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Caso Clínico

Treatment of prediabetes with sodium glucose type 2 cotransporter inhibitors (SGLT2 inh)?: report of a non obese, non insulin resistant patient with impaired glucose tolerance treated with dapagliflozin

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RESUMEN

Además de cambios intensivos del estilo de vida con descenso significativo de peso corporal y cirugía bariátrica, varios fármacos antihiperglucémicos y/o anti obesidad han confirmado la factibilidad de reducir la conversión de prediabetes a diabetes tipo 2. Estos agentes comprenden acarbosa, tiazolidindionas (TZD), orlistat y el agonista del receptor de GLP1 liraglutide. No existe evidencia definitiva de alto nivel que muestre que esto puede también ser el caso de los inhibidores del SGLT2.

ABSTRACT

In addition to intensified life style changes with significant body weight loss and bariatric surgery, several antihyperglucemic and/or antiobesity drugs have demonstrated the feasibility of reducing the conversion of prediabetes to type 2 diabetes. The latter include acarbose, thiazolidinediones (TZD), orlistat and the GLP1 R agonist liraglutide. High quality evidence supporting SGLT2 inhibitors for this purpose is lacking.

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INTRODUCTION

Prediabetes, defined by IFG, HbA1c cutoffs values of 5.8-6.4%, or IGT (an abnormal OGTT: a 2-hour post-75g glucose oral challenge value between 140 and 199 mg/dL), not only increases the risk of progressing to type 2 diabetes but cardiovascular and overall mortality as well[1]. Prediabetes is an identifiable clinical entity, likely reflecting the very early stages of the disease, and it is treatable. A substantial body of evidence confirms that the progression to diabetes can be delayed or even prevented through various therapeutic approaches, including intensified lifestyle changes[2,3], metabolic surgey[4] and drugs such as acarbose[5], thiazolidinediones (TZD)[6, 7], orlistat[8] and the GLP-1 receptor analog liraglutide[9]. Most subjects in the corresponding prospective controlled randomized clinical trial (RCT) were selected because of IGT.

CASE REPORT

A 64-year-old white patient with long-standing impaired fasting glucose (IFG) consulted seeking specialized advice. His plasma glucose values ranged from 98 to 115 mg/dL over the past eight years. Five years ago, during a consultation with his physician, he had borderline results on an oral glucose tolerance test (OGTT), with a reading of 133 mg/dL at 2 hours, and a fasting glucose (FG) level of 113 mg/dL. HbA1c measurements consistently remained below 5.7% during that period. He was physically active, had a normal weight, and was non-hypertensive, non-smoker, and otherwise healthy, except for gastro esophageal reflux disease and chronic benign prostate hyperplasia.

Physical examination of the patient revealed normal findings, with a height of 1.79 meters, weight of 71 kg, and a BMI of 22.18 kg/m2. His waist circumference was of 83 cm measured at the midpoint between the 12th rib and the iliac crest. His blood pressure was 125/75 mmHg. His diabetes risk, assessed using the FINDRISK scale (15 points), was high at 33%.

Family medical history revealed a 91-years-old father who was still alive, lucid, independent, and physically active, despite being diagnosed with type 2 diabetes in his seventies and afterward hypertension. His blood pressure was well-controlled with valsartan-amlodipine and his lipid profile was normal without medication. His diabetes had been well-controlled without micro or macrovascular complications; firstly, treated with sulfonylurea and metformin, then with vildagliptin/metformin with progressively lower doses of metformin, due to non albuminuric chronic kidney disease and finally with linagliptin alone. The A1c patient's values along the last two years were 6.2%, 6.3% and 6.2%

A new OGTT was conducted, the fasting plasma glucose (FPG) 99 mg/dL and the 2-hour post-load was 174 mg/dL, showing a change to impaired glucose tolerance (IGT Basal insulin value was 2.2 mU/ml, C-peptide was of 1.12 ng/dl (normal range1 to 4 ng/ml), and HOMA-B was significantly reduced to a value of 19.3 (normal value >70). The HOMA-R index was within the low-normal range at 0.5, and tests for anti-GAD 65 and anti-IA2 antibodies were negative. Serum creatinine was 1.18 mg/dL (eGFR 68 mL/1.73 m2), uric acid was 4.1 mg/dL, and ultrasensitive CRP was 0.6 mg/L.

Although acarbose is no longer available in Argentina, it was obtained as a generic form and administered at a low dose of 50 mg/day for 3 months only. This, combined with amateur competitive tennis, swimming, and daily gym workouts, appropriately managed the condition. Due to the absence of overweight or obesity and insulin resistance, an off-label prescription of dapagliflozin was initiated thereafter. The SGLT2 inhibitor was well-tolerated but led to an unwanted yet predictable weight loss of 2.5 kg, which was managed by increasing total daily calorie intake with additional protein and unsaturated fats, finally achieving a body weight of 70 kg.

A third OGTT was performed 1 year later under the new treatment, revealing a fasting glucose of 111 mg/dL and a 2-hour post-load glucose of 96 mg/dL, with an A1c level of 6.02%. Basal glucosuria was of 1297 mg/dL. Although the possibility of a carry-over effect from acarbose cannot be excluded, the pharmacodynamics of the SGLT2 inhibitor[10] plausibly explain the return to normal glucose tolerance while remaining with IFG and A1c above normal values, yet consistent with prediabetes. The treatment will be followed by a daily dose of 5 mg of dapagliflozin or an equivalent 10 mg dose every other day for another year or more.

CONCLUSION

Apparently to date, no randomized controlled trial (RCT) has directly assessed the efficacy of SGLT2 inhibitors for the prevention of type 2 diabetes. Nonetheless, a recent meta-analysis[11] of trials of non diabetic subjects treated either for heart failure or chronic kidney disease has shown a reduction in new onset type 2 diabetes diagnosed by Hb A1c .This case report provides valuable insights into the potential use of SGLT2 inhibitors in prediabetic patients but should be considered alongside existing medical guidelines and ongoing research in the field. It also suggests that a potentially positive outcome may be achieved particularly in those with IGT.

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