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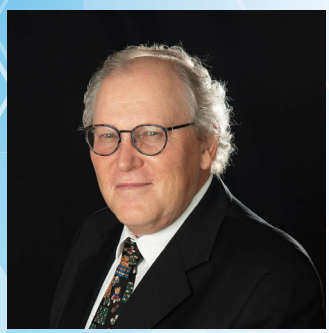
Diabetes

Case study 3 of 3

A type 2 diabetes patient with kidney disease

Presented by:



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Learning objectives

This case study aims to:

- Provide an opportunity to implement evidence-based international guidelines and clinical trial data in the management of an anonymised patient with type 2 diabetes mellitus (T2DM) and diabetic kidney disease (DKD)
- Provide expert input on the common dilemmas encountered by clinicians in the treatment of these patients
- Develop an understanding that in order to avoid the development of severe kidney disease, kidney function needs to be assessed early in the management of T2DM.

Patient information

Mrs RT, 66 years old, has come for a routine T2DM follow-up appointment. She was diagnosed with T2DM six years before, is currently asymptomatic and regularly attends her six-monthly follow-ups.

Upon T2DM diagnosis, she initially responded well to metformin plus sulphonylurea therapy (↓ HbA_{1c} 7.5%). Mrs RT's glucose control deteriorated to HbA_{1c} 11.5% within a year of using this regimen and fixed-dose biphasic insulin treatment was then introduced to positive effect; within a few months, her HbA_{1c} levels reached 8.5% and then 6.5%.

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Comorbidities and family history

- Family history not known to her
- Concomitant hypercholesterolaemia being treated with simvastatin
- Lumbar spondylosis.

Habits and lifestyle

- Non-smoker, does not use alcohol, no other lifestyle risk factors.

Physical examination

- Weight 90.3kg
- Height 160cm
- Body mass index (BMI) 35.2kg/m^2
- Blood pressure (BP) 130/95mmHg.

Laboratory tests

Date	Sep 2016	Mar 2017	Jun 2017	Aug 2018	Feb 2019	Apr 2020	Oct 2020	Feb 2024
HbA_{1c}, %	7.3	11.5	7.2	8.5	6.5	7.5	9.6	7.6
Estimated glomerular filtration rate (eGFR), ml/min/1.73m^2							79	86
Urine albumin-creatinine ratio (UACR), mg/mmol							0.48	5.6

Clinical questions

1. **What is the HbA_{1c} target for this T2DM patient?**
   - A. 6%
   - B. 7%
   - C. 8%

Expert comment

According to the Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) and most international guidelines, HbA_{1c} 7% is the desired target. Age and comorbidities may increase or decrease the target.

2. **Which low-density lipoprotein cholesterol (LDL-c) target is appropriate for T2DM patients with established cardiovascular disease (CVD)?**
   - A. 3.0mmol/l
   - B. 2.5mmol/l
   - C. 1.8mmol/l
   - D. 1.0mmol/l

Expert comment

The current LDL-c target for a T2DM patient with established CVD is 1.8mmol/l and in some cases even lower - 1.4mmol/l. In general, over recent years, there has been a tendency in both local and international dyslipidaemia and diabetes guidelines towards lowering LDL-c targets for these patients.

3. **UACR is an important marker of early kidney disease:**
   - A. True
   - B. False

Expert comment

According to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines, eGFR and UACR must be used to classify kidney diseases.

4. **In a recent meta-analysis, progression to end-stage kidney disease can be reduced by …% if a sodium-glucose co-transporter-2 (SGLT-2) inhibitor is prescribed:**
   - A. 20%
   - B. 30%
   - C. 37%
   - D. 52%

Expert comment

A meta-analysis of 13 clinical trials including a total of 90 143 participants demonstrated that compared with placebo, SGLT-2 inhibitor therapy reduced the risk of kidney disease progression by 37%;[1] this reduction was similar between chronic kidney disease (CKD) patients with or without diabetes. Furthermore, these benefits were similar across the range of studied kidney function (eGFR 37-85ml/min/1.73m^2) and were seemingly unmodified by primary kidney diagnosis.

