

Medicines and the kidney

CATAG Teaching Tool

Introduction

Medicines can have a profound effect on the kidneys, and reduced kidney function can impact the safety and effectiveness of many medicines. Reduced kidney function is a problem that is commonly identified in hospitals and is a major risk factor for serious adverse reactions to medicines.^{1,2}



1 in 3 people with reduced kidney function are prescribed medicines that are either contraindicated or prescribed doses that are inappropriately high.³

This case scenario should be used as a teaching tool by clinical educators in teaching sessions for medical officers, nurses, pharmacists, and students. It provides a clinical example of managing medicines in reduced kidney function.

It can be used by educators to stimulate discussion of current practice and opportunities for quality improvement. Medicines and Therapeutics Advisory Committees should share this teaching tool along with the [‘Medicines and the kidney’ Practice tool](#) with clinical educators.

Applying eGFR to medicines

Medicine dosage adjustments in people with reduced kidney function should be anticipated at the point of prescribing,¹⁴ and must take into consideration the clinical situation of the person, including trends, rather than rigid calculations based on reported numbers alone.

- Use adjusted estimated glomerular filtration rate (eGFR) to estimate kidney function for medicine dosage.⁴
- Applying eGFR where estimated creatinine clearance (eCrCl) is recommended for medicine dosage adjustments, is not likely to result in a clinically significant difference.^{4,14}
- Use therapeutic monitoring for medicines with a narrow therapeutic index, when available.¹⁴
- In acute kidney injury (AKI), eGFR calculations are not reliable and should not be used to dose medicines.¹⁶ The trend in serum creatinine concentrations over multiple measurements should instead be used to judge the degree of decline or improvement in GFR.¹⁶

Refer to the [‘Medicines and the kidney’ Practice tool](#) for further information.

Case Scenario for medicines and the kidney

Admission

John Brown is a 75-year-old retired male brought in by ambulance after his wife, Mary, found him lying in the yard with worrisome neurological symptoms. He may have been lying there for up to 24 hours as his wife has been interstate and last spoke to him the previous day. His medical history includes hypertension, type 2 diabetes, hip pain and benign prostatic hyperplasia.

Diagnosis

John is diagnosed with an ischemic stroke, rhabdomyolysis secondary to a prolonged period of lying, dehydration, and acute kidney injury (AKI). To ensure effective communication throughout John's treatment (and appropriate clinical coding), these diagnoses are clearly documented in John's progress notes. A best possible medication history is obtained (see Table 1) and he is admitted to the hospital's high dependency unit.

Clinical features

- Diffuse muscle pain
- Confusion
- Weakness in the left arm and the left leg
- Difficulty enunciating words

Observations

- BP 95/55
- HR 115 bpm
- RR 18
- Saturation 99% on room air
- Temperature 36.5°C
- Height – 156 cm
- Weight – 103 kg
- Urine output: 15 mL dark brown urine within 30 minutes of urinary catheter placement

Initial investigations

- Creatinine 250 micromol/L
- Urea 15 mmol/L
- eGFR of 23 mL/min/1.73m²
- Sodium 150 mmol/L
- Potassium 5.4 mmol/L
- Chloride 120 mmol/L
- Bicarbonate 15 mmol/L
- Normal blood count
- Serum creatine kinase 25 000 units/L
- Blood glucose 5.6 mmol/L
- CT brain showing subacute ischemic changes in the territory of the right middle cerebral artery
- Normal renal ultrasound

Table 1: John's best possible medication history on admission

Medicine and strength	Prescribed dose	Actual dose	Additional information from John and Mary
amlodipine 5 mg	1 daily	1 tablet in the morning	
furosemide 40 mg	Half to 1 daily when needed	1 tablet in the morning when needed	John has been experiencing swelling in the ankles. He was taking the furosemide every day for about a week, but it didn't work very well so he stopped taking it 3 days ago.
gliclazide MR 60 mg	1 mane	1 tablet in the morning	Able to swallow tablet whole. Often skips breakfast. John monitors his blood glucose levels once weekly on Saturday mornings.
metformin 1,000 mg	1 twice daily	1 tablet twice daily	No swallowing issues reported. Occasionally forgets the evening dose.
paracetamol MR 665 mg	2 tablets 8 hourly when needed	2 tablets 8 hourly when needed	John reports occasional use; twice a week on average.
ramipril 10 mg	1 daily	1 tablet in the morning	No cough reported. John does not monitor his blood pressure at home.
rosuvastatin 5 mg	1 daily	1 tablet at night	Sometimes forgets to take this medicine (on average 1-2 times per week).
tamsulosin 400 microgram	1 daily	1 tablet in the morning	Able to swallow tablet whole. Experiences minor dizziness on standing but this is settling. John thinks his symptoms have improved since starting this medicine.
Allergies and adverse reactions to medicines:			Nil known



Best Possible Medication History

John's medicines plan

As John has an AKI, any estimates of his kidney function (e.g. eGFR, eCrCl) are unreliable and should not be used to guide dosage adjustments.⁴ With only a single initial elevated serum creatinine concentration available, his GFR should be assumed to be 0 mL/min and medicines dosed accordingly⁴ until further investigations are available (refer to Table 4 of 'Medicines and the kidney' Practice tool).

