Medication-induced diabetes urgencies

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Many medications commonly used by people with diabetes have potential adverse effects or interactions with other medications that can result in emergency care being required. Red flags identifying people at high risk of such problems are renal impairment, patient frailty, polypharmacy and nonadherence.

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People with type 2 diabetes are often taking hypotensive and hypolipidaemic medications and antiplatelet agents as well as medications for their diabetes. They also may be taking other prescription medications to treat comorbidities, using various complementary medications and intermittently adding further medications and/or stopping current ones. Both the polypharmacy and the changing mixture of medications put these patients at risk of direct medication side effects and of medication interactions, some of which can be dangerous (Table 1).

Using two cases, this article reviews the problems that can occur from medications commonly used in type 2 diabetes – hypoglycaemic, hypotensive and hypolipidaemic medications and antiplatelet agents. 'Red flags' that identify patients with diabetes who are likely to have medication-induced emergencies are also discussed.

HYPOGLYCAEMIC AGENTS

Case 1 – background

Sally is 82 years old and was widowed seven years ago but continues to live in the small house in which she and her husband raised their family. She manages the house and garden with help from a weekly cleaner and one of her daughters, Anna, who lives in the area. Anna has arranged for her mother to ring her at 8 a.m. each morning so Anna will know she is okay. Sally has had diabetes for 11 years and over the past two to three years her blood glucose level has gradually crept up (glycosylated haemoglobin

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[A_{1c}] now 9.7%) but she has refused to start using insulin. Her hypoglycaemic medication includes maximum doses of glimepiride (4 mg/day), metformin (1 g twice daily) and pioglitazone (45 mg/day).

Potential disasters

The following are disasters waiting to happen with Sally.

- *One morning Anna does not get her 8 a.m. call. She goes to her mother's house and finds Sally unconscious on the kitchen floor.*
- *When gardening one afternoon, Sally notes some chest discomfort and feels 'dizzy'. She contacts Anna, who takes her to the Emergency Department of the local hospital. Sally is admitted, but dies later that night.*
- *Sally is very fond of Chinese food and on her birthday Anna and another of Sally's daughters take her to a Chinese banquet. That night, Sally becomes progressively short of breath, is frightened and rings for an ambulance.*

Side effects of oral hypoglycaemic agents

Most of the side effects associated with the oral hypoglycaemic agents (OHAs) are a 'nuisance' but some are dangerous (Table 2). The above scenarios of severe hypoglycaemia, lactic acidosis and cardiac failure are some of these dangerous problems.[1]

Severe hypoglycaemia

The long-acting sulfonylureas, glibenclamide and glimepiride, can cause severe and prolonged hypoglycaemia if renal function is impaired because these sulfonylureas and/or their active metabolites accumulate as renal function deteriorates. This may be interpreted as the onset or worsening of dementia, and may only become apparent as hypoglycaemia when unconsciousness occurs.

Given Sally's age, gender and diabetes, it is quite likely she has a glomerular filtration rate (GFR) of around 30 mL per minute; any worsening of this could initiate the build-up of glimepiride metabolites. A situation that is potentially dangerous but stable today can become dangerous tomorrow, next week or next month. The long-acting sulfonylureas are convenient to use because of their once-daily dosage (also, glimepiride is available in tablet strengths of 1, 2, 3 and 4 mg so one pill can be prescribed for doses of 1 to 4 mg/day) but they become progressively more dangerous in older people like Sally.

TABLE 1. POTENTIAL MEDICATION-RELATED PROBLEMS IN PATIENTS WITH TYPE 2 DIABETES

Commonly used medications	Potential problems
OHAs	Hypoglycaemia Lactic acidosis
Hypotensives	Hypotension Hyperkalaemia Renal impairment
Hypolipidaemics	Muscle weakness/damage Abnormal liver function tests
Antiplatelet agents	Gastrointestinal and cerebral haemorrhage
Others*	Hypotension Renal impairment

* Especially cardiovascular agents, NSAIDs and antidepressants.
ABBREVIATION: OHA = oral hypoglycaemic agent.

