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Research Article

Evolution of anthropometric and biochemical parameters after 6 months of treatment with exenatide compared to dapagliflozin in patients with type 2 diabetes

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Abstract. Aim: to conduct a Real-World Study to investigate the effect of 6 months treatment with GLP-1RAs vs. sodium-glucose co-transporter 2 inhibitors (SGLT2i) on anthropometric (body mass index-BMI) and biochemical parameters (lipid profile and HbA1c) in an outpatient clinic setting. Material and methods: We included 65 patients that were previously diagnosed with T2D, which could not reach adequate glycemic control with the prior antidiabetic treatment and needed the intensification of treatment. They were given GLP-1 or SGLT2i. The decision of treatment was made by their physician, and it was based on the HbA1c criteria and National Guidelines. One group included 36 consecutive patients that received treatment with GLP-1RAs, once-weekly exenatide (exenatide QW). The other group included 29 patients treated with SGLT2i dapagliflozin. At the inclusion visit, we recorded demographic, anamnestic, clinical data. Results: We observed a statistically significant decrease of HbA1c and triglycerides and an increase in HDL-cholesterol after six months of treatment. The total cholesterol values were lower after six months of treatment, but the difference was almost at the threshold of statistical significance. The mean value of HbA1c in the SGLT2 group at the initial moment was 7.9±0.9, and at six months was 7±0.5. The mean value of HbA1c in the exenatide group at the initial moment was 8.5±1.4, and at six months was 6.8±0.8. The HbA1c decrease was statistically significant greater in the exenatide group, as compared to the SGLT2 group. The decrease of triglycerides or the increase in HDL-cholesterol was not influenced by the type of antidiabetic medication. Conclusion: the treatment with GLP-1Ras or SGLT2i lowered the HbA1c value, although exenatide was more effective.

Key Words: type 2 diabetes, sodium-glucose co-transporter 2 inhibitors, glucagon-like peptide-1 receptor agonists

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Introduction

Diabetes mellitus (DM) is a chronic disease affecting a large proportion of the population. The prevalence of DM in Romania it is estimated to be 11.6%, type 2 diabetes (T2D) being the most frequent (Mota et al 2016). According to the Romanian National Guidelines (2016), several classes of glucose-lowering agents are currently available for the treatment of T2D, each with different mechanisms of action and therapeutic effect. The newest editions are the sodium-glucose co-transporter 2 inhibitors (SGLT2i), which are known to prevent glucose reabsorption in the kidney and increase glucose urinary excretion improving glycemic control, weight, and blood pressure (Saleeem 2017; Kuhn et al 2017). The second newest non-insulinic class of glycaemia lowering therapy available in Romania are the glucagon-like peptide-1 receptor agonists (GLP-1RAs) which act on the glucagon-like peptide-1 (GLP-1) receptor on pancreatic beta cells and increase insulin secretion, decrease glucagon secretion, slow gastric emptying, and increase satiety, decrease body weight, postprandial glucose excursions, and some cardiovascular risk factors (Chaudhury et al 2017; Knop et al 2017; Levin et al 2017; American Diabetes Association 2018). Both classes have a low risk of hypoglycemia observed mostly when used in combinations with other classes of glycaemia lowering therapy which are known to have hypoglycemia as a side effect (Chaudhury et al 2017; Santos et al 2017).

Our aim was to conduct a Real-World Study to investigate the effect of 6 months treatment with GLP-1RAs vs. SGLT2i on

anthropometric (body mass index-BMI) and biochemical parameters (lipid profile and HbA1c) in an outpatient clinic setting.

Material and methods

The study was observational, longitudinal, analytical, prospective, case-controlled.

The patients were recruited from the Diabetes Centre of Cluj County Emergency Hospital in Cluj-Napoca, from January 2014 to July 2017. We included 65 patients that were previously diagnosed with T2D, which could not reach adequate glycemic control with the prior antidiabetic treatment and needed the intensification of treatment. They were given GLP-1 or SGLT2i. The decision of treatment was made by their physician, and it was based on the HbA1c criteria and National Guidelines.

One group included 36 consecutive patients that received treatment with GLP-1RAs (dapagliflozin), once-weekly exenatide (exenatide QW). The other group included 29 patients treated with SGLT2i dapagliflozin and were matched with the patients from the exenatide group, for age, gender and duration of the disease.

