CASE STUDY

Challenges in type 2 diabetes control: slipping control and weight gain

Introduction

This case study presents an everyday clinical situation for you to review with guidance from experts in the field. It aims to highlight complications such as appropriate therapies for individual patients, providing insight and latest clinical reviews.

Grand Rounds: Test your clinical skills

Active businessman with type 2 diabetes – a challenge for diabetes control

The patient: Mr PP

- Married
- Active businessman
- 66 year old obese gentlemen with a history of type 2 diabetes mellitus and dyslipidaemia

Reason for visit

- Mr PP presented for his routine 6 month follow up visit.
- He has noted worsening of his glycaemic control over the last 6 months. He was self-monitoring his glucose. He noticed that fasting and postprandial readings were increasing. He was not experiencing new symptoms.
- He is conscientious with self-monitoring at home, and was documenting morning and evening glucose levels. However, he was not monitoring at work and so did not have a record of lunchtime values. Furthermore, he did not take his monitor with him when he travelled and did not monitor during those times.
- Shows both elevations in fasting and post prandial glucose. See above.
- Most of the concern relates to his post prandial glucose levels that are rising. See above.

- He is also concerned about his weight gain. There has been slow, but progressive weight gain over the last 18 months. His weight was being monitored at his follow-up visits and there has been a 1-2kg increase in weight per visit over the last 2-3 visits. He has also started attending gym and was monitoring his weight there, and had noticed that it was increasing.
Case Study – Type 2 Diabetes

Patient History
• Mr PP was first diagnosed with type 2 diabetes mellitus in 2006, for which he had been prescribed metformin 500mg twice daily. At the same time he was noted to have dyslipidaemia for which he had been prescribed simvastatin 20mg daily.
• Over the next few years his metformin was increased to 1g twice daily and then changed to metformin XR 2g daily due to gastrointestinal side effects.
• During this period HbA1c was optimal at below 7%.
• Thereafter, his glucose control worsened.
• He was still overweight and was doing minimal exercise.
• Gliclazide MR 120mg was added to his therapy over a year in incremental doses to improve his glucose control, but the HbA1c remained suboptimal (8.2% at this current review).
• Simvastatin was changed to atorvastatin 10mg as he was not achieving acceptable control (based on SEMDSA targets for lipids).
• His lifestyle over the past 6 years had improved with regular exercise at the gym 4-5 times per week.
• His diet had improved, but was still not optimal. He was still adding sugar to his tea and was consuming a lot of rice on a daily basis. He had made attempts to reduce consumption of other carbohydrates.
• Currently he has no further complaints except for intermittent nocturia.

Co-morbid conditions and family history
Mr PP had no other background history of note except that:
• He had previously been treated for depression with fluoxetine 20mg daily. No longer on medication.
• He had been previously been treated by an ophthalmologist (4 years earlier) for a retinal detachment, which had subsequently stabilised. There is no established diabetic retinopathy.
• Family history included type 2 diabetes mellitus on the paternal side as well as hypertension on both maternal and paternal sides.

Habits and lifestyle
• Owns a very busy textile company
• Frequently travels overseas on business. Due to the nature of his work and busy schedule at work, he often finds it difficult to monitor his glucose at work.
• He is an ex-smoker; stopped smoking 3 years ago.
• Consumes alcohol on a social basis – mainly wine and vodka.
• He has no known allergies.
CASE STUDY – TYPE 2 DIABETES

Physical examination
• Weight 109.4kg
• BMI 37.4kg/m²
• BP 148/80mmHg
• Pulse 80b/min, regular. All pulses were palpable and he had no carotid or renal bruits.
• Neurological examination revealed decreased vibration sense bilaterally with normal 10g monofilament assessment.
• Cardiac, respiratory and abdominal examinations were all normal.

Latest test results
• U&E: Na 137mmol/l, K 4.5mmol/l, CL 105mmol/l, Urea 4.5mmol/l, Creatinine 64mmol/l
• GFR = 97ml/min/1.73m²
• Urine microalbumin: Normal
• Lipids: Total Cholesterol 3.4mmol/l, LDL cholesterol 1.6mmol/l, HDL cholesterol 1.0mmol/l, Triglycerides 1.74mmol/l
• HbA1c: 8.2%

Clinical Questions

1. Weight gain is due to:
   a) Suboptimal diet and lifestyle
   b) Gliclazide

Expert comment
Patient concerned about his weight gain which is most likely due to his lifestyle, particularly his business travel. Gliclazide is associated with weight gain¹, but a very recent systematic review has shown this to be in the order of 1.8kg, less than the other sulphonylureas. He put on much more than that (±4.5kg over the past 18 months).