Lactic acidosis

As with use of a long-acting sulfonylurea, the high dose of metformin that Sally is taking may not cause a clinical problem until a second setback occurs, such as pulmonary oedema and hypoxia associated with her myocardial infarction.

Both metformin and hypoxia promote glycolysis and lactic acid production. Lactic acid impairs cardiac function, worsening cardiac failure and completing a vicious and frequently lethal cycle of

TABLE 2. OHAS: NUISANCE AND SERIOUS SIDE EFFECTS

OHA*	Nuisance side effects	Serious side effects
Sulfonylureas	Weight gain	Severe hypoglycaemia
Metformin	GI disturbance	Lactic acidosis
Glitazones	Oedema Weight gain	Cardiac failure Fractures
Glucagon-like peptide-1 (GLP) agents		
Saxagliptin Sitagliptin Vildagliptin	Nasopharyngeal symptoms, dizziness, headache	Possibly pancreatitis
Exenatide	Gastrointestinal disturbance	Possibly pancreatitis

* The less commonly used OHAs (acarbose, repaglinide) are not included.
ABBREVIATION: OHA = oral hypoglycaemic agent.

TABLE 3. RED FLAGS FOR MEDICATION PROBLEMS

Medication	Medication problem	Red flags for problem
General medication use	Medication accumulation	Renal impairment
	Minor problems potentially becoming major problems	Patient frailty*
	Increased likelihood of adverse effects	Polypharmacy Nonadherence
OHAs	Hypoglycaemia†	Past history of hypoglycaemia Neuropathy Living alone
	Lactic acidosis	Cardiac/pulmonary failure Shock Vitamin B_1 deficiency
	Cardiac failure	Past history of cardiac failure Oedema/diuretic use NSAIDs/insulin use

* Patient frailty = biological age older than 85 years.
† For a more complete list of factors predisposing to hypoglycaemia, see reference 2.
ABBREVIATION: OHA = oral hypoglycaemic agent.

hypoxia – lactic acidosis – cardiac impairment – hypoxia – and so on. This vicious cycle is most commonly precipitated by cardiac failure or pulmonary failure causing hypoxia or by severe renal impairment causing metformin accumulation.

Cardiac failure

The same considerations apply to Sally's cardiac failure as to potential severe hypoglycaemia or lactic acidosis – potential precipitants may not cause a problem in their own right but combined with an OHA precipitate the urgency. Sally's cardiac failure was acutely precipitated by the sodium load of her Chinese meal but chronically predisposed to by her taking pioglitazone. This predisposition would have been further increased were Sally to start insulin, which, like the glitazones, promotes renal sodium retention.

Potential precipitants include a high sodium meal (which can contain 200 to 300 mmol of sodium), worsening of cardiac function, missing diuretic doses and starting another sodium-retaining drug (like insulin).

Also, the full effects of starting, stopping or changing the dose of a glitazone are not evident for several weeks. Like the use of a long-acting sulfonylurea and metformin, the use of a glitazone can be a disaster that is waiting to happen.

'Red flags'

The four 'red flags' that are useful indicators of patients who may have problems with medications are renal impairment, frailty, polypharmacy and nonadherence (Table 3). Renal impairment may cause medication accumulation as well as contributing to the serious side effects of OHAs. For example, hypoglycaemia is contributed to by the neuropathy, reduced renal capacity to release glucose from stored glycogen and decreased renal excretion of medication that occur in renal impairment. Patient frailty may or may not directly cause a side effect but can turn a potentially minor problem into a major one. Polypharmacy and nonadherence increase the likelihood of all adverse effects associated with medication.

Extra 'red flags' for the specific side effects associated with OHAs are listed in Table 3.

