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Canaglifozin in the Diabetic-Obese and Poorly Controlled

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Abstract

Objective: To analyze the metabolic evolution in patients with previous poor control after starting treatment with canagliflozin.

Methodology: A retrospective observational study in patients with poor glycemic control assigned to several health centers of Albacete and Cuenca provinces in which treatment with canagliflozin has been started after 6 months. Variables are analyzed: age, sex, weight, height, BMI. Analytical variables: glycemia, glycated hemoglobin, total cholesterol, HDL, LDL, triglycerides, uric acid, C-reactive protein, urea, creatinine proteinuria

Results: 107 diabetic patients participated, 45.5% men, Average age 61, 16-23 years. Basal variable 6 months level signify Glucemia fasting 157.41-126.89, p>0.002 Hemoglobin glycated 8.55-6.91, p>0.003, Weight 84.31-80.21, p>0.002, BMI 31.66-30.04, p>0.04, Cholesterol T 199.05-188.61, p>0.03, LDL 113.36-97.102, p>0.05, TG 195.18-176.80, p>0.05.

Conclusion: The treatment with Canaglifozin 100 has been effective for the metabolic control of patients previously poorly controlled.

Keywords: Diabetes; Obesity; Bad control canaglifozina

Introduction

Diabetes mellitus type 2 (DM2) is a health problem of the first order. It is a chronic pathology with a growing prevalence associated with the increase of obesity, sedentary lifestyle and the aging of the population.

Obesity and diabetes mellitus constitute one of the most frequent associations and with the highest cardiovascular comorbidities. Since the first results of the Framingham study both conditions were considered as risk factors for coronary disease, and in recent years the explosive incidence of obesity in developed countries [1,2] together with the growing understanding of their interrelation with the appearance of the syndrome. Insulin resistance syndrome and the onset of non-insulin-dependent diabetes mellitus has led to numerous studies have been conducted to address this issue [3,4].

The treatment of this disease, once established, is oriented toward preventing the development of acute decompensation and the chronic complications that determine morbidity and mortality. The bases of this treatment are hygienic-dietetic measures and metformin. For many years, the only alternative to metformin was sulfonylureas (SU) and insulin. Subsequently, inhibitors of glycosidases and thiazolidinediones (TZD) were incorporated. Throughout last few years, many other therapeutic targets have been developed that have led to the appearance of several pharmacological groups.

There is a general consensus that the drug of choice for the management of DM2 is metformin. More controversial or controversial is the attitude to take when the goals of glycemic control with hygienic-dietetic measures and metformin are not achieved, when considering the next therapeutic step. The guides of the most respected scientific societies, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD), propose the selection of the next drug based on the preference's patients [5-7].

The glucosuric drugs are selective inhibitors of the sodium-glucose cotransporter type 2 (SGLT2), responsible for 80-90% of renal glucose reabsorption. These drugs reduce the reabsorption of glucose at the level of the proximal tubule and cause an increase in urinary glucose excretion, so that, due to their mechanism of action, they are only useful in patients with preserved renal function. The glucosuric drugs approved by EMA are dapagliflozin, canaglifozin and empagliflozin. The most recent systematic review comparing them with active drugs confirms a reducing effect of HbA1c levels added to metformin, a weight reduction that oscillates around 2 kg at the end of the observation period and a low frequency of hypoglycaemia [8,9].

The results of EMPA-REG and CANVAS change the paradigm of how to reduce cardio-renal risk in high-risk patients. Primary care physicians, internal medicine, endocrinology and cardiology should be familiar with this class of drugs. This class of drugs should be considered as a cardiovascular drug, not just another glucose-lowering agent [10].

Research Methodology

A retrospective observational study in patients with poor glycemic control of several health centers of Albacete and Cuenca provinces in which treatment with canagliflozin has been started after 6 months. Patients diagnosed with Type 2 Diabetes Mellitus with Body Mass Index greater than 25 who met the diagnostic criteria in force at the time of presentation and who were in follow-up at the Health Center in the period between January 2017 to May 2018 were included regardless of age or association with other comorbidities.