For the treatment of ischaemic stroke, the treating team decides to initiate aspirin.

[The Renal Drug Database](#) is consulted, which recommends to dose as per normal renal function for GFR <10 mL/min, and so John is prescribed aspirin 300 mg for one dose, followed by 100 mg daily.

Due to his acute illness and AKI, all of John's regular medicines are omitted initially; his blood glucose levels are managed with an insulin infusion and his blood pressure remains within acceptable limits without his usual medicines, likely due to dehydration.

For the first few days, John's medicines plan is reviewed and altered according to his clinical status at least once per day. As his clinical condition stabilises and kidney function improves, his medicines are re-introduced slowly, as clinically indicated.

Discussion Points

How would you manage John's medicines at admission?

How often should John's medicines be reviewed and what clinical factors would influence your decision?

Reintroduction of medicines

After 7 days of acute care, John's dehydration has been corrected, rhabdomyolysis has been managed, and his serum creatinine has been stable at around 180 micromol/L for 3 days. His blood pressure and blood sugar levels are rising and it is decided to reintroduce his metformin and ramipril slowly.

John's eGFR is calculated, based on actual body weight, and used to guide renal dosage adjustment for his regular medicines. For interest, a comparison of the different results yielded from different equations and body weights is shown in Table 2, which highlights the issues of variance in estimates of kidney function. The preferred formula to guide dosage is currently uncertain,⁵ though adjusted eGFR is generally used.^{5,6}

Discussion Points

Discuss the different formulae used in estimating glomerular filtration rates and which calculations would be beneficial to use when reviewing and reinitiating John's medicines?

Discuss when and how John's regular medicines should be reintroduced?

Medicines dosage adjustments must take into consideration the clinical situation of the person, including trends, rather than rigid calculations based on reported numbers alone.



The Renal Drug Database

Table 2: Comparisons of John’s estimated kidney function using different equations, for an automated eGFR 33 mL/min/1.73 m²

	Adjusted eGFR	Cockcroft-Gault eCrCl
Using actual body weight (103 kg)	40 mL/min	46 mL/min
Using ideal body weight (54 kg)	N/A	24 mL/min
Using adjusted body weight (73 kg)	N/A	32 mL/min

* Ideal body weight (IBW) and BSA calculated using the AMH online calculator. Adjusted ideal body weight (kg)= IBW + 0.4 x (weight – IBW).⁵

Metformin

- The Australian Medicines Handbook is consulted which recommends a maximum of 500 mg and 1000 mg daily where CrCl is 15 to 30 mL/min and 30 to 60 mL/min, respectively.⁷ Applying eGFR where eCrCl is recommended for dosage adjustments, is not likely to result in a clinically significant difference.^{5, 6}
- John is recommenced on metformin 500 mg daily, with a plan to titrate to 1000 mg daily slowly as indicated and tolerated. He is monitored closely for gastrointestinal symptoms or lactic acidosis and has blood glucose levels checked four times daily.

Ramipril

- The [Australian Medicines Handbook](#) cautions use in reduced kidney function due to potential to worsen renal impairment, and increased risk of hyperkalaemia. In people who are elderly, have reduced kidney function, or are taking a diuretic, the recommended initial dose is 1.25 mg daily.
- John is recommenced on ramipril 1.25 mg daily with careful monitoring of serum

creatinine, potassium, blood pressure, and tolerance (headache, dizziness).

This same process (checking renal dosage recommendations and low initial dose with careful titration and monitoring) should be applied to each of his medicines as they become required, except for amlodipine and furosemide which are ceased; the furosemide was added to treat peripheral oedema, which can be caused by amlodipine.

Discharge

John remains in hospital for 4 weeks, including rehabilitation, before being discharged home. His creatinine at discharge remains stable at around 180 micromol/L.



The Australian Medicines Handbook



Discussion Points

What should be included in John’s discharge communications regarding his kidney function?

Does your hospital have a standardised discharge template including a medicines plan?