5. **When initiating empagliflozin treatment, what adverse reactions can be expected for a small percentage of patients?**
   - A. Urinary tract infections (UTIs)
   - B. Initial lowering of eGFR
   - C. Nausea and vomiting
   - D. Mycotic infections
   - E. B and D

Expert comment

Meta-analysis demonstrated no increased risk for UTIs with use of empagliflozin, other than the intrinsic UTI risk of diabetes. An increased risk of mycotic infections is more common for females and uncircumcised males, although this risk can largely be mitigated through adequate daily hygiene. The initial reduction of eGFR associated with empagliflozin normalises within 1-4 months after commencing therapy.

6. **What is the starting dose of empagliflozin?**
   - A. 5mg/day PO
   - B. 5mg bd PO
   - C. 10mg/day PO
   - D. 25mg/day PO

Expert comment

Empagliflozin therapy should be started at 10mg/day PO. If tolerated, the empagliflozin dose can be increased to 25mg/day. For Mrs RT, we elected to start with a dose of 10mg/day.

7. **What would this patient's DKD classification be?**
   - A. G1 A1
   - B. G1 A2
   - C. G2 A2

Expert comment

Mrs RT has a normal eGFR (G1) and albuminuria of 3-30mg/mmol (A2).

CKD is classified based on:
Cause (C)
GFR (G)
Albuminuria (A)

GFR categories (ml/min/1.73m²) Description and range				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severerely increased
				<30mg/g <3mg/mmol	30–299mg/g 3–29mg/mmol	>300mg/g >30mg/mmol
	G1	Normal to high	≥90	Screen 1	Treat 1	Treat and refer 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat and refer 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat and refer 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat and refer 3	Treat and refer 3
	G4	Severely decreased	15–29	Treat and refer 3	Treat and refer 3	Treat and refer 4+
	G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

Low risk (if no other markers of kidney disease, no CKD)
Moderately increased risk
High risk
Very high risk

Source: ADA and KDIGO consensus report on diabetes management in CKD[2]

8. **What measures should be taken when eGFR worsens?**
   - A. Discontinue SGLT-2 inhibitor therapy
   - B. Follow up after 3-4 months
   - C. Increase SGLT-2 inhibitor dose
   - D. Increase angiotensin receptor blocker (ARB) dose

Expert comment

The eGFR-lowering effect of a SGLT-2 inhibitor is transient and usually normalises by 1-3 months.

Three months later

9. Which biomarkers should be measured after three months of SGLT-2 inhibitor therapy?

- A. eGFR
- B. UACR
- C. HbA_{1c}
- D. Lipids
- E. Urea and electrolytes (U+E), creatinine
- F. BP
- G. Liver functions
- H. Thyroid functions
- I. Full blood count (FBC)
- J. A, B, C, E and F

Expert comment

During follow-up, evaluate the efficacy of empagliflozin and possible side effects.

10. During major surgery or any condition of hypovolaemia in the patient using empagliflozin, it is recommended that empagliflozin treatment be:

- A. Maintained
- B. Permanently discontinued
- C. Withdrawn at 48 hours pre-surgery and for six days after surgery; reinitiate after one week if there are no postoperative complications
- D. Withdrawn seven days prior to surgery and reinitiated one month after surgery

Expert comment

SGLT-2 inhibitors should be halted when patients are acutely ill, when unable to maintain adequate fluid intake, when undergoing major surgery or when there is a sudden acute decline in renal function.

References

Click on reference to access the scientific article

1. The Nuffield Dept of Population Health Renal Study Group and the SGLT-2 inhibitor meta-analysis Cardio-renal Trialists Consortium. Impact of diabetes on the effects of sodium glucose-co-transporter-2 inhibitors on kidney outcomes: Collaborative meta-analysis of large placebo-controlled trials. *Lancet* 2022; **400**(10365): 1788-1801.
2. De Beer IH, Khunti K, Sadusky T, *et al*. Diabetes management in chronic kidney disease: A consensus report by the American Diabetes Association (ADA) and Kidney Disease Improving Global Outcomes (KDIGO). *Diabetes Care* 2022; **45**(12): 3075-3090.

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Making best practice, everyday practice

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