Hypoglycaemia

Neuropathy is likely to be present in patients with long-standing diabetes (for more than about 15 years). This includes autonomic neuropathy, which silences the sympathetic nervous system response to falling blood glucose levels, making the person unaware that he or she is hypoglycaemic and therefore not being alerted to the need for carbohydrate to counteract the hypoglycaemia.[2]

Similarly, a past history of a severe hypoglycaemic event (one requiring help from another person for recovery) reduces hypoglycaemic awareness acutely and warns that unless the precipitant of the hypoglycaemia is identified and removed, another severe and potentially lethal hypoglycaemic episode is likely.

Lactic acidosis

Lactate is produced from glucose (via pyruvate) by anaerobic glycolysis (lactic acid fermentation) when aerobic glucose oxidation (via acetyl CoA and the Krebs cycle) cannot produce energy because of hypoxia (Figure 1). Any condition reducing oxygen or blood circulation or increasing oxygen demand will increase lactate production and blood lactate levels. Both the lactate and hydrogen ions are excreted by the kidney and/or removed by the liver (which converts lactate to pyruvate and then to glucose in the presence of adequate oxygen – gluconeogenesis). If either removal process is impaired, lactate levels increase faster and reach higher levels, which increases the likelihood of initiating the vicious cycle.

Also, vitamin B_1 (thiamine) is required as a cofactor for the enzyme (pyruvate dehydrogenase) that converts pyruvate

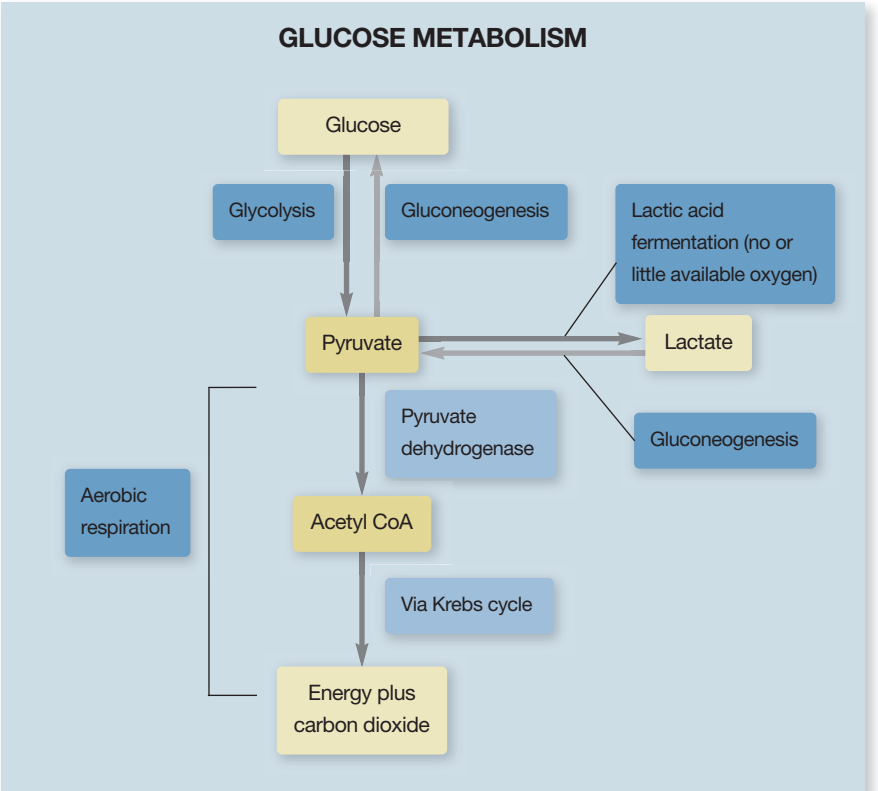

Figure 1. Glucose metabolism and lactate production.

to acetyl CoA, which then enters the Kreb's cycle to produce energy. Thiamine deficiency from a 'tea and toast' or other limited diet occurs in some older, disadvantaged or substance-misusing people, increasing their potential for lactic acidosis.