The study protocol was approved by the Ethics Committee of "Iuliu Haţieganu" University of Medicine and Pharmacy and was conducted according patients' rights established by the Declaration of Helsinki revised in 2000. All patients were included in the study after signing an informed consent.

At the inclusion visit, we recorded demographic, anamnestic, clinical data: age, gender, duration of the disease, current diabetes treatment, the presence of arterial hypertension, dyslipidemia, diabetic polyneuropathy, retinopathy or nephropathy, and body mass index. The following biochemical data were recorded at the study inclusion and after six months of uninterrupted treatment: total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides and HbA1c.

Statistical analysis was performed using the MedCalc Statistical Software version 17.9.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2017). Quantitative data was analyzed for normality of distribution with the Kolmogorov-Smirnov test, and were described by means and standard deviation, or median and interquartile range, whenever appropriate. Qualitative data were characterized by frequency and percentage. Comparison between group at the initial moment where performed using the t test for independent variables, Mann-Whitney test or chi-square test, whenever appropriate. The differences recorded between the two visits were analyzed by paired t-test or ANOVA for repeated measures, whenever appropriate. A p value <0.05 was considered statistically significant.

Results

The characteristics of study patients are summarized in table 1. The comparison of the two groups (table 2) revealed differences at the inclusion, regarding the BMI, HbA1c, and the use of basal insulin and sulfonylureas. The other variables did not differ between groups, showing good homogeneity.

The biochemical and clinical measurements at the initial moment and after six months of treatment with once weekly exenatide or dapagliflozine can be found in table 3. We observed a statistically significant decrease of HbA1c and triglycerides and an increase in HDL-cholesterol. The total cholesterol values were lower after six months of treatment, but the difference was almost at the threshold of statistical significance.

Table 1. Primary antibodies

Variable		Group characteristics
Therapy	**Dapagliflozin**	29 (44.6%)
	Exenatide QW	36 (55.4%)
Age (years)		57±9.3
Gender	**Male**	31 (47.7%)
	Female	34 (52.3%)
Duration of diabetes (years)		6 (3-9)
Metformin		62 (95.4%)
Basal insulin		9 (13.8%)
Prandial insulin		1 (1.5%)
Sulfonylureas		29 (44.6%)
Thiazolidinediones		1 (1.5%)
α-glycosydase inhibitors		2 (3.1%)
Glinide		1 (1.5%)
Dipeptidyl peptidase IV inhibitors		8 (12.3%)
Hypertension		48 (73.8%)
Dyslipidemia		42 (64.6%)
Diabetic Neuropathy		9 (13.8%)
Diabetic Retinopathy		3 (4.6%)
Diabetic Nephropathy		-

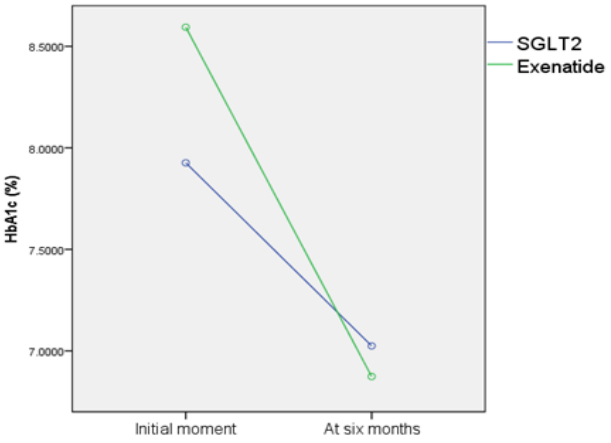

Fig. 1. The variation of HbA1c according to the medication

The mean value of HbA1c in the SGLT2 group at the initial moment was 7.9±0.9, and at six months was 7±0.5. The mean value of HbA1c in the exenatide group at the initial moment was 8.5±1.4, and at six months was 6.8±0.8. The HbA1c decrease was statistically significant greater in the exenatide group, as compared to the SGLT2 group (p=0.02; fig. 1).

The decrease of triglycerides or the increase in HDL-cholesterol was not influenced by the type of antidiabetic medication.

