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CASE REPORT
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The use of dapagliflozin in the treatment of type 1 diabetes in a 36-year-old patient

ABSTRACT

Until recently, insulin was the only medicine used in therapy of type 1 diabetes mellitus (T1DM). As our knowledge of pathomechanisms involved in diabetes evolves, other promising drugs are being introduced, e.g. metformin in the patients with insulin resistance or sodium-glucose cotransporter 2 (SGLT-2) inhibitors in patients with poor metabolic control. The first SGLT-2 inhibitor (dapagliflozin) has been recently approved by the National Institute for Health and Clinical Excellence (NICE) for additional treating of poorly controlled type 1 diabetes. This article presents a case of patient with type 1 diabetes successfully treated with insulin and dapagliflozin at a daily dose of 5 mg. (Clin Diabetol 2021; 10; 2: 200–203)

Key words: diabetes mellitus type 1, dapagliflozin, continuous glucose monitoring

Introduction

Type 1 diabetes mellitus (T1DM) is characterized by an absolute insulin deficiency, therefore it is necessary to supplement the lacking hormone with exogenous insulin. Functional intensive insulin therapy is the method of choice in treatment of T1DM. It consists of multiple insulin injections with insulin pens or continuous subcutaneous insulin infusion with personal insulin pomp mimicking the profile of its pancreatic secretion in healthy population [1].

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As our understanding of metabolic disorders in T1DM changes, novel drugs are being introduced to the therapy. Presently, metformin is being widely used as an additional drug in T1DM therapy reducing the insulin requirements in patients with severe symptoms of insulin resistance. Moreover, numerous studies suggest that metformin promotes weight reduction, lowers low-density lipoprotein (LDL) cholesterol concentrations and slows atherosclerosis progression [2, 3].

In 2019 the first drug from the group of sodium-glucose cotransporter 2 (SGLT-2) inhibitors, dapagliflozin at a dose of 5 mg/day, was approved by the National Institute for Health and Clinical Excellence (NICE) for additional treating of patients with T1DM. SGLT-2 inhibitors, also known as "flozins", act in the proximal tubules of the nephrons reducing the reabsorption of glucose in kidneys and increasing the excretion of glucose (and calories) into the urine [4]. As the SGLT-2 cotransporter is responsible for nearly 90% of glucose reabsorption, it leads to decrease in glucose blood concentration and subsequent weight loss [5]. Additionally, flozins increase diuresis and lower the blood pressure [6].

Dapagliflozin is indicated in patients with inadequately controlled T1DM and a body mass index ≥ 27 kg/m^2, who cannot achieve metabolic goals with optimal insulin therapy [7, 8]. After introducing dapagliflozin, patients must not reduce their insulin doses by more than 20%.

The most common adverse effects of dapagliflozin are: urinary tract infections, euglycemic ketoacidosis and, when used simultaneously with insulin, hypoglycaemia [6, 9].

Case presentation

A 36-year-old female with a 23-year history of T1DM was referred to the outpatient clinic. At the visit she was 176 cm tall, and weighted about 90 kg. The

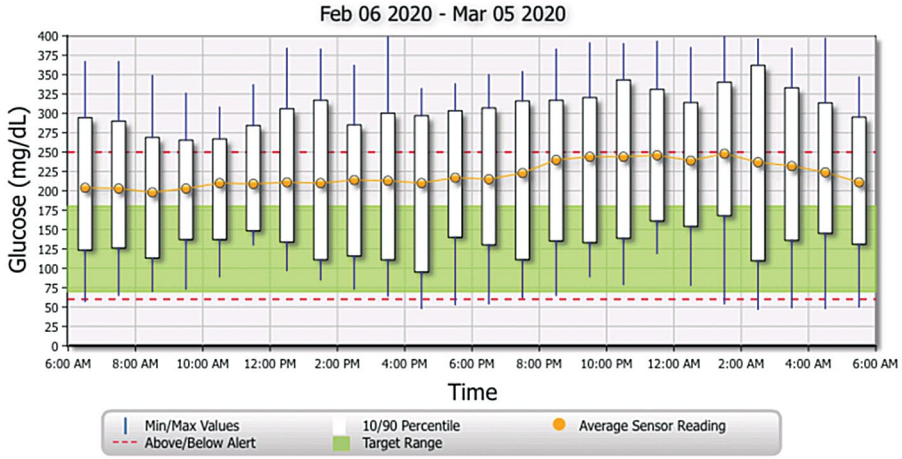

Figure 1. Monthly glycemic profile without dapagliflozin (registered by Eversense)