John's discharge summary includes:

- clear documentation of the diagnoses of stroke, rhabdomyolysis, and AKI
- eGFR results
- current medicines list, reasons for medicines changes and plan (see Table 3)
- a recommendation for the GP to review within one week:
 - John to measure BSL daily and visit local pharmacy at least once in the next week for blood pressure check and take these results to his GP
 - GP to review blood pressure and BSLs and, together with John and Mary, formulate a management plan
 - GP to check kidney function; *no improvement anticipated*
- a note to the GP that John's kidney function is not expected to improve, and that once he meets the diagnostic criteria for chronic kidney disease (i.e. GFR < 60 mL/min/1.73m² for more than 3 months) his diagnosis should be updated and John made aware
- a recommendation for a [Kidney Health Check](#) (eGFR, urine albumin/creatinine ratio, and blood pressure) every year, due to AKI and ongoing risk factors of hypertension and diabetes⁸
- a recommendation for a post-discharge comprehensive medicines review once kidney function has stabilised
- his rehabilitation exercise plan
- a recommendation for referral to a community dietitian for weight loss, optimal nutrition and diabetes care
- provision of a [sick day action plan](#): advice that John discontinue metformin, gliclazide, ramipril, and indapamide and to seek medical attention in the event of acute illness or dehydration.⁸

are recognised by the mnemonic SADMANS: Sulfonylurea, ACE inhibitors, Diuretics, Metformin, Angiotensin Receptor Blockers, NSAID, SGLT2 inhibitors.⁸

These points are also clearly communicated to John and Mary, with ample opportunity provided for any questions.

The ward pharmacist issues John and Mary a medicines plan (see Table 3) and provides counselling including the importance of medicines for stroke prevention and risk of hypoglycaemia with the use of metformin and gliclazide and reminds of hypoglycaemia awareness. They recommend that John consider purchasing a home blood pressure monitor and keep a blood pressure diary; providing the '[Measuring your blood pressure at home](#)' resource from the Heart Foundation. John is advised he is at increased risk of having another stroke and is provided a brochure '[Understand and prevent stroke](#)' and both he and Mary are educated on the F.A.S.T. (face, arms, speech, time) signs of stroke and importance of calling an ambulance immediately.

The ward dietitian provides education around optimal nutrition and diabetes care, including:

- regularly scheduled meals and healthy snacks
- smaller portion sizes
- increasing high-fibre foods such as non-starchy vegetables, fruits, and wholegrains
- fewer starchy vegetables, refined grains, and sweets
- modest servings of low-fat dairy, low-fat meats and fish.

A sick day action plan provides information to people or their carers about what to do when unwell, including which medicines may need to be temporarily withdrawn. These medicines



Kidney Health Check



Sick day action plan



Measuring your blood pressure at home



Understand and prevent stroke

Table 3: John's medicines plan at discharge (4 weeks after hospital admission)

Medicine and strength	Prescribed dose	Action and reason
aspirin 100 mg	1 tablet in the morning	NEW MEDICINE for secondary stroke prevention.
gliclazide MR 60 mg	Half a tablet in the morning	Dose reduced due to reduced kidney function, with advice to monitor BSLs daily until GP review in one week.
indapamide 1.25 mg	1 tablet in the morning	NEW MEDICINE for blood pressure control. (Replaces amlodipine).
metformin XR 1,000 mg	1 tablet in the morning	Dose reduced due to reduced kidney function. Changed to controlled release formulation in the morning to improve compliance.
paracetamol MR 665 mg	2 tablets three times daily, when needed	Continued at same dose; paracetamol and analgesia education given and advised on importance of avoiding and risks associated with NSAID use.
ramipril 2.5 mg	1 tablet in the morning	Dose reduced due to kidney function.
rosuvastatin 20 mg	1 tablet in the morning	Dose increased due to stroke, changed to morning to increase compliance.
tamsulosin 400 microgram	1 tablet in the morning	Continued at same dose.
CEASED (and reason)		SICK DAY ACTION PLAN
<ul style="list-style-type: none"> • Amlodipine – changed to indapamide as causing peripheral oedema • Furosemide – no longer needed as was for peripheral oedema <p>Do not take these medicines; return unused tablets to your local pharmacy.</p>		<p>If you are unwell or dehydrated, STOP TAKING:</p> <ul style="list-style-type: none"> • Metformin • Gliclazide • Ramipril • Indapamide <p>AND contact your doctor.</p>

Follow-up

John sees his GP 7 days after discharge for follow-up review. He and Mary purchased a home blood pressure monitor and checked his blood pressure and blood sugar levels daily; these have remained stable and within acceptable ranges. The GP advises John he can decrease to second daily blood sugar monitoring, and three times weekly blood pressure monitoring. The GP refers John for a comprehensive medicines review.

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