Variables are analyzed: age, sex, weight, height, BMI. Analytical variables: glycemia, glycated hemoglobin, total cholesterol, HDL, LDL, triglycerides, uric acid, C-reactive protein. Urea, Creatinine Proteinuria in several health centers of Albacete and Cuenca in which treatment with canagliflozin has been started after 6 months of treatment. Variables are analyzed: age, sex, weight, height, BMI. Analytical variables: glycemia, glycated hemoglobin, total cholesterol, HDL, LDL, triglycerides, uric acid, C-reactive protein, Urea, Creatinine Proteinuria.

Statistical analysis

Excel database (Microsoft®) was designed ad hoc in which all the data collected and the identifiable data of the participants that were protected and encrypted were archived. The statistical analysis was performed with the statistical package SPSS® (Statistical Package for Social Sciences) in its version 23.0.

A descriptive analysis of the variables of interest was carried out in which its distribution was observed in order to define cut-off points depending mainly on the typical scores and to detect abnormal or erroneous values. The qualitative variables were presented by the frequency distribution of the percentages of each category, while the quantitative variables were explored whether or not they followed a normal distribution using the Kolmogorov-Smirnov test, and central tendency indicators were given (mean or median) and dispersion (standard deviation or percentiles).

The association between these factors was investigated by hypothesis testing, with comparison of proportions when both were qualitative (chi square, Fisher's exact test); comparisons of means when one of them was quantitative (Student's t test, ANOVA), and if the normal distribution did not follow the Mann-Whitney U test, Kruskall-Wallis and Friedman in the case of repeated measures (I have taken them all as normal moment). Linear regression tests were performed when the dependent variable was quantitative. In the case of qualitative variables, relative risk (RR) was calculated for the different proportions and their confidence intervals (CI). The analysis was complemented with graphic representations. The level of statistical significance for this study was $p \leq 0.05$.

Ethical aspects

The study was carried out following the recognized deontological norms and the Good Clinical Practice Standards. The data was protected from uses not allowed by people outside the investigation and confidentiality was respected on the Protection of Personal Data and the law 41/2002, of November 14, basic law regulating the autonomy of the patient and rights and obligations regarding information and clinical documentation. Therefore, the information generated in this study has been considered strictly confidential, between the participating parties.

Results

107 diabetic patients participated, 45.5% men, average age 61, 16-23 years. BMI at baseline 31.66 with glycated Hgb mean baseline of 8.55. The results of the variables at the beginning and at 6 months are described in Table 1 next to the level of significance (p).

In the Table 1 and the Figure 1, after taking Canaglifozin 100, a 6-month reduction in glycemia -30.52, of glycated hemoglob -1.54, can be seen. The weight has decreased 4.10 kg and the BMI 1.62. In the relationship of variables, a statistically significant relationship between weight and poor glycemic control is observed (p>0.0002).

Variables	Basal	6 months	I Significant level
Glycemias fasting	157.41	126.89	p>0.002
Hemoglob glicated	8.55	6.91	p>0.003
body	84.31	80.21	p>0.002
BMI	31.66	30.04	p>0.04
Cholesterol T	199.05	188.61	p>0.03
LDL	113.36	97.102	p>0.05
TG	195.18	176.80	p>0.05
HDL	51.15	50.98	P<0.05
Prot C	1.39	1.24	p>0.07

Table 1: Values at the beginning and at 6 months.