Cardiac failure

As for hypoglycaemia, a past history of cardiac failure is a warning that unless the precipitating cause is identified and removed, a further episode is likely. The presence of peripheral oedema suggests that the person's physiology is already abnormally sodium retentive, as does the use of diuretics. Moreover, diuretics may be missed, stopped or reduced by the patient; this may not cause an acute problem but can result in gradual fluid accumulation precipitating cardiac failure over the medium to longer term.

As noted earlier, insulin promotes sodium retention and will add to the effects of pioglitazone. NSAIDs are other commonly used sodium-retentive medications; corticosteroids (including prednisolone) also promote sodium retention but are used less often.

HYPOTENSIVE AGENTS

Case 2 – background

Graham is 78 years old and has had type 2 diabetes for more than 20 years. In his younger days, Graham played Aussie Rules football for the local team, and he still takes pride in keeping trim (weight, 74 kg; height, 170 cm; BMI, 23 kg/m^2). His glycaemia is moderately controlled (A_{1c} between 7.5 and 8.5%) on night-time isophane insulin and metformin 500 mg twice daily. However, his blood pressure has always been difficult to control. This difficulty has been attributed to renal impairment (serum creatinine 160 µmol/L; normal range 50 to 120 µmol/L). He is taking telmisartan plus hydrochlorothiazide (80/12.5 mg/day) and amlodipine (10 mg/day) and you add metoprolol 50 mg/day. His other medications include simvastatin 80 mg/day, which is controlling his cholesterol (total cholesterol, 3.4 mmol/L), and intermittently a proton pump inhibitor for oesophageal reflux.

Potential medication urgencies

The following are some of the potential medication urgencies for Graham.

- *Graham gets out of bed to make a cup of tea for his wife, collapses heavily on the floor and feels a crack in his left hip that 'hurt like hell'. His wife calls for an ambulance.*
- *On a subsequent visit you check Graham's renal function and are contacted by the laboratory because the serum potassium is 7.1 mmol/L (normal range, 3.2 to 4.5 mmol/L).*
- *Graham complains about the pain in his hips that has been present for years but has recently got much worse. A friend gives him a few of his arthritis pills to try. Several days later Graham feels terrible, visits the Emergency Department at his local hospital and is admitted with acute renal failure.*

Problems associated with hypotensive agents

Hypotensive agents are particularly likely to cause problems in people with diabetes because these patients are prone to falling, postural hypotension and hyperkalaemia. Any renal impairment makes people with diabetes more prone to acute kidney injury,[3,4] and because their blood pressure is often difficult to control they are often also taking an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor antagonist (ARA) and a diuretic. These patients then only need to take an NSAID to complete the 'triple whammy' of ACE inhibitor/ARA, diuretic and NSAID, and develop acute renal failure.

All the hypotensive agents can cause postural hypotension, and each class has its own particular adverse effects in people with type 2 diabetes. These side effects are summarised in Table 4.

Although the nitrates are not used as hypotensive agents, they are often used in patients with coronary heart disease. Their use is of special concern in patients with autonomic neuropathy who are using a further vasodilator (one of the 'afil' family: silden-, tidal- and vilden-afil) to treat erectile dysfunction caused by this neuropathy because this combination may occasionally precipitate severe hypotension.

TABLE 4. HYPOTENSIVE AGENTS: SIDE EFFECTS IN PATIENTS WITH TYPE 2 DIABETES

Hypotensive agent class	Side effects
All hypotensive agents can cause hypotension and falls	
ACE inhibitors and ARAs	Increased potassium levels, decreased BGL (decreased insulin resistance)
Thiazide diuretics (including indapamide)	Decreased potassium levels, increased BGL (decreased insulin secretion), increased uric acid levels, abnormal lipid levels (increased LDL cholesterol, decreased triglycerides, decreased HDL cholesterol), erectile dysfunction
Beta blockers	Increased BGL (decreased insulin secretion), abnormal lipid levels (decreased HDL cholesterol levels, increased triglycerides), erectile dysfunction
Calcium channel blockers	Dihydropyridines (e.g. amlodipine): increased heart rate, oedema, angina Nondihydropyridines (e.g. verapamil, diltiazem): constipation, oesophageal reflux
Sympatholytics	Depression, nasal congestion, constipation
Alpha blockers	Cardiac failure, urinary incontinence

ABBREVIATIONS: ACE = angiotensin converting enzyme; ARA = angiotensin II receptor antagonist; BGL = blood glucose level; HDL = high density lipoprotein; LDL = low density lipoprotein.