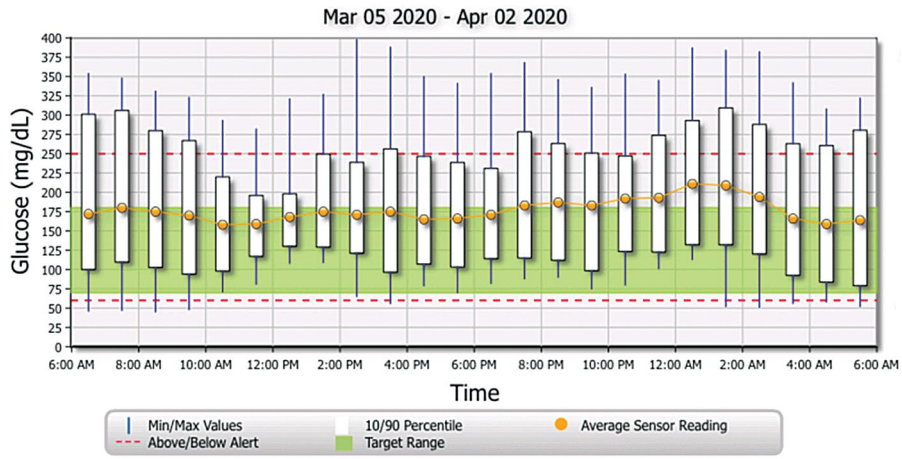

Figure 2. Monthly glycemic profile with dapagliflozin (registered by Eversense)

patient used a personal insulin pump (Accu-Chek Spirit) together with a continuous glucose monitoring system (Eversense). She already had chronic diabetes complications including non-proliferative diabetic retinopathy.

Despite comprehensive educational interventions and use of the up-to-date devices, patient's diabetes was poorly controlled — the glycated hemoglobin (HbA1c) concentration remained at the level of about 9%. The patient had sufficient theoretical knowledge about her disease and treatment, but she had not been putting enough effort into meeting everyday glucose targets.

At first, as the patient was overweight and required a large dose of insulin (0.8–1.0 U/kg/day), she was prescribed metformin at a dose of 1 g/day that turned out to be ineffective after 12 months of use (Figure 1).

After the discussion about possible benefits and adverse effects, the patient consented to dapagliflozin at a dose of 5 mg/day. Due to the additional risk of ketoacidosis she was instructed not to reduce insulin dose by more than 20% and test for ketones daily or more often when feeling unwell.

After a month of dapagliflozin therapy at the dose of 5 mg per day, the glycemic profile improved significantly (Figure 2).

During the first month of therapy patient has lost weight and noted lowered insulin requirements. The daily dose of insulin decreased by more than 10%. The basal insulin and the average number of boluses did not change. On the other hand, the bolus amount decreased, which resulted in a change in the basal-bolus ratio (Figures 3, 4). Moreover, the percentage of time spent within blood glucose levels in target range (time-in-range; TIR) doubled, while the time above target range (TAR) decreased (Table 1).

The patient is not diagnosed with celiac disease, however, due to gastric problems, remains on a gluten-free diet. During the control visit at the outpatient clinic,

