Contents lists available at ScienceDirect

Primary Care Diabetes

journal homepage: http://www.elsevier.com/locate/pcd

Brief report

Effects of selected antidiabetics on weight loss – A retrospective database analysis

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ARTICLE INFO

Article history:
Received 8 February 2014
Received in revised form
27 March 2014
Accepted 1 April 2014
Available online 6 May 2014

ABSTRACT

Aims: In published studies metformin was often associated with weight loss in type 2 diabetes patients. Until now, no epidemiological studies have directly compared the effects of DPP-4 and GLP-1 versus metformin on weight loss. Our study is a comparison of sulfonylurea, DPP-4 and GLP-1 with metformin regarding body weight in type 2 diabetes patients.
Methods: Data from 2641 patients initiated therapy with either metformin, sulfonylurea, DPP-inhibitors or GLP-1 with baseline BMI >30 were retrospectively analyzed (Disease Analyzer Germany: 11/2008–10/2012). Comparison was performed for the weight change after 1 year of therapy compared with the last value prior to therapy. Differences between SU, DPP-4, GLP-1 versus metformin were estimated using regression model adjusted for age, gender, health insurance status, defined co-diagnoses and body weight at baseline.
Results: In absolute values, metformin patients lost an average of 2.6 kg, subjects treated with SU gained 0.3 kg, body weight in the DPP-4 group decreased by 1.8 kg and GLP-1 patients lost 3.3 kg in body weight after 1 year. After adjustment for other variables, comparisons with metformin revealed the following results: SU +3.4 kg ($p < 0.001$), DPP-4 +1.0 kg ($p = 0.003$) and GLP-1 −0.4 kg ($p = 0.589$).
Conclusion: Our study showed that GLP-1 treatment was comparable to metformin regarding the weight reduction, while sulfonylurea and DPP-4 are inferior in this regard.

1. Introduction

Diabetes is a global epidemic and the majority of Type 2 diabetics (T2D) are overweight, meaning that these patients have a negative cardiovascular risk profile [1,2]. As most of these patients are treated with oral antidiabetics it would be desirable for these drugs to promote weight loss. However, a common side effect of most antidiabetics is weight gain, which in turn causes therapy adherence [3,4] to deteriorate. So far, Metformin is the only antidiabetic which leads to weight loss [5–7], but it also causes serious side effects such as lactic acidosis and may not be used in patients with impaired kidney function (which is relatively often the case in diabetics) or heart insufficiency.

In recent year, two new oral antidiabetics have been introduced to the market: dipeptidyl peptidase-4 inhibitor

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http://dx.doi.org/10.1016/j.pcd.2014.04.001
1751-9918/

Table 1 – Basic patient demographic data.

Characteristics	Metformin	Sulfonylurea	DPP-4	GLP-1	*p*-Value
N	1200	252	1107	82	
Male sex (%)	54.3	49.6	56.0	58.6	0.263
Age (years)	64.9 (11.0)	67.4 (10.2)	65.0 (10.6)	56.8 (10.7)	<0.001
Private insurance status	3.6	2.9	4.0	7.5	0.1296
HbA_{1c} (%)	7.2 (1.2)	8.2 (4.6)	7.5 (1.2)	7.8 (1.3)	<0.001
Weight (kilograms)	100.7 (17.9)	100.9 (17.2)	101.5 (16.9)	114.6 (25.6)	<0.001
BMI	35.4 (5.1)	35.4 (5.2)	35.5 (4.8)	38.6 (6.9)	<0.001
Coronary heart disease (%)	23.9	23.4	23.5	11.0	0.064
Myocardial infarction (%)	8.3	6.0	6.4	0.0	0.016
Heart insufficiency (%)	13.3	18.3	12.0	9.8	0.030
Stroke (%)	6.2	2.4	3.8	0.0	0.002
Lipid disorders (%)	59.1	51.6	61.3	56.1	0. 040
Hypertension (%)	79.7	83.0	80.9	78.1	0.587
Retinopathy (%)	1.8	3.6	2.5	4.9	0.113
Nephropathy (%)	5.7	12.3	9.5	8.5	<0.001
Peripheral artery disease (%)	2.1	5.6	3.6	6.1	0.007

