POORLY CONTROLLED TYPE 1 DIABETES MELLITUS – CASE REPORT

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Abstract: *The two major forms of diabetes mellitus (DM) are type 1 and type 2 diabetes. People having T 1 DM require multiple daily injections of insulin. The standard method for insulin replacement is called Intensive Insulin Therapy. Diabetes can lead to complications and can increase the overall risk of dying prematurely, especially in poorly controlled, when they appear earlier and are more severe. Insulin resistance can reflect in high insulin doses, obesity and poor glycaemic control. We report the case of a patient with type 1 DM for 37 years, with micro- and macrovascular complications, with poor glycaemic control despite high insulin doses on a 5 injections/day regimen. Overcoming insulin resistance leads to good metabolic control.*

INTRODUCTION

Diabetes mellitus (DM) is the most common metabolic disorder worldwide. Although progress in medicine has allowed us to find the aetiology of many forms of DM, all gathered in the group of specific types of diabetes due to other causes, the two major forms are type 1 diabetes (which requires insulin injections for survival) and type 2 diabetes (where the body cannot properly use the insulin it produces).(1)

Treating diabetes can be a tough road to follow, especially for those with type 1 diabetes mellitus (T 1 DM) diagnosed in the '70's and '80's. People having T 1 DM require multiple daily injections of insulin. This is called Intensive Insulin Therapy, and most closely mimics natural insulin production. It is the standard method for insulin replacement.(2)

Diabetes can lead to complications and can increase the overall risk of dying prematurely. Over time, diabetes can damage the heart, blood vessels, eyes, kidneys, and nerves. In pregnancy, poorly controlled diabetes increases the risk of fetal death and other complications.(1)

Complications appear earlier and are more severe in poorly controlled diabetes. Some of the factors involved in poor glycaemic control are genetic factors, lower economic status, and psychological factors, including lack of motivation, emotional distress, depression and eating disorders.(3,4)

But why all diabetics, but especially those with type 1 should have a strict control of their glucose levels? Many of them are diagnosed in their youth, and later in life complications can have a major negative effect on both the patient and the society. A poor glycaemic control is associated with depression, and they have an increased tendency to ketoacidosis.(4,5) A study showed the cost for the health system increases with ~ 4, 10, 20 30% for every successive 1% increase in Hb A1c above 6%.(6)

The Diabetes Control and Complications Trial (DCCT) and the Stockholm Diabetes Intervention Study (SDIS) showed that intensive therapy, maintaining Hb A1c < 7% significantly reduced the incidence and progression of microvascular complications in patients with type 1 diabetes. But in these patients the risk of hypoglycaemia is a real obstacle to achieving glucose targets.(7) DCCT trial showed a threefold increased risk of severe hypoglycaemia in patients who followed intensive insulin therapy.(8) This is one reason for which type 1 diabetics tend to maintain suboptimal glycaemic control, especially those treated with conventional therapy at a point in their life.

I present the case of a woman, with poorly controlled Type 1 Diabetes Mellitus (T 1 DM) diagnosed 37 years ago.

CASE PRESENTATION

I present the case of a woman, S. S., 54 years old, from Medias city, diagnosed in 1979 with T 1 DM, at the age of 17, with poor glycaemic control. The family history records are without pathological meaning, no alcohol consumption, non-smoker.

The patient was admitted for investigations and adjustment of therapy in the Diabetes and Nutrition Department Sibiu, accusing worsening of paraesthesia and pain in lower limb, pain in the left hip and the left shoulder. Her glycaemic profiles and random tests at self-monitoring of blood glucose (SMBG) showed high values (fasting between 167-193 mg/dl, and at 2 hours postprandial between 174-265 mg/dl).

From the patient's history we have recorded that in 1996, she was diagnosed with diabetic polyneuropathy and non-proliferative diabetic retinopathy; in 2001 she was diagnosed with high blood pressure and ischaemic cardiomyopathy, and started treatment. In 2015, she was diagnosed with Paroxysmal supraventricular tachycardia, successfully treated with radiofrequency catheter ablation.

The onset of the symptoms was insidious, but worsened 3 months ago, when she observed high values at Smbg glucose tests. She experienced intense pain and paraesthesia in lower limb, especially during the night. Her insulin regimen included 5 injections/day: Insulin Aspart = 24 – 24 – 24 U (hours 08^{00} - 13^{00} - 19^{00}) and Insulin Detemir = 26 – 0 – 0 – 58 U (hours 08^{00} - 22^{00}). The fear of hypoglycaemia stopped her to increase the insulin units.

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At admission, the patient was conscious and cooperative. Subcutaneous tissue was well - represented, with predominance of abdominal obesity (waist = 106 cm) - BMI = 33 kg/m^2. She presented muscular hypotonia, with normal kinetics, pain at rest and during mobilization in both left hip and shoulder. Blood pressure at admission was 140/80 mm Hg, heart rate of 80 bpm, rhythmic, and had lower limbs varicose veins. At screening for diabetic neuropathy she had diminished protective sensation, in both pinprick and monofilament test and diminished temperature perception, associated with diminished osteotonic reflexes. The rest of the clinical exam was in normal range.

Laboratory investigations at the time of admission revealed a Hb A1c of 8,3%, with the following glycaemic profile: 07^{00}= 188 mg/dL; 13^{00}= 200mg/dL; 19^{00}= 175 mg/dL; 03^{00}= 155 mg/dL; 06^{00}= 178 mg/dL. She also had severe dyslipidemia (total cholesterol = 298 mg/dL; HDL-cholesterol = 20 mg/dL; LDL-cholesterol = 145,2 mg/dL; Triglycerides = 664 mg/dL), and a C reactive protein of 17,79 mg/L.