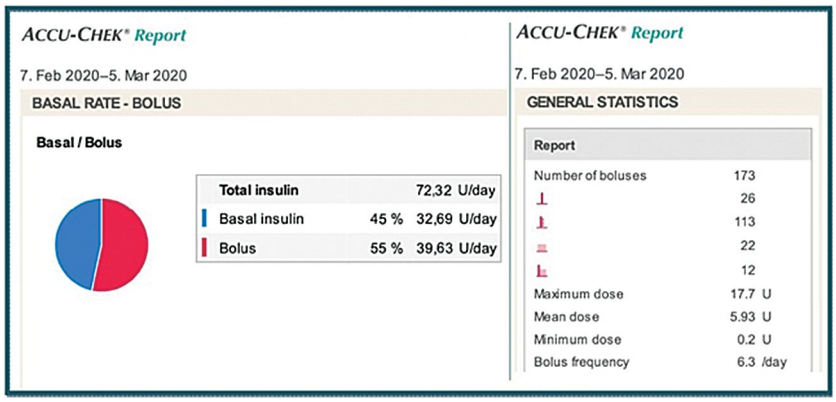

Figure 3. Basal-bolus ratio and bolus report without dapagliflozin (registered by Accu-Chek)

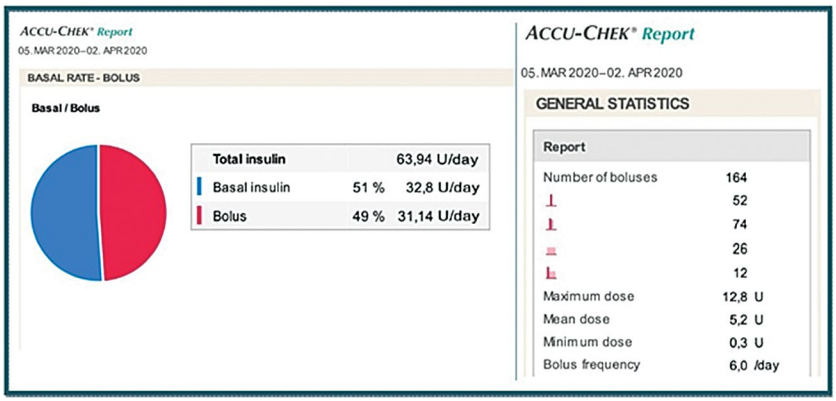

Figure 4. Basal-bolus ratio and bolus report with dapagliflozin (registered by Accu-Chek)

Table 1. Changes to selected parameters before and after 30 days of dapagliflozin use

	Before flozin	After flozin
Body weight [kg]	91	88
BMI [kg/m^2]	29.4	28.4
Mean glucose [mg/dl]	221	177
Glycemic variability (%)	31	34.6
TIR 70–180 mg/dl (%)	28.1	58.7
TAR >180 mg/dl (%)	70.9	39.5
TBR < 70 mg/dl (%)	1	1.8
Daily insulin dose/ /basal insulin dose [U]	72.3 / 32.7	63.9 / 32.8

BMI — body mass index; TAR — time above range; TBR — time below range; TIR — time in range

has reported that she noticed some changes in food preferences. She feels an earlier need to eat another meal (she gets hungry faster after meals) and reports an increased craving for sweet things.

Summary

This case stands as an example of successful introduction a novel oral hypoglycemic drug into a T1DM therapy.

Over the years, many studies have assessed the positive effect of SGLT-2 inhibitors on diabetes control and cardiovascular risk. Moreover, flozins have been also demonstrated to have nephroprotective properties [10–12].

Some patients with T1DM, despite the satisfactory knowledge and use of the modern devices like personal insulin pumps or continuous glucose monitoring systems, still struggle to meet therapeutic goals. In described case, the addition of dapagliflozin doubled the time-in-range and resulted in decreased insulin requirements and patient's weight loss. Nevertheless, the patient still has not met the metabolic goals depicted by i.e. the Polish Diabetes Society or the Consensus of the 12th International Conference on Advanced Technologies & Treatment for Diabetes [13, 14]. There-

fore, adding a novel drug to therapy do not exempt the patient from further education and maintaining glycemic control.

Moreover, SGLT-2 inhibitors are not without adverse effects. Therefore, every patient with T1DM willing to take flozins should be informed about the necessity of continuous adequate insulin administration and ketone testing as well as proper hygiene to prevent urinary tract infections.

Despite the lack of long-term observational studies, dapagliflozin seems to stand as a sensible option for patients with T1DM, whose metabolic control can be improved and who would benefit from its cardio- and nephroprotective effects.

Conflict of interest

No conflict of interest to declare.

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