Falls and postural hypotension

People with diabetes are often at high risk of falling because they may lose their peripheral vision and adaptation to the dark because of retinopathy and laser therapy. They may also lose motor power and proprioception because of neuropathy.

Graham is 78 years old and has had type 2 diabetes for more than 20 years, and almost certainly has neuropathy. He is also likely to have impaired hearing, which would compromise spatial orientation, and low vitamin D levels, which would further impair motor power. Even if he were not prone to falling, his neuropathy makes him likely to have postural hypotension, as does his taking a vasodilating calcium channel blocker (amlodipine). The addition of the β-blocker (metoprolol) may well have been the 'last straw' in causing his collapse. His nontraumatic hip fracture (he fell from less than standing height) suggests he also has osteoporosis, probably the result of his age, renal impairment and his likely low vitamin D level, low calcium intake and use of a proton pump inhibitor (which reduces calcium absorption).

An inquiry about falls and unsteadiness should be part of the annual cycle of diabetes care. Any problem should prompt a review looking for modifiable factors. Examples of such factors are other 'ataxiagenic' medications (e.g. those with sedating side effects); personal habits (e.g. use of bifocals, non-use of hearing aid, inappropriate footwear); and features of the personal environment (e.g. slippery floors, loose mats, stairs [can be replaced by ramps]). Potential aids for patients include nightlights, walking sticks and walking frames.

As Graham was so likely to have postural hypotension, his blood pressure should have been checked at least seated and standing, and ideally also supine. Graham could then have been counselled to move from being in a supine position to standing in stages and to make sure he could immediately resume the seated position if he felt unsteady – for example, sit up in bed, then put legs over edge, then put feet on the floor with buttocks still on bed, then stand and finally move away from the bed, with or without a walking aid.

Hyperkalaemia

Serum potassium levels reflect both the overall balance of potassium in the body (oral intake versus excretion – mainly by the kidney) and the balance between the potassium concentrations in the intra- and extracellular compartments (physiologically controlled by aldosterone, insulin, β2-adrenergic activity and acid base and osmolar status), as shown in Figure 2. Both type 1 and type 2 diabetes can affect these balances.

Renal impairment impairs capacity to excrete potassium, as do certain medications (including ACE inhibitors, ARAs and potassium-sparing diuretics) and/or associated hypoaldosteronism. In both type 1 and type 2 diabetes, the ability of