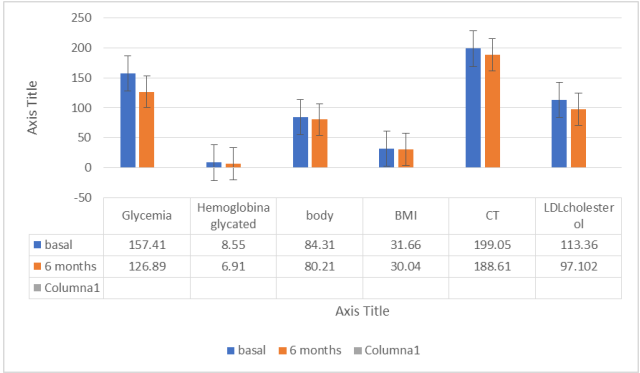

Figure 1: Evolution of the main metabolic parameters.

There is also a statistically significant relationship between weight reduction and reduction of glycated hemoglobin (p>0.001). At 6 months there is a reduction in cardiovascular risk Score of 2.52 points.

Discussion

Diabetes mellitus is a chronic metabolic disease with important complications both micro and macrovascular, 90% suffer from type 2 diabetes, one of the main conditions associated with diabetes is obesity and overweight; which proportionally increases the cardiovascular risk of these patients [11].

The incidence of diabetics has doubled in recent years, among other reasons, due to the increase in the incidence of obesity and overweight. In fact, it has been proven that 60 percent of the Spanish population already suffers from excess weight. In this sense, it is key to fight obesity in order to prevent diabetes, since another of the problems of diabetes is that at the beginning it does not present symptoms.

In any case, controlling our weight is not only possible, but an important and substantial part of a diabetes management plan. Losing weight can help improve blood glucose levels, blood pressure and cholesterol levels. The benefits of losing weight have been recognized and supported by research, especially in patients with type 2 diabetes [12,13].

The most challenging lifestyle change for people living with type 2 diabetes is balanced eating and regular physical activity as an essential part of managing the disease, losing a few pounds through exercise and balanced meals can help control of diabetes. Several studies have shown that even a moderate amount of weight loss (5 percent of body weight) can improve the action of insulin and reduce fasting sugar levels [14].

In our study we can observe the close relationship between obesity and poor metabolic control in general and the glycemic in particular.

The main cause of death in people with type 2 diabetes, which is caused by overweight and lack of exercise is cardiovascular disease. It seems that decreasing the glycemic figures has an impact on mortality due to cardiac and vascular causes, however, there is controversy in this regard, especially no oral antidiabetic drug has shown a reduction in the risk of death and because others have been associated with greater adverse effects (Rosiglitazone).

The inhibitors of the sodium cotransporter glucose type 2, are a new family of drugs, work by forcing the elimination of glucose through the urine, thereby also generating fluid elimination and other effects such as reduction of systolic blood pressure, increase in HDL cholesterol (the good) and decrease of one or two kilograms of weight. For this reason, both the decrease in glucose and weight and its possible effect on blood pressure and lipid parameters, it may be all in global what will reduce mortality [15].

In comparison with placebo, these drugs cause a reduction in HbA1c levels of -0.79% (95% CI -0.96 to -0.62) in monotherapy, and -0.61% (95% CI of 0.69 to -0.53) in combined treatment. With regard to weight, absolute reductions of -1.74 kg (95% CI -2.03 to -1.45) are observed compared to placebo and -1.11 kg (95% CI -1.46 to -0.76) in comparison with active drugs and corresponding approximately 2% of the initial weight of the subjects. A reduction of about 4 mmHg in systolic blood pressure and 2 mmHg diastolic has also been described in both the studies compared with placebo and those compared with active drugs [8,16].

Conclusion

Our study in patients treated with Canaglifozin 100 we can see a significant reduction of both the glycemic parameters and the weight and lipid parameters. Although in our study there are limitations of a small sample and a relatively short term if we can appreciate the trends in these diabetic patients with obesity and poor control in the reduction mainly of glycemic parameters and weight. We can observe a tendency of Canaglifozin to reduce cardiovascular risk factors and therefore of the risk itself, so it can be considered an effective tool in secondary prevention.

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