(DPP-4) and glucagon-like-peptide-1 agonist (GLP-1). Both influence the glucagon-like peptide (GLP-1) [8,9], which is an incretin hormone released into the circulation in response to nutrients. Its major functions are the stimulation of insulin and reducing the secretion of glucagon. Initial studies were promising with regard to glycemic control and weight loss [10–14], prompting hopes that an appealing addition to the current options for treating type-2-diabetes may finally have been developed. However, until now, no studies have directly compared the effects of DPP-4 and GLP-1 versus metformin on weight loss because in most studies DPP-4 and/or GLP-1 are only administered as complementary treatments. Consequently, we performed a direct comparison of SU, DPP-4 and GLP-1 with metformin and regarding their effects on body weight in a T2D population.

2. Methods and patients

The Disease Analyzer database (IMS® Disease Analyzer, IMS Health, Germany), a well-established statistical tool for data collection, was used for this retrospective study. It allows direct access to drug prescriptions, diagnoses, and basic medical and demographic data from computer systems used in the practices of registered doctors and the adequacy of the data is monitored by IMS.

The study collective included T2D patients who was treated with either metformin, sulfonylurea, DPP-4 or GLP-1 for at least 1 year. The time of therapy was calculated as the number of days from the first till the last prescription of metformin, sulfonylurea, DPP-4 or GLP-1 given in the time period November 2008–October 2012. Patients receiving a combination of drugs were excluded from analysis. Body mass index (BMI) was calculated as follows: body weight (in kilograms (kg)) divided by body height (in meters) squared. Obesity is defined as BMI ≥30. In addition, the different treatment arms (SU/DPP-4/GLP-1) were compared directly with metformin, again separately for patients with BMI >30. Comparison was performed for the weight change after 1 year of therapy compared with the last value prior to therapy. Differences between SU, DPP4, GLP1 versus metformin were estimated using regression model adjusted for age, gender, health insurance status, body weight at baseline and co-diagnoses of coronary heart disease, myocardial infarction, stroke, lipid disorders, hypertension, retinopathy, nephropathy, peripheral artery disease and heart insufficiency. A p-value <0.05 was said to represent statistical significance and all analyses were carried out with the application of SAS 9.2. (SAS Institute, Cary, USA).

3. Results

Data was collected within a 48-month period (11/08–10/12) from 812 general practices and 30 specialized diabetes practices in Germany. Of 5900 patients treated with metformin, sulfonylurea, DPP-4 or GLP-1 for at least 1 year with documented weight values prior to and after the therapy, 1392 were excluded due to combination therapy and 1867 due to BMI below 30. A total of $n = 2641$ patients met the inclusion criteria, of which $n = 1200$ received metformin, $n = 252$ sulfonylurea (SU), $n = 1107$ dipeptidyl peptidase-4 inhibitor (DPP-4) and $n = 82$ glucagon-like-peptide-1 agonist (GLP-1). Basic demographic data is provided in Table 1.

In absolute values, metformin patients lost an average of 2.6 kg (95% CI: 2.5–2.9), subjects treated with SU gained 0.3 kg (95% CI: −0.2 to 0.8), body weight in the DPP-4 group decreased by 1.8 kg (95 CI: 1.4–2.1) and GLP-1 patients lost 3.3 kg (95% CI: 1.9–4.6) in body weight after 1 year (Fig. 1). After adjustment

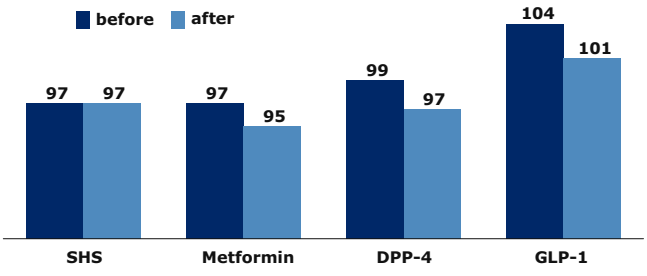

Fig. 1 – Median weight changes (in kg, after vs. before treatment start).