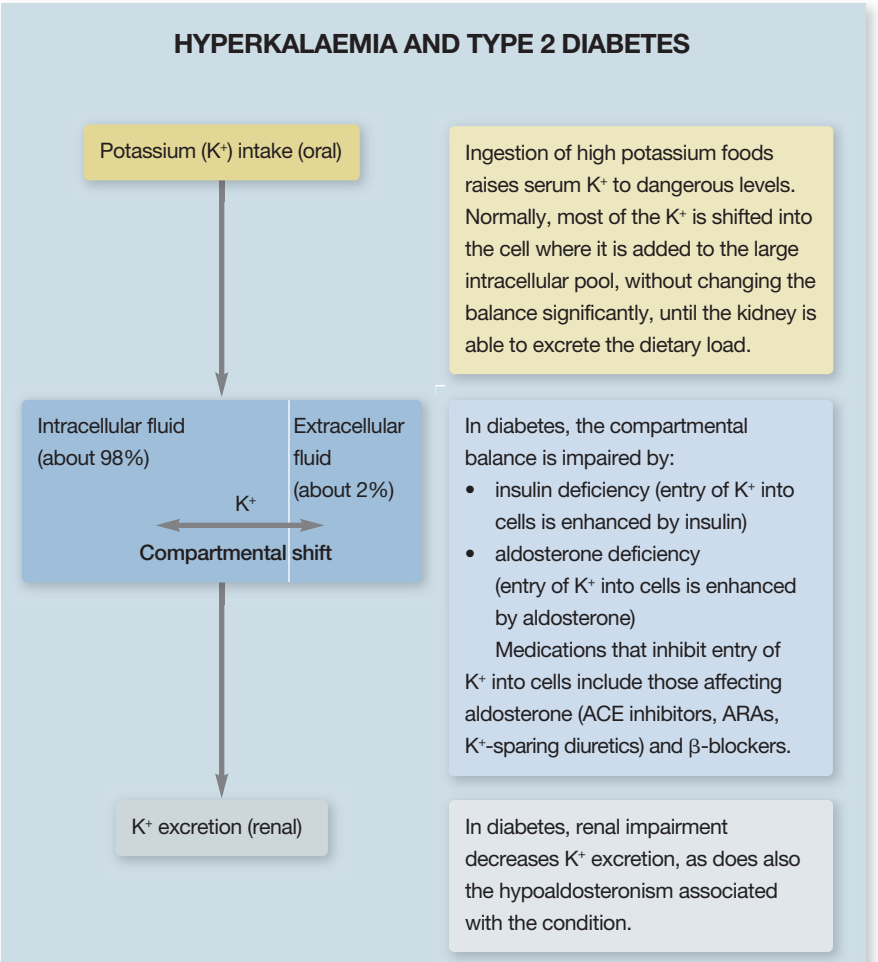

Figure 2. Potassium balance and the effect of diabetes.

potassium to change insulin secretion is absent or reduced, further impairing compartmental balance. Beta-2 adrenergic effects are reduced because of autonomic neuropathy and, in Graham's case, may also have been affected by his β-blocker (metoprolol, which has relative rather than absolute β_1-selectivity). Other medications (e.g. NSAIDs) can also affect the compartmental balance.

Monitoring potassium levels is especially important in patients with diabetes, checking for both hypokalaemia (because of diuretic therapy) and hyperkalaemia (as noted above).

Acute renal failure

Graham's friend unwittingly provided the NSAID, completing the 'triple whammy' of ACE inhibitor/ARA, diuretic and NSAID. As noted, people with renal impairment (reduced GFR and/or proteinuria) are particularly prone to acute kidney injury, and Graham did have a low GFR (his serum creatinine of 160 μmol/L giving a calculated GFR [creatinine clearance] of 36 mL/min [see the box on this page]).

The use of an ACE inhibitor or ARA can be expected to reduce GFR because these medications dilate the efferent arterioles of the glomeruli, reducing glomerular pressure and thus filtration. However, the serum creatinine should not increase by more than 30%.[5] Any greater increase should prompt investigation for other contributors (e.g. renal artery stenosis where efferent arteriole vasoconstriction may be the major factor maintaining glomerular pressure).

Including the medications forming the 'triple whammy', there are 'nine nephropathic nasties' (Table 5).[6] It is important to be especially aware of these medications in patients with abnormal renal function (decreased GFR and/or proteinuria).

GLOMERULAR FILTRATION RATE AND MEDICATION ADJUSTMENT

Calculating GFR (creatinine clearance) mL/min

Glomerular filtration rate (GFR) is the best overall index of kidney function.

Theoretically, the total GFR should be used for medication adjustment, and not the estimated GFR, which needs to be adjusted for body surface area.[1] One easy formula for calculating total GFR, or creatinine clearance, is a modified form of the Cockcroft–Gault equation:[3]

For women:
GFR = [(140 – age in years) x healthy weight in kg] ÷ serum creatinine in mmol/L

For men:
As above x 1.25 to allow for the greater muscle mass per kg of body weight. (Using 1.25 rather than 1.23 allows easier calculation.)