The ankle-brachial index was 0,92 in the right leg, and 1,1 in the left, showing an increased risk for peripheral artery disease (PAD). At dilated eye exam non-proliferative diabetic retinopathy and early cataract in both eyes was found.

The diagnosis after neurological exam was diabetic polyneuropathy; S1 radiculopathy and carpal tunnel syndrome.

Pelvic radiograph showed minimal narrowing of the bilateral polar superior cox-femoral articular space and loose bodies in the left lower pelvis; allowing the physiotherapist to establish the diagnosis of early left coxarthrosis.

The rest of the clinical and paraclinical investigations showed no pathological changes.

Treatment:

Taking in consideration the duration of diabetes, her age, the complications and comorbidities, we had to establish a plan for care, based on the following steps:

- Re-evaluation of diet: lower carbohydrate and lipid content;
- Set a realistic goal for Hb A1c and intensification of insulin therapy;
- Aimed therapy for the complications of DM;
- Initiate statin therapy for dyslipidemia;
- Re-evaluation of cardiovascular therapy;
- Specific neurological, ophthalmologic and physiotherapeutic treatment

We prescribed a hypocaloric diet with 160 g carbohydrates, low in saturated fats (≤ 7%), low in cholesterol (≤ 200 mg/dL), rich in PUFA (≈ 12%)

The goal for Hb A1c was set at 7%, because she is a young person, with a history of heart disease and non-proliferative diabetic retinopathy and neuropathy. In order to achieve it we replaced insulin Detemir with insulin Glargine – 300 (Gla – 300), so the insulin regimen became:

- Insulin Aspart = 24 – 24 – 22 U hours 08^{00} - 13^{00} - 19^{00}
- Insulin Glargine = 0 – 0 – 0 – 62 U (at 22^{00})

Our decision was based on the pharmacokinetic and pharmacodynamic profiles of Gla-300, suited for this difficult-to-control patient that requires unusually high doses of insulin for a type 1 diabetes.(9) Also, the flatter and longer profile of Gla-300 and it is lesser intra-/inter-variability, translated in a lower risk of hypoglycaemia, especially at night, makes it the right choice for T1 DM patients.(10)

We also recommended moderate increase of physical activity, in accordance with the cardiologist's permission.

For complications and comorbidities the following treatment was initiated:

- Vitamin therapy prescribed by the ophthalmologist for retinopathy (Mirtilene Ginkgo 1 tb/day);
- Milgamma N 2 tb/day; Gabapentinum 300 mg 3 tb/day for the polyneuropathy and her neurological conditions;
- Atorvastatin 20 mg 1 tb/day; Lipanthyl nano 145 mg 1 tb/day and Omacor 1000 mg 2 tb/day for dyslipidemia;
- Dafiro 10/320/25 mg 1tb/day; Aspenter 75 mg 1 tb/day, for a better control of HBP
- Tador 25 mg 2 tb/day, 1 week, for the pain.

After 3 months of therapy, the glycaemic profile was improved significantly: 07^{00}= 147 mg/dL; 13^{00}= 155 mg/dL; 19^{00}= 143 mg/dL; 03^{00}= 140 mg/dL; 06^{00}= 131 mg/dL. Random fasting glucose test at SMBG: 160 mg/dL, 92 mg/dL. Also her lipidic profile improved: total cholesterol = 228 mg/dL; Triglycerides = 288 mg/dL. For personal reasons she was not able to determine Hb A1c at this follow-up.

Case specifics:

It is about an obese patient who requires unusually high doses of insulin for a type 1 diabetic, and even at 1,67 U/kg she did not achieve glycaemic control.

Even though she received 84 U of insulin Detemir daily, she needed a much lower dose of Gla-300 (62 U); despite the proven necessity to increase the dose in order to obtain the same metabolic response.

DISCUSSIONS

The patient had insulin resistance, reflected in high insulin dose/kg, associated with class I obesity, high W/H ratio and severe dyslipidemia. In time, she did develop micro- and macrovascular complications, as reflected from an analysis of DCCT data.(11)

Switching to a more concentrated insulin, with a longer profile and a better flexibility in the time of injection, has proven to be a good choice for this patient. Also, lowering the dose of insulin to 1,41 U/kg allowed up-regulation of insulin receptors.

The dose for Gla-300 needed to be reduced, even though subcutaneous degradation is higher than that seen in Gla-100, all patients requiring an increment of the dose up to 10 U, in order to achieve the same Hb A1c.

Diet is a daily "must" for all diabetic patients, especially for those treated with insulin, who are at risk of gaining weight because of it is anabolic effect.

Of-label use of Metformin can be useful to overcome insulin resistance in type 1 diabetic patients, especially when associated with obesity or metabolic syndrome.

CONCLUSIONS

This case supports the importance of diagnosis and treatment of insulin resistance in type 1 diabetic patients.

Research of new insulin analogues that mimic physiological secretion and intensive insulin therapy will reduce the incidence of complications in both type 1 and type 2 DM.

Hypoglycaemia is still an obstacle in treatment of diabetes, therefore hypocaloric diet is not always possible in these patients, especially type 1, who also have diminished counter regulation response to it.

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