Discussions

In a real world setting once weekly exenatide was statistically significant more effective than dapagliflozin in lowering HbA1c. The difference in the HbA1c value in the two groups, at the

Table 2. Comparison between exenatide QW and dapaglifozin groups at the first visit

Variable		Dapagliflozin	Exenatide QW	p
Age		58.6±8.8	55.7±9.6	0.2
BMI		34.6±6.01	39.7±6.6	0.002
Cholesterol (mg/dl)		173.1±22.2	183.5±33.8	0.1
LDL-cholesterol (mg/dl)		102.3±28.5	109.03±36.6	0.4
HDL-cholesterol (mg/dl)		38.8±6.2	37.6±9.2	0.5
Creatinine (mg/dl)		0.81±0.13	0.87±0.18	0.2
HbA1c (%)		7.9±0.9	8.6±1.4	0.03
Duration of diabetes		6 (3.5-9)	6 (2-8.7)	0.4
Triglycerides (mg/dl)		191 (135-258)	166 (140.2-218.2)	0.6
Sex	**Male**	14 (48.3%)	17 (47.2%)	1
	Female	15 (51.7%)	19 (52.8%)	
Metformin		26 (89.7%)	36 (100%)	0.08
Basal insulin		1 (3.4%)	8 (22.2%)	0.03
Prandial insulin		1 (3.4%)	-	0.4
Sulfonylureas		7 (24.1%)	22 (61.1%)	0.005
Thiazolidinediones		-	1 (2.8%)	1
α-glycosylase inhibitors		2 (6.9%)	-	0.2
Glinide		-	1 (2.8%)	1
Dipeptidyl peptidase IV inhibitors		2 (6.9%)	6 (16.7%)	0.2
Hypertension		22 (75.9%)	26 (72.2 %)	0.9
Dyslipidemia		21 (72.4%)	21 (58.3%)	0.3
Diabetic Neuropathy		2 (6.9%)	7 (19.4%)	0.1
Diabetic Retinopathy		-	3 (8.3%)	0.2

Table 3. The biochemical and clinical measurements at the initial moment and after six months of treatment

Variable	Initial	At 6 months	p
BMI (kg/m^2)	37.5±6.8	37.2±6.4	0.5
Total cholesterol (mg/dl)	178.8±29.5	174.3±27.3	0.06
Triglycerides(mg/dl)	183 (140-238.5)	170 (146-200)	0.01
LDL-cholesterol (mg/dl)	106.03±33.2	111.1±46.7	0.2
HDL-cholesterol (mg/dl)	38.1±8.04	40.8±8.2	0.01
Creatinine (mg/dl)	0.84±0.16	0.87±0.15	0.2
HbA1c (%)	8.2±1.2	6.9±0.7	<0.001

initiation moment, was probably due to the fact that each of the two glycaemia lowering agents have different reduction of HbA1c capacity (−1.3% to −1.9% for exenatide QW (Knop et al 2017; Genovese et al 2017) and -0.8% to -1.2% for dapagliflozin (Steen & Goldenberg 2017; Kuhn et al 2017; Cefalu et al 2015) and were selected according to the reduction needed to reach the HbA1c target. The difference in the decrease of the HbA1c favoring the exenatide QW was expected as seen in prior randomized controlled trials (Knop et al 2017; Frías et al 2017). Both therapies decrease the levels of triglycerides and increase the value of HDL-cholesterol, but only after the groups were merged the modifications in lipid profile were statistically significant.

BMI remained unchanged after 6 months of therapy with either exenatide QW or SGLT2i. This was unexpected, both therapies being known for their effect on decreasing BMI (Levin et al 2017; Frías et al 2016; Santos et al 2017).

The differences in insulin and sulphonylurea use seen between the combinations of glycaemia lowering drugs used prior to the initiation of the two therapies are due to the switching from basal insulin regime to GLP-1RA in order to facilitate weight loss and to different regulatory approvals for the use of the two drugs. Exenatide QW can be administered in triple therapy according to the National Guidelines and dapagliflozin can only be administered in dual therapy, limiting its use.

A major study limitation was the number of patients, which was reduced due to the fact that the classes of drugs are relatively new and the National Guidelines are restrictive.

Conclusion

The treatment with GLP-1Ras or SGLT2i lowered the HbA1c value, although exenatide was more effective.

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