In Graham's case:
GFR = [(140-78) x 74] ÷ 160 = 28.7
28.7 x 1.25 = 36 mL/min

HYPOLIPIDAEMIC AND ANTIPLATELET AGENTS

The cases – continued

Case 1: *Sally recently started taking low-dose aspirin for cardioprotection but*

is now concerned because a copious nosebleed that lasted about four hours obliged her to visit the Emergency Department. She was told to stop taking the aspirin. When you ask about other medication she is taking, Sally comments that she had recently added gingko and fish oil to her medication list because they were on special offer at her health food shop.

Case 2: *Graham feels 'awful'. His muscles ache and he feels 'as weak as a kitten'. He wonders if his problem is related to a respiratory tract infection and if the roxithromycin he has been taking for the infection should be changed to another antibiotic.*

TABLE 5. NEPHROPATHIC MEDICATIONS

Medication	Comment
Nephrotoxic	
Radiocontrast agents	Use low ionic agents instead and avoid dehydration
NSAIDs (including COX-2 'specific' NSAIDs)	Use paracetamol instead
ACE inhibitors	Check renal function
Dose adjustment needed if GFR is reduced	
Allopurinol	Use 10 mg/day per 30 mL/min of GFR
Digoxin	Check levels
Sulfonamides	Use half dosage if GFR below 30 mL/min/
Not to be used if GFR below 30 mL/min	
Certain hypoglycaemics (glibenclamide, glimepiride, metformin)	–
Potassium-sparing diuretics (amiloride, triamterene, spironolactone)	–
Tetracyclines	–

ABBREVIATIONS: ACE = angiotensin-converting enzyme; COX-2 = cyclo-oxygenase 2; GFR = glomerular filtration rate; NSAIDs = nonsteroidal anti-inflammatory drugs.

Antiplatelet agents

Sally's problem was caused by a predictable but little known antiplatelet effect of both gingko and fish oil.[7] Some people and some health professionals may think that complementary medications do not have any effect – therapeutic or adverse. They are wrong. Some of these medications have been shown to be effective in rigorous randomised controlled clinical trials (e.g. St John's wort for depression) and many have adverse side effects and/or interact with other prescription or nonprescription medications.

Sally is 82 years old, probably has impaired renal function and is taking three hypoglycaemic medications, aspirin and almost certainly other known prescription medications. A Home Medications Review (HMR) would have identified any medication likely to cause problems and provided an opportunity to counsel Sally not to take any medication without asking an informed health professional (her doctor or pharmacist) about potential adverse effects or interactions with any of her other medications. Doctors, pharmacists and patients are very aware that they need to be ultracautious about the use of warfarin but they may forget that gastrointestinal and cerebral haemorrhage can be equally lethal with antiplatelet therapy (aspirin or clopidogrel). This is especially so in a high-risk patient like Sally, who has at least two major risk factors for gastrointestinal haemorrhage: being aged over 80 years and having type 2 diabetes.

People with type 2 diabetes usually fill one or more of the criteria for a HMR. Such a review should be considered whenever a new medication is started (prescription or nonprescription).

Hypolipidaemic agents

Graham's muscle pain was probably caused by the interaction of his macrolide antibiotic (roxithromycin) and his statin (simvastatin). Several other commonly used medications also interact adversely with statins (Table 6).[8]

The muscle damage associated with statin use may be minor and asymptomatic, causing only a two or threefold increase in creatine kinase level, or be very severe and associated with rhabdomyolysis, profound weakness and renal failure. Statins are also associated with significant liver damage.

It is worth remembering that statistics from randomised controlled trials of statins may underestimate these risks as many of these trials had a 'run-in' period where all participants took the statin at the dose to be prescribed for the active arm and those who had adverse effects were excluded. The 'rule of sixes' should also be remembered – doubling the dose of a statin increases the hypocholesterolaemic effect by 6% but more than doubles the risk of adverse effects.[8] A further red flag in Graham's case was his renal impairment, which should have made his doctor more cautious.