2. What additional concerns should be addressed in this patient?
   a) Poor glycaemic control
   b) Blood pressure
   c) Lipid profile
   d) All of the above

Expert comment
Poor glycaemic control, blood pressure and lipid profile will all contribute to cardiovascular risk.

3. What target HbA1c would you be aiming for?
   a) < 6.5%
   b) < 7%
   c) < 8%

Expert comment
The patient has no co-morbidities, he does not complain of any other symptoms and is keen to not suffer any further weight gain or a worsening of his diabetes. He shows a willingness to strive for better glucose control again.
4. What factors would you regard as important in choosing additional therapy for his diabetes?
   
a) Obesity  
b) Lifestyle  
c) Both of the above  

**Expert comment**
Patient has a busy lifestyle with frequent overseas trips on his own, therefore he requires treatment with agents with a lower propensity to hypoglycaemia.

5. Which one of the following agents would you consider adding to his treatment?
   
a) Basal Insulin  
b) Biphasic Insulin twice daily  
c) DPP-4 inhibitor  
d) Pioglitazone  
e) GLP-1 agonist  

**Expert comment**
Insulin is not a good option in view of possible weight gain, and bearing in mind that he already has grade II obesity. The treatment decision should also take into account risk of hypoglycaemia.

The HbA1c reduction required is 1.2%, which is beyond the achievable (expected) reduction for all DPP-4 inhibitors.

A GLP-1 agonist is a good choice as it is associated with a low risk of hypoglycaemia and with weight loss, which would be beneficial for this patient. Weight loss might motivate him to make and persevere with healthy lifestyle and dietary changes in order to continue that positive trend.

6. What target BP would you be aiming for?
   
a) <130/80mmHg  
b) <140/80mmHg  
c) <150/80mmHg  

**Expert comment**
The current SEMDSA guidelines advise doctors to aim for a BP of £130/80mmHg.

7. Based on the results of his lipid profile, what changes would you make to his therapy?
   
a) Optimize glycaemic control, then reassess  
b) Add fibrates  

**Expert comment**
The total cholesterol and LDL cholesterol are within target. However, the triglycerides are elevated. The recommendation is to optimize glycaemic control then reassess the patient’s lipid profile.

**Any changes to medication at this stage?**
The decision is taken to add liraglutide 1.2mg daily, starting with 0.6mg daily for one month and then increasing the dose.
8. What are the advantages of this agent in this particular patient?

- Low risk for hypoglycaemia
- Weight loss
- Daily dosing
- All of the above

**Expert comment**
Liraglutide has all of the above advantages. The opportunity for weight loss may also create a further opportunity for diet modification. It is worthwhile to refer the patient to a dietitian after the first month of therapy.

9. What are the risks, if any, of adding liraglutide onto his current therapy?

- The risk of hypoglycaemia is increased when it is combined with a sulphonylurea
- Pancreatitiss

**Expert comment**
The main concern is hypoglycaemia. Although liraglutide itself is not associated with hypoglycaemia, there is an increased risk of hypoglycaemia when adding another antidiabetic drug to a sulphonylurea.

Studies (mainly early animal studies) suggested that pancreatitis may be a consideration when using liraglutide. However, clinical and post marketing studies have failed to demonstrate a significant association between GLP-1 receptor agonists and pancreatitis.

Nevertheless, it may be prudent to use the GLP-1 receptor agonist cautiously in patients at increased risk of pancreatitis (e.g., alcohol abuse, history of pancreatitis, cholelithiasis).3, 4, 5

10. In view of the elevated blood pressure, what agent would you choose for BP control?

- ACE inhibitor/ARB
- Calcium Channel Blocker

**Expert comment**
Losartan 50mg was added to treatment for blood pressure control.

**Recommended management**

**Expert comment**
There is an advantage of adding liraglutide to therapy in this patient. Liraglutide itself is not associated with weight gain, but rather may be associated with stable weight or weight loss. Clinical studies indicate a modest weight loss of 2-3kg over 1-2 years.

A disadvantage of adding insulin is that insulin is associated with weight gain. The addition of insulin would be a next step in this patient.

**Follow up six months later**
- Repeat lab tests included
- BP 128/80mmHg.
- Weight 107.6kg (weight loss of 2kg).
- HbA1c 6.8%.
- Total cholesterol 3.7mmol/l, LDL cholesterol 1.8mmol/l, HDL cholesterol 1.0mmol/l and Triglycerides 2.09mmol/l.
11. What are your concerns and what treatment would you consider?

  a) Triglycerides are increased despite improvement in HbA1c – Consider fibrate as additional therapy
  b) Increase atorvastatin to 20mg
  c) Both of the above

Expert comment
His triglycerides are increased despite improvement in HbA1c and a fibrate should be considered as additional therapy. Atorvastatin should also be increased to 20mg once daily.

References