pill burden and improve medication adherence

The use of combination formulations is an emerging method to reduce pill burden, particularly in patients with multiple chronic conditions, and is an appropriate approach in Ontario, where such formulations are covered by the Ontario Drug Benefit Program. Combination formulations have been shown to produce cost savings and reduce nonadherence by up to 26%.^{14,15} We combined metformin and sitagliptin, as well as amlodipine and atorvastatin, thereby cutting 8 pills down to 3. Twice-daily labetalol was switched to once-daily bisoprolol with the internist's agreement, while gliclazide MR dosing was switched from two 30 mg tablets to one 60 mg tablet daily to further reduce pill burden. The dose of allopurinol was decreased slightly so that one pill could be taken instead of two and a half; this medication change was well tolerated with no resulting episodes of gout during the 12-week program admission.

TABLE 3 Intervention timeline

Initial pill burden: ≈ 29 pills/day Initial number of medications: 27	
Week 1	<ul style="list-style-type: none"> • Decrease amlodipine dose to 2.5 mg daily every morning
Week 3	<ul style="list-style-type: none"> • Increase amlodipine dose to 10 mg daily every morning (blood pressure: 192/83 mmHg)
Week 6	<ul style="list-style-type: none"> • Stop tramadol • Decrease allopurinol to 200 mg daily
Week 9	<ul style="list-style-type: none"> • Stop vitamin B₁₂ • Stop pantoprazole • Start rabeprazole 10 mg daily every morning for 2 weeks, then stop
Week 10*	<ul style="list-style-type: none"> • Stop aliskiren, hydralazine, labetalol, valsartan, metformin, sitagliptin, amlodipine, simvastatin and fluticasone • Start bisoprolol 10 mg every morning • Start valsartan/hydrochlorothiazide 320/12.5 mg every morning • Start metformin/sitagliptin 1000/50 mg twice daily • Start amlodipine/atorvastatin 10/10 mg every morning • Decrease calcium to once daily every morning
Final pill burden: ≈ 14 pills/day Final number of medications: 20	

*During the first part of the admission, efforts focused on understanding and addressing barriers to adherence, clarifying indications with prescribers and monitoring control of chronic disease. Once this took place, we established that the dosages for most medications were appropriate, which allowed us to consolidate using combination or once-daily pills. Medications not needed (hydralazine, fluticasone) or contraindicated (aliskiren) were stopped.

These changes allowed for a simplified twice-daily dosing regimen with a much reduced overall pill burden. The nurse next focused on teaching filling of the dosette in a stepwise approach: reading the vial label, turning the vial upside down once that medication was added to the dosette and doing a visual double-check before closing the lid. With written instructions and continued monitoring by the nurse at each visit, the number of filling errors was noted to be greatly reduced. A medication chart, outlining specific reasons for each medication, and a description of and rationale for changes, was prepared by the pharmacist and reviewed periodically with the patient; a final copy was sent to the family doctor with the discharge summary. The patient was encouraged to share this chart as a communication tool with all health care providers. At the end of her admission, the patient was judged by both the GDH team and her family to have much improved medication awareness and adherence.

Conclusion

This case demonstrates how a team (including the patient and family) can work together to improve medication adherence and, as a result, control of chronic disease. A complex medication regimen, high pill burden and multiple medication changes can lead to nonadherence and poor management of chronic conditions. Careful reduction in the use of unnecessary or unsafe medications, use of combination and once-daily formulations, and patient education and monitoring were all shown to be effective strategies in managing polypharmacy, reducing pill burden and improving medication management. We have previously identified cases of intentional medication nonadherence due to lack of medication awareness and complex medication regimens.¹⁶ All of these cases highlight the importance of simplifying dosing regimens and providing education and monitoring. We encourage all pharmacists, whether they work

in hospital or primary care settings, to adopt these strategies and work together with other health care professionals to help older adults feel more confident in managing their medications.

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KEY RESOURCES

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