Like Sally, Graham is eligible for a HMR, which would have identified the potential medication adverse effects and interactions. Graham would have been

TABLE 6. MEDICATIONS REDUCING STATIN CLEARANCE*

Medication	Use in patients with diabetes
Gemfibrozil, nicotinic acid	Dyslipidaemia
Macrolide antibiotics (azithromycin, clarithromycin, erythromycin, roxithromycin)	Skin and respiratory infections
Antidepressants (fluvoxamine, fluoxetine, nefazodone)	Depression
Cyclosporin	Transplant for diabetic nephropathy

* Reduced statin clearance may also occur with azole antifungal agents (e.g. ketoconazole, itraconazole), and is a theoretical possibility with diltiazem and also grapefruit juice because these can affect the hepatic metabolism of statins.

given the same advice as Sally:

'Never take a medication before being advised by an informed health professional.'

SUMMARY

- Many commonly used medications have the potential to cause serious side effects or to interact with other drugs. These effects can have severe consequences for patients with type 2 diabetes because these patients often one or more of the 'red flags' of being at risk of medication side effects (i.e. renal impairment, patient frailty, polypharmacy and nonadherence).
- All the OHAs have both nuisance and serious side effects. 'Red flags' indicating problems specific to OHAs include: history of hypoglycaemia and neuropathy for hypoglycaemia; cardiac/pulmonary failure and shock for lactic acidosis; and history of cardiac failure and oedema/diuretic use and NSAID/insulin use for cardiac failure.
- All the hypotensive agents can cause postural hypotension, which increases the already high risk of falls in people with diabetes. Asking about or testing for falls or unsteadiness should be part of the annual cycle of care for patients with diabetes.
- Each class of hypotensive medications has its own profile of side effects that are relevant in patients with diabetes, including hyperkalaemia and renal impairment. These adverse effects should be considered and sought after prescribing any hypotensive agent.
- Antiplatelet agents can cause the same haemorrhagic disasters as warfarin. Patients (and their doctors) should remember not to take (or prescribe) any medication before checking that it is unlikely to have adverse effects or interactions with any other prescribed or nonprescribed medication.
- Most people with diabetes fulfil one or more of the criteria for a HMR. Such a review would identify potential diabetic urgencies related to medications and would provide an opportunity to counsel the patient (and doctor) about avoiding them. MT

ACKNOWLEDGEMENT

This article discusses some of the same problems as a previous article by the same author published in Current Therapeutics.[9]

REFERENCES

1. Harris P, Mann L, Phillips PJ, Bolger-Harris H, Webster C. Diabetes management in general practice. Guidelines for type 2 diabetes. 17th ed. 2011/12. Canberra: Diabetes Australia; 2011. Available online at: www.racgp.org.au/guidelines (accessed October 2011).
2. Phillips P. Hypoglycaemia: a major barrier to glycaemic control. Medicine Today 2011; 12(8): 55-60.
3. James MT, Hemmelgarn BR, Wiebe N, et al. Glomerular filtration rate, proteinuria, and the incidence and consequences of acute kidney injury; a cohort study. Lancet 2010; 376: 2096-2103.
4. Grams M, Coresh J. Proteinuria and the risk of acute kidney injury. Lancet 2010; 376: 2046-2048.
5. Bakris GL, Weir MR. Angiotensin-converting enzyme inhibitor-associated elevations in serum creatinine: is this a cause for concern? Arch Intern Med 2000; 160: 685-693.
6. Yong TY, Phillips PJ, Coates PTH. Neglected nephropathy. Aust Fam Physician 2008; 35: 398-402.
7. Moses GM, Maguire TM. Drug interactions with complementary medicines. Aust Prescriber 2010; 33: 177-180.
8. Phillips P. ABCss: C is for cholesterol. Medicine Today 2006; 7(12): 65-70.
9. Phillips P, Braddon J. Dangerous drugs in diabetes. Current Therapeutics 1999; 4: 46-53.

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