Excess weight loss in a patient with type 2 diabetes mellitus treated with an SGLT-2 inhibitor

Edyta Cichocka, Janusz Gumprecht

School of Medicine with the Division of Dentistry in Zabrze, Medical University of Silesia, Katowice, Poland, Department of Internal Medicine, Diabetology, and Nephrology

Key words: weight loss; diabetes; SGLT-2 inhibitor

Case report

A 62-year-old obese male patient with a 12-year history of type 2 diabetes was hospitalised in 2018 in the Department of Diabetes to optimise diabetes treatment. The patient had previously been treated with multiple injections of insulin (regular human insulin before meals and insulin glargine at night, daily dose of insulin = 140 IU) and metformin (3000 mg/day). Out-patient HbA1c level was 12% (108 mmol/mol). Additionally, the medical history revealed dyslipidaemia and hepatic steatosis. The patient was in the process of getting divorced, which exposed him to additional stress. The patient did not follow the rules of healthy nutrition, meal consumption was irregular, and regular physical activity was not undertaken. The non-smoking patient who consumed 2–3 bottles of beer per week showed poor knowledge about diet and diabetes.

On admission, physical examination did not reveal any significant abnormality except for obesity (BMI 30 kg/m²) and elevated blood pressure (160/100 mm Hg). Laboratory tests showed HbA1c level 12% (108 mmol/mol), mixed dyslipidaemia, and elevated liver function tests (ALT 68 U/L, AspAAT 52 U/L). The glycaemic profile is given in Table I.

The patient was instructed in terms of diet, the need to increase physical activity, and basic information related to diabetes. The subject was prescribed an antihypertensive drug (ramipril) and a statin (rosuvastatin). Diabetes treatment was modified: a full dose of metformin and insulin were maintained, and an SGLT-2 inhibitor was added (empagliflozin). A decrease in insulin requirement (from 140 IU to 100 IU/day) and an improvement in glycaemic control were observed during hospitalisation.

Six months later the patient was re-admitted. He had lost 21 kg of body weight (from 98 kg to 79 kg). During that period, prandial insulin was gradually reduced and then discontinued (treatment of diabetes included metformin 3000 mg, empagliflozin 10 mg, insulin glargine 20 IU). Glycaemic control was good, and the HbA1c level was 6.7% (50 mmol/mol). Due to low blood pressure the patient also discontinued the antihypertensive drug. There were no “self-reported”

Table I. Glucose measured using a glucometer

<table>
<thead>
<tr>
<th>Date</th>
<th>Glucose level [mg/dL]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fasting</td>
</tr>
<tr>
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<td>386</td>
</tr>
<tr>
<td>20 Feb 2018</td>
<td>349</td>
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<td>204</td>
</tr>
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<td>22 Feb 2018</td>
<td>181</td>
</tr>
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<td>23 Feb 2018</td>
<td>137</td>
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Clinical vignette

the result of a caloric deficit caused by the elimination of glucose and higher renal water excretion (osmotic diuresis). SGLT-2 inhibitors reduced body weight by as much as 4.7 kg [3–4]. Body weight reduction using SGLT-2 inhibitors gradually slows down and becomes stable after 26–34 weeks [5].

In the presented patient, we observed excess weight loss and, above all, an improvement in glycaemic control that was associated with the use of empagliflozin. In our opinion, the progressive weight loss cannot be attributed to a change in lifestyle. However, other factors that contributed to high response to treatment should be considered: diuresis, water loss due to reduction in glycogen, and probably reduced calorie intake unnoticed by the patient [5].

The loss of 1 kg of body weight is equivalent to the loss of 7000 kcal. The patient lost 21 kg within about 180 days, which would mean the loss of 205 grams of glucose in urine daily (820 kcal). That rate of urinary glucose excretion also exceeds generally accepted rates of efficacy of these drugs. But is it possible? Does it result from the hyper-reactivity of SGLT-2 or a mechanism of drug action that has not been discovered yet?

References

Discussion

Gliflozins are used at every stage of diabetes treatment [1]. The most important feature of these drugs is their beneficial effect on the reduction of cardiovascular risk. Their action is related to the inhibition of SGLT-2 in the proximal convoluted tubule to prevent reabsorption of glucose and sodium and facilitate its excretion in urine thereby promoting a decrease in blood pressure and glycosuria [2]. They also result in a decrease in body weight, which is associated with renal loss of glucose — as much as 80 g/day (320 kcal/day). Weight loss is the result of a caloric deficit caused by the elimination of glucose and higher renal water excretion (osmotic diuresis). SGLT-2 inhibitors reduced body weight by as much as 4.7 kg [3–4]. Body weight reduction using SGLT-2 inhibitors gradually slows down and becomes stable after 26–34 weeks [5].

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Table II. Glucose measured using a glucometer

<table>
<thead>
<tr>
<th>Date</th>
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<th>2 h after breakfast</th>
<th>Before dinner</th>
<th>2 h after dinner</th>
<th>Before supper</th>
<th>2 h after supper</th>
<th>Before bedtime</th>
<th>At 3 a